Perioperative Pain Control: Tools for Surgeons

A Practical, Evidence-Based Pocket Guide

Peter F. Svider
Anna A. Pashkova
Andrew P. Johnson
Editors

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Preface

There are many reasons for preparing a manual for perioperative analgesia targeted at surgical trainees. It is our hope that this text provides an easy-to-use reference and acts as an educational tool to improve the use of analgesia in an evidence-based manner. All three of us have witnessed firsthand the consequences of the paucity of dedicated analgesia prescribing education in surgical training programs, as this results in both the undertreatment and overtreatment of pain issues.

Both inadequate and overzealous treatment of pain issues lead to needless suffering, both on the societal level as well as the individual level. Importantly, we hope texts such as this can act as an easy-to-access reference and provide a foundation for understanding contemporary evidence-based practices relating to pain management in the perioperative setting. We have prepared this in an interdisciplinary fashion, with the editors including an academic anesthesiologist and interventional pain specialist (Dr. Pashkova), an academic otolaryngology-head and neck surgeon (Dr. Johnson), and an otolaryngologist and rhinologist/endoscopic skull base surgeon (Dr. Svider). Furthermore, the authors represent a combination of surgeons with expertise in various specialties, anesthesiologists and pain physicians, as well as individuals with a diverse array of experience, ranging from trainees to experienced attending physicians.

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I would like to thank my husband, Peter, for his encouragement and support throughout this project – *Anna Pashkova*

I thank my wife, Anna, for her support during challenging times, including throughout my training and beyond. Without her encouragement, projects such as this would not have been possible. I would also like to thank Melissa Johnson for allowing her husband, Andrew, to collaborate on this project. – *Peter Svider*

I would like to thank Bella for her inspiration and encouragement – *Andrew Johnson*

We would like to thank our fellow residents, attending physicians, and staff for all of their support during our residency training in the Department of Otolaryngology – Head and Neck Surgery at Wayne State University in Detroit, Michigan. Our experiences during those 5 years provided the foundation for us to be competent surgeons and clinicians, as well as teaching us important life lessons extending far beyond the operating room and clinic. – *Andrew Johnson and Peter Svider*

Finally, all three of us would like to thank Abha Krishnan, Samantha Lonuzzi, and all of the other staff from Springer for their encouragement and coordination during this project. Without their help, this project would not have been possible.

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Part I

Overview Chapters

1 Perioperative Pain Control: Practical Tools for Surgeons

Peter F. Svider, Anna A. Pashkova, and Andrew P. Johnson

Overview of Perioperative Analgesia

Prescription drug abuse has played an outsize role in the rise of the opioid epidemic over the past two decades [1–4]. As repeated throughout this text, one of the reasons responsible for this deals with the role of government in promoting pain as an under-recognized fifth "vital sign" during this time period [5–7]. Hence, individuals and healthcare providers have paid special attention to whether patients are having their pain treated appropriately, and critics have suggested that this has come at the expense of recognizing whether there is appropriate analgesia.

In the past 5 years alone, prescription drug abuse has outpaced illicit opioid use and is responsible for overdoses and deaths. In

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2017 alone, greater than 40,000 Americans died from prescription opioid overdose [8]. Consequently, the pendulum has swung the other way, and there is greater recognition of these phenomena. Programs have been formed to address these issues and deal with individuals who have abused opioids; however, oftentimes, these programs have represented "too little too late." Understanding strategies for mitigation as well as minimizing the illicit use of these substances will be key as we move on from this phase of overdose and death.

In addition to the above issues, there has been little formalized opioid prescribing education (OPE) among those who prescribe these medications [9, 10]. There have been myriad studies examining the role of OPE in recent years, as trainees play an important role in the dispensation of these substances. The role of surgical trainees is particularly important, as half of the 33,000 opiate-related deaths per year are attributed to prescription opioids [11]; surgical trainees play an important role in the spread of these medications in our society. Study after study has shown a paucity of formalized training both in undergraduate medical training and during residency and fellowship, despite the fact that these are the individuals responsible for patients taking these medications. Hence, gaining further appreciation for the special role of OPE takes on greater importance in our contemporary healthcare environment.

One of the most important components of appropriate OPE has to do with the need to learn about opioid alternatives. There are certainly correct ways to prescribe opioids and incorrect ways to dispense these medications. Nonetheless, recent decades have witnessed the advent and popularization of alternatives that are as effective but do not harbor many of the same addictive side effects and potential adverse events. For example, nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen work through different mechanisms but oftentimes have the same impact, decreasing the need for rescue opioids and controlling pain in an effective manner. There is an entire body of literature, discussed in this text, which focuses on their effectiveness. The same can be said in many situations about gabapentinoids, as these are another alternative to opioids.

In addition to "pill" alternatives, there are alternate routes to PO opioids that play an important role in our therapeutic repertoire. Local blocks play an outsize role, and they are discussed in several chapters, particularly when examining the abdomen and genitourinary tract. Furthermore, there are a variety of blocks acting at the spine and other parts of the body that obviate the need for PO opioids.

The alternatives discussed above can be addressed together as they were noted in evidence-based, controlled studies. The past three decades have witnessed the increased importance of evidence-based medicine alternatives (EBM), and the rise of EBM is important in fighting the unnecessary prescription of opioids that has ravaged our healthcare system and societal discourse. In addition to the rise of EBM for use of these drugs as monotherapy, many of these drugs can be used in combination with opioids, and this strategy has also gained popularity in recent years.

As opioid-related events creep into public consciousness and a greater number of overdoses are reported, legislation has played an increasingly important role. Although often passed at the state level, surgeons should be familiar with the basics of what goes into these laws, as this certainly impacts them at both the individual and societal level. Consequently, there is a chapter dedicated to understanding some of the unique undertakings related to such legislation. A shared feature among these laws addresses limits as to how many opioids can be prescribed for acute pain following a procedure, although exceptions exist for nearly all of these laws. Understanding local practice patterns is paramount in avoiding trouble and making sure patients do not abuse medications.

Understanding the role of preoperative optimization for perioperative analgesia is important in preventing unnecessary prescribing practices and facilitating appropriate postoperative care. Part of this deals with an appropriate preoperative evaluation delineating what medications patients can and cannot receive. For example, understanding whether there are contraindications to NSAIDs, acetaminophen, gabapentinoids, or opioids is important in formulating an effective perioperative plan. This includes a

discussion of renal or liver issues, presence or absence of obstructive sleep apnea or other respiratory conditions, concurrent use of sedatives, and understanding what home medications the patient has been taking. Optimization also includes renally dosing certain medications in patients with renal insufficiency. Obviously, a lot more goes into this process, but having the basics down is important for the surgical trainee as well as the practicing surgeon.

In addition to special considerations to optimize patients, one must consider issues arising in those who are already being treated for chronic pain. Importantly, the physician writing for chronic pain medications should ideally be involved in formulating a perioperative analgesic plan in order to minimize the chances that anything added will be disruptive. An estimate must be made as to the level of postprocedural pain, as the procedure will add to the chronic pain, and based on that additions can be made to the chronic pain regimen with a plan to withdraw these additions as soon as appropriate. Patients with chronic pain who do not undergo counseling for perioperative analgesia may be a setup for trouble down the line, particularly with opioid use.

In addition to some of the physical manifestations of pain, pain psychology plays an important role in one's reaction to pain and should be considered in at-risk patients undergoing surgery. Importantly, patients with psychiatric comorbidities or patients already on chronic pain medication regimens may require multidisciplinary care with a pain psychologist after their procedure. Methods such as cognitive behavior therapy (CBT) play an important role in considering the way one reacts to pain, and understanding the role of CBT is of paramount importance as a result.

Special Populations

Pain is expressed in different ways by various populations. For example, individuals who report chronic pain and are treated for this oftentimes experience pain differently than the elderly or pediatric populations. In the elderly, polypharmacy represents a troubling concern, and opioids, respiratory depressants, and sedatives should be avoided when possible, making familiarity of

evidence-based alternatives paramount [12]. Elderly patients represent one of the fastest-growing surgical populations in the United States, and taking a conservative approach to managing their perioperative analgesia is an important consideration for avoiding untoward complications.

In addition to elderly populations, there are several unique aspects of treating pain when it comes to children and adolescents, further described in a dedicated chapter. Briefly, younger children have trouble articulating their pain levels, meaning providers need to be more attuned to this potential and have a lower threshold for managing such pain. As children become older and are better able to articulate their pain, guidelines must be followed regarding appropriate pain medications. Opioids are absolutely appropriate in children in the correct settings, but it is important to be familiar with these guidelines. For example, codeine represents a controversial medication in some situations, as some children are slow metabolizers and others fast metabolizers [13]. Understanding the appropriate situations to use opioids and opioid alternatives is paramount for staying out of trouble when addressing analgesia in the pediatric population.

Pain Throughout the Body

Pain manifests itself differently throughout different parts of the body and in different locations. Understanding how individuals react to pain throughout different parts of the body is important for surgical trainees and practicing surgeons. For example, there are significant differences in how our bodies perceive gastrointestinal pain versus urologic/gynecologic pain issues versus those in the head and neck, and the chapters in this text reflect these unique differences. Importantly, this text can be used as a reference for providers treating these patients when these individuals require perioperative analgesia.

In addition to specific locations throughout the body, the authors would be remiss not to comment upon the types of surgeries that are being performed, as this harbors a profound impact on perioperative analgesia. For example, we discuss evidence-based

approaches to patients undergoing plastic and reconstructive surgery. This encompasses a diverse array of individuals, with a portion of these patients undergoing purely cosmetic, elective procedures while others requiring surgery to reconstruct and restore issues impacting quality of life.

Conclusion

There are many considerations responsible for the rising opioid epidemic in the United States over the past two decades. Much of this crisis stems from policies aimed at addressing pain as the fifth vital sign which lead to overprescription of opioids, while poor opioid prescribing education programs have led to a lack of familiarity with evidence-based alternatives among surgical trainees and practicing surgeons. In recent years, the pendulum has started swinging the other way, with increasing recognition of these societal problems and legislation aimed at stemming the tide of opioid overprescription.

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2 The Surgeon's Role in the Opioid Epidemic

Hope Schneider, Emma Hassell, and Peter F. Svider

The opioid epidemic was declared a public health emergency in October 2017 [1], the same year that nearly 43,000 individuals died from opioid overdoses [2]. The two decades preceding this declaration played an important role in the rise of prescription opioid use in our society to crisis proportions, including federal agencies labeling pain as a "fifth vital sign" and consequently encouraging more attention toward treating pain complaints. A combination of other factors, including tying patient satisfaction to reimbursement practices in some situations, facilitated the prescription of narcotics and has led us to where we are today.

As noted, there are numerous factors contributing to the opioid epidemic. One important area to understand is the role that surgeons play in propagating these trends. For many patients, their introduction to prescription opioids comes after they have had a procedure or are given extra prescription pills by a friend or family member [3]. Many of these prescriptions are written by

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surgeons, with studies demonstrating a tendency to overprescribe prescription opioids both in amount and in potency. This leads to patients who were opioid-naïve prior to surgery being exposed to opioids when alternatives are available and/or unused medications are being given to others.

As an example of overprescription, one study encompassing 2392 surgical patients demonstrated that only 27% of opioids prescribed were actually taken. When patients bring home larger prescriptions, they are more likely to consume more pills, with every ten additional pills prescribed leading to a patient using five more pills [4]. In another example examining 1199 orthopedic procedures including total hip arthroplasty, knee arthroplasty, carpal tunnel release, rotator cuff repair, and lumbar decompression, 61% of patients reportedly had unused opioid pills following surgery [5].

Although orthopedists have been suggested to be the leaders in opioid overprescription, this may be due to the fact that this topic has been well studied in the specialty, as overprescription is actually rampant throughout all surgical specialties. For example, multiple studies in otolaryngology have noted prescription of excess opioids [6, 7]. A lack of formalized opioid prescribing education (OPE), whether in medical school or in residency, has been suggested as one reason why this occurs on such a frequent basis. In many institutions, surgical trainees or physician extenders are the ones writing postoperative prescriptions, and their first real-time practical exposure to opioid prescription is when they are actually writing a prescription. One survey noted only a minority of students seeking surgical residency positions felt adequately prepared to prescribe postoperative opioids [8]. Deficiencies in OPE are further described in a dedicated chapter in this text.

Brief Overview of Recommended Prescribing Practices

Because under 50% of patients who undergo surgery report acceptable pain management, the American Pain Society put together a set of 32 recommended guidelines for postoperative pain management. The first guideline set by the American Pain Society encourages physicians to discuss postoperative pain and its management with patients before surgery. The recommenda-

tion comes from studies which suggest patient education reduces postoperative opioid use as well as postoperative anxiety [9]. After conducting a preoperative health history, physicians should develop a treatment plan with the patient, taking into account factors such as psychiatric conditions, chronic pain history, and past substance abuse disorders [9]. The American Pain Society recommends using the treatment plan as a guide, making adjustments along the way if the pain control is inadequate.

One strong recommendation with a high quality of evidence is the use of multimodal analgesia, which is defined as combining various medications and techniques with different mechanistic targets to provide stronger pain relief [9]. A multimodal treatment plan can also include integrative medicine techniques such as acupuncture, acupressure, and transcutaneous electrical nerve stimulation. Nonopioid medications as well as physical therapies should be incorporated as it has been suggested that postoperative opioid use is linked to long-term opioid use. Patients receiving opioid prescriptions within 7 days of surgery are 44% more likely to use opioids in the long term [10].

Because orthopedic surgeons are one of the leaders in overprescribing of opioids [11, 12], an evidence-based approach was developed to improve the use of opioids by orthopedists. In agreement with the American Pain Society, a preoperative consultation is recommended to determine which patients are at risk for opioid misuse and to also develop a postoperative pain management plan with multimodal anesthesia [11]. It is also suggested that physicians complete a training program or continuing medical education on evidence-based opioid prescribing, as medical schools do not provide adequate education on this topic or pain management [11]. When using opioids to manage severe, acute postoperative pain, the initial prescription for home use should not exceed a 2-week supply of medication [13].

Potential Solutions

Over the past 5 years, an increasing number of states have passed legislation aimed at mitigating the opioid epidemic. Several states have passed laws limiting the amount of opioid medication that physicians can prescribe in the acute care setting, namely, follow-

ing surgery. For example, many of these laws limit opioids following procedures to a 5–7-day supply. Early results suggest this has cut down on unnecessary opioid use; however, longer-term analysis is needed to measure the effectiveness of these measures. Importantly, the popularity of these measures illustrates the first concerted attempts by states to recognize and address the opioid crisis. Further details on legislative attempts to stem the opioid crisis are detailed in Chap. 3.

In addition to legislative attempts to address opioid prescribing practices, patient education has been playing an increasingly important role [14]. The importance of OPE for trainees and practicing physicians has been mentioned and is further detailed in Chap. 4; however, patient education initiatives have been long underappreciated. Particularly for opioid-naïve patients, the importance of following instructions regarding opioids, discarding unused opioids appropriately, and avoiding overuse is paramount. All too often patients are prescribed these medications following procedures without any instruction, a trend that can be addressed by active initiatives [15, 16].

While educating opioid-naïve patients is an important strategy for decreasing societal opioid misuse, addressing chronic pain patients is equally important. It is important to identify patients who suffer from chronic pain and are on pain medications regularly. Any of these patients who are undergoing procedures should have a plan prior to any intervention, a plan involving their prescribing physician, surgeon, and ideally the anesthesiologist. This plan should take them through the preoperative, intraoperative, and postoperative phase in a way that does not increase narcotic use in a long-term fashion. The authors cannot emphasize enough that simply performing an intervention on these patients and adding opioids is dangerous. The importance of preoperative optimization is further reviewed in Chap. 5.

Preoperative optimization is important for all patient populations, whether addressing chronic patients, opioid-naïve patients, or other individuals undergoing surgical intervention. All patients need to have a plan ideally discussed between their surgeon and anesthesiologist that involves multimodal analgesia (MMA) for before, during, and after surgery. Each patient cannot have the

same plan; as illustrated above, there are different needs for different patient populations. A perfectly healthy opioid-naïve patient has differing needs from a chronic pain patient, a child or adolescent, an elderly individual, or someone known to misuse opioids. Familiarity not only with opioids but also, more importantly, with evidence-based alternatives, is paramount for addressing the opioid epidemic.

Surgeons have played a significant role in the overprescription of opioids and consequent opioid epidemic. Understanding evidence-based alternatives available, such as NSAIDs, acetaminophen, gabapentinoids, local blocks, and other modalities, is important in contemporary practice. The importance of patient education in decreasing opioid abuse in situations in which opioids are prescribed cannot be overstated. By understanding the role of surgeons in the opioid epidemic, surgeons can change their practices and most importantly improve patient outcomes.

Conclusion

The opioid epidemic has impacted tens of thousands of individuals over the past two decades. Thousands of individuals die every year, with an increasing proportion of these deaths relating to prescription opioids. A multitude of evidence-based alternatives to opioids are available, including nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and gabapentinoids (gabapentin, pregabalin). Overprescription of opioids by surgeons following procedures plays a significant role in the opioid epidemic, as patients often misuse opioids prescribed and divert extra opioids to friends, family members, and other individuals. There has been historically poor patient education and physician education practices, both of which have been emphasized increasingly in recent years to address opioid overprescription and misuse. Furthermore, recent legislation at the state level has been passed in an attempt to limit opioid overprescription. By embracing educational initiatives and evidence-based alternatives, surgeons can become leaders in the drive to mitigate the opioid epidemic.

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3 Pain Prescription Legislation: What You Need to Know as the Surgeon

Jay Majmundar, George Zhou, and Peter F. Svider

Introduction

While people of the world have alleviated their pain with various substances throughout history, laws and regulations regarding pain medication and prescription of pain medication is a relatively recent phenomenon. Throughout the 1800s, narcotics were marketed and prescribed for all sorts of complaints, from diarrhea to toothaches, to menstrual cramps. The first federal law that began the regulation of narcotic medications was the Pure Food and Drug Act of 1906, which mandated labeling of products that contained "addictive" substances, including morphine and other opioids. This was followed by the Harrison Narcotics Tax Act in 1914, in response to rising street heroin abuse. The overall effect

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of this legislation was discourage physicians and patients from prescription and use of opiate medications [1].

Controlled Substance Act

The Controlled Substance Act categorizes substances into five schedules based upon potential for medical use, potential for abuse, and liability of safety and dependence [Table 3.1]. Schedule 1 substances are those with no accepted medical use and possess a high potential for abuse such as heroin, LSD, marijuana, methaqualone, and peyote. Schedule II substances are those with high potentials for abuse with usage that can potentially lead to severe psychological or physical dependence. These substances however do possess medical benefits. Examples of Schedule II substances include hydrocodone, methamphetamine, methadone, hydromorphone, oxycodone, and fentanyl. Schedule III substances are defined as drugs with moderate to low potential for physical and psychological dependence, and their abuse potential is less than the drugs that belong to Schedule I and II but still greater than those in Schedule IV. Examples of some Schedule III drugs are

Table 3.1 Drug schedules [2]

Drug schedule	Accepted medical use	Abuse/ dependence potential	Examples
Schedule I	No	High	Heroin, LSD, marijuana, ecstasy, methaqualone, peyote
Schedule II	Yes	High	Hydrocodone, methamphetamine, methadone, hydromorphone, oxycodone
Schedule III	Yes	Moderate/low	Tylenol with codeine, ketamine, anabolic steroids, testosterone
Schedule IV	Yes	Low	Xanax, Valium, Ativan, Ambien, Tramadol
Schedule V	Yes	Low	Robitussin AC, Lyrica, or Lomotil

Tylenol with codeine, ketamine, anabolic steroids, and testosterone. Schedule IV drugs are those with low abuse and dependence potential such as Xanax, Valium, Ativan, Ambien, and Tramadol. Schedule V are those with even lower potential for abuse than Schedule IV and consist of preparations of drugs with limited narcotic quantities such as Robitussin AC, Lyrica, or Lomotil. Essentially, the greater the schedule number, the lower the potential for abuse and dependency. The rules and regulations in the United States for controlled substances are enforced by the Drug Enforcement Agency [2].

State Laws

By the end of 2018, at least 27 states have introduced laws that limit the use of opioids in the outpatient setting in response to the growing recognition of the negative effects associated with their use. The earliest law was made in 1989 in Missouri. However, wide variations exist in the characteristics of each state's law, with differing stipulations on the amounts and durations that opioids may be used for patients with acute pain [Fig. 3.1]. First-time opioid prescriptions are limited to 7 days in Alaska, Hawaii, Colorado, Utah, Oklahoma, Louisiana, Missouri, Indiana, West Virginia, South Carolina, Pennsylvania, New York, Maine, Connecticut, and Massachusetts. First-time prescriptions for acute pain are limited to 5 days in Arizona. However, in Arizona and North Carolina, postsurgical prescriptions are limited to 14 days and 7 days, respectively. Kentucky, Tennessee, and Florida have the strictest limit of 3–4 days for the duration of an opioid prescription, whereas Hawaii, Illinois, Missouri, and Tennessee impose limits of 30 days. South Carolina limits Schedule II drugs to 31 days. On the other hand, Maryland has no limitations on the duration of initial opioid prescriptions [3].

This wide variation also exists in the total amount of opioids than can be prescribed. Since there are several different opioid medications with different strengths, most legal guidelines discuss quantity of opioids in units of morphine milligram equivalents (MME). One MME is defined as the amount of morphine, in

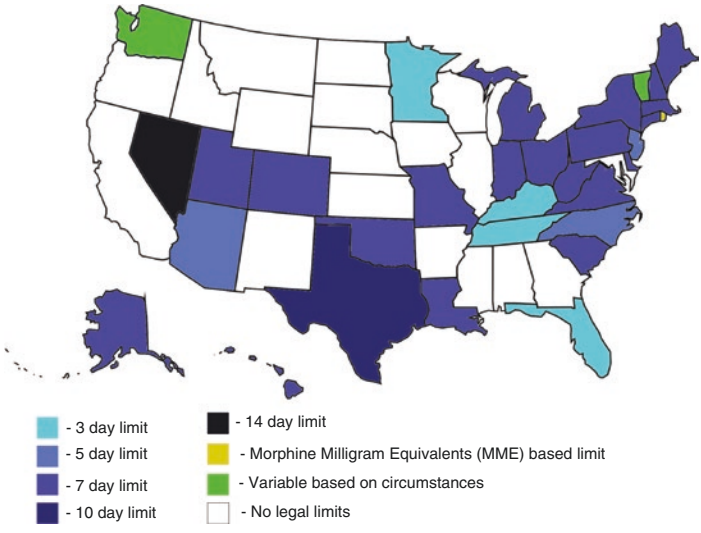

Fig. 3.1 Map of state limitations on opioid prescription for acute pain [3]

milligrams, that would provide equivalent opioid strength as the dose of other opioid medication prescribed. Ohio and Rhode Island restrict daily dosage to 30 MME with further day limits. Maine instead restricts daily dosage to 100 MME, which can be prescribed for a maximum of 7 days. In Vermont, limitations can vary by the patient's pain level from 24 MME for moderate pain to 50 MME for extreme. New Jersey limits opioid prescriptions to the "lowest effective dose" limited to a 5-day supply. Vagueness in the laws also exists with New Hampshire limiting opioid prescriptions to the "lowest effective dose for a limited duration," without actually defining how long the duration is, and Maryland law limits the prescriber to the "lowest effective dose" without any time limit other than that it "shall be based on an evidence-based clinical guideline" that is appropriate for the patient [4]. The non-homogenous nature of these laws can be challenging for surgeons and clinicians as they care for their patients.

Medication coverage by state laws also varies. While over half of states apply these opioid prescribing laws only to opioid

medications, some states also include all Schedule II drugs or possibly even Schedule III or IV drugs. Providers should check their own state laws for specific detail of which medications are covered under state prescribing laws.

There are many exceptions to the rules listed above as well, depending on the state. In some states, there are further restrictions on opioid prescriptions to minors, either through the quantity of medication or through a requirement for parental consent. In other states, physicians may deviate from restrictions if treatment of the patient requires it; this usually must be documented.

Furthermore, each state has its own guidelines for practitioner education regarding the prescribing of controlled substances. Individual states have their own requirements either in statute, regulation, or board guidelines for practitioners to obtain continuing education hours in areas such as prescribing controlled substances, pain management, and substance use disorder identification, among others. Some states have mandated training by statutes, whereas others allow the state medical board to decide what is required [5]. Even within a state, there may be differences in requirements based on whether the prescriber is an allopathic or osteopathic physician – as is the case in Nevada and Oklahoma, which each board having their own requirements [6]. Practitioners therefore must remain informed regarding controlled substances regulations in their geographic area of practice. This information can be found within in each state's individual legal code; a broad overview of each state's requirements can be found in various resources, like the Federation of State Medical Boards CME overview [6].

Other initiatives exist such as the Prescription Drug Monitoring Programs (PDMP), which are statewide databases that contain information regarding controlled substances that are dispensed in the state [3]. Providers can use the PDMP to receive information on the dose, supply, and prescriber of scheduled drugs that a patient has filled in the past [7]. These programs are available in all 50 states and the District of Columbia except for Missouri, in which a PDMP is only available in St. Louis county [8]. The PDMP is used as a tool to identify and address prescription drug abuse and addiction.

For surgeons, this database can be used to identify patients who may have sought opioid prescriptions from multiple providers or for the early detection of those patients who have had unintended prolonged use, which may clue the provider in to patient who are at high risk for opioid abuse postoperatively. As of 2019, 40 states have statutes or rules in place that require prescriers of opioid mediations to use PDMPs, but rules regarding when to utilize the PDMP vary by state law [9]. Some states only mandate the use of PDMP if the patient is suspected of opioid abuse, which may be less relevant to the surgeon in the perioperative enviornment. Other states require the use of PDMP before prescription of any scheduled substance at all or if the prescription will exceed a certain number of days [7].

Federal Laws

In 2016, the CDC created guidelines and recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care [10]. These guidelines focused on determining when to initiate or continue opioids for chronic pain; the selection of the opioid, dosage, duration, follow-up, and when to discontinue; and the assessment of risk and addressing the harms of opioid use. However, it is important to note that postoperative patients fall outside of the scope of these guidelines, as stated in the document itself [11]. The CDC has published no specific guidelines on acute pain in perioperative patients.

Furthermore, the Centers for Medicaid and Medicare Services has introduced many initiatives that focus on limiting opioid prescription, such as sending letters to physicians who prescribe these drugs at higher levels than their peers [12]. Additionally, the FDA has initiated the Opioids Risk Evaluation and Mitigation Strategies program for long-acting opioids, which focuses on educating all healthcare providers who are involved in the management of patients with pain, including nurses and pharmacists [13].

The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act

(SUPPORT) was passed in 2018 as federal law and includes a many new laws pertaining to opioid prescription and addiction treatment [14]. Some of the laws most relevant to surgeons will be discussed below.

The Combating Opioid Abuse for Care in Hospitals Act (COACH) is one such law. The overall goal of this law, as one might surmise from its title, is to decrease opioid abuse resulting from hospital care. This includes a few provisions relevant to surgeons. As a part of this law, the Department of Health and Human Services will publish guidance for hospitals regarding pain management and opioid abuse prevention strategies. In the future, this will likely affect hospital policies on pain prescriptions that surgeons must follow. Additionally, the act establishes a technical expert panel in order to collect data on perioperative opioid use. The goal of this panel is to produce recommendations and guidelines in order to decrease use of opioids perioperatively and post-discharge. While no legal changes have been made by this committee, there may be future legislation on pain prescriptions pending the results of this government panel.

The Expanding Oversight of Opioid Prescribing and Payment Act and Dr. Todd Graham Pain Management, Treatment, and Recovery Act involve review of payment for opioid and non-opioid by Medicare, with the goals of financially incentivizing non-opioid pain management for many clinical contexts, including perioperative care. These acts may impact Medicare reimbursement in the future [14].

Federal Prescription Rules for Controlled Substances

In order to prescribe controlled substances, a practitioner must be registered with the DEA and include their DEA number on the prescription. For Schedule II drugs, a written prescription must be presented by the patient to the pharmacy, and no refills are allowed. Therefore, a new prescription is required for each time the patient needs more medication. In emergency conditions, a prescription may be phoned in by the physician but only for the

amount of medication required to treat the patient for the emergency period. Following the oral prescription, a written and signed prescription must be presented to the pharmacy within 7 days with the words "authorization for emergency dispensing" written on the prescription. If this follow-up is not completed, pharmacists are obligated to report the incident to the DEA.

For Schedule III and IV drugs, written or oral prescriptions are allowed. Refills are allowed up to a maximum of five times, and only for 6 months following the date listed on the prescription. Schedule V drugs can be prescribed in similar fashion, with no specific limitations on refills aside from those of noncontrolled substances.

Beginning in 2010, electronic prescriptions were allowed for controlled substances, provided that the electronic prescription application used complies with DEA requirements [15, 16]. This compliance is determined by a third-party auditor of the application provider, and the application provider should provide a copy of the auditor report to the health practitioners. In the past few years, many states have begun to institute mandatory electronic prescription. At the federal level, the section 2003 mandate, part of the SUPPORT act of 2018, states that, "a prescription for a covered part D drug under a prescription drug plan…for a schedule II, III, IV, or V controlled substance shall be transmitted by a health care practitioner electronically" [14]. There are some exceptions to this law. There is a waiver system for physicians who cannot implement electronic prescribing due to economic or technological reasons, but these waivers only last for 1 year at a time. There is also an exception in situations where an electronic prescription would result in unreasonable delay in the patient obtaining their medication. This law applies to prescriptions starting from 2021 [14].

Conclusion

The legislative landscape regarding controlled substances is ever changing. Currently, in the United States, there is a raging overuse of opioids, and its fatal consequences have reached staggering

numbers. To address this crisis, government regulatory agencies and physician licensing boards have released many statements and recommendations over the years resulting in varied stances. A coordinated effort among physicians, lawmakers, state bodies, and the general public are required to ensure clarity for the practitioner and safety for the patient.

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4 Opioid Prescribing Education in Surgical Training

Elizabeth Boscoe, Kenny D. Rodriguez, and Andrew P. Johnson

Introduction

Physicians and policymakers alike have been working to combat the opioid epidemic decades. The United States started to see a rise in opioid prescription rates in 2006, and this rise peaked in 2012 at a rate of 81.3 opioid prescriptions per 100 persons. Since 2012, we have started to see the amount of opioid prescriptions trend downward; however, it remains exceptionally high with an average of 58.7 prescriptions per 100 persons, and in some states, this rate is as much as seven times higher [1].

Resident physicians play a significant role in opioid prescriptions. These physicians represent the future of medicine and can play an important part in combating needless opioid prescriptions. As far as surgical residents are concerned, opioids are often prescribed for acute postoperative pain. In a study examining almost 800,000 patients across 315 medical centers, 97% of them received an opioid prescription after surgery [2]. Surgeons are estimated to

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prescribe 36% of all opioid medications dispensed in the United States [3]. Patients often receive more pills than they need, and instead of disposing of the excess pills, patients often hold on to them, increasing the risk of misuse. In addition, initial opioid prescriptions in opioid-naïve patients increase the risk of chronic opioid use by 44% [4]. Surgeons, therefore, are intimately tied to the opioid epidemic, and this explains the effort to increase resident education in opioid prescribing. Furthermore, surgical residents play a significant role in the care of patients at teaching hospitals and surgical centers. Studies comparing prescription rates among teaching hospitals versus nonteaching hospitals *demonstrated a larger average oral morphine equivalents prescribed at teaching hospitals* [5].

Postoperative tasks such as prescriptions of discharge medications are commonly assigned to residents, including newly appointed interns. However, there remains no comprehensive guidelines available or widely accepted instruction on proper opioid prescription or proper tapering after surgery. This leaves residents to learn on their own mostly by following more senior physicians' examples, resulting in large variability in prescription practices [6, 7]. Additionally, significant research is still warranted when it comes to prescription trends among residents. The following attempts to shed some light on opioid prescription trends highlight the variation among residents and further demonstrate the need for formal opioid education in residency.

Opioid Prescriptions in Surgical Training Programs

Bhashyam et al. performed a study surveying 83 orthopedic residents from four orthopedic residency programs in a single state and looked at their prescribing patterns for postoperative analgesia after open reduction and internal fixations of distal radius fractures. Thirty-seven percent of residents surveyed had completed some form of opioid training. Senior residents were more likely to prescribe larger amounts of opioids to younger patients than junior residents. Nineteen percent of residents prescribed more than 7 days of opioids after surgery. Interestingly, these residents were training in a state which had passed a law limiting first-time opioid

prescriptions to no more than a 7-day supply [8]. This further emphasizes the need for structured opioid prescription education.

In another study examining both US and Canadian plastic surgery residents, Grant et al. found that 53.4% of Canadian residents surveyed had received some form of opioid prescription training, while only 25% of US residents reported any training. This varied significantly based on the geographic region of where the resident was training in the United States. In order to compare opioids, the oral morphine equivalent was reported. Eight different plastic surgery procedures were looked at, and US residents prescribed significantly more oral morphine equivalents for seven of the eight procedures than their Canadian counterparts. When surveyed about factors that impacted their prescription patterns, attending and senior resident preference played a large role for the majority of residents (72% of Canadian and 68% of Americans) indicating that opioid prescription patterns are very much a learned behavior. Regarding the concern for potential opioid abuse, 70% of Canadians considered this a factor in their prescription decision, compared to only 49% of Americans. Potentially even more alarming is that 24% of US residents and 14% of Canadian residents surveyed noted that the amount of opioids prescribed did not vary based on the surgery performed, which indicates a lack of consideration for necessary analgesia and likely contributes to excess opioid prescription practices [9].

Another study by Chiu et al., looking only at general surgery residents at a single institution, showed similar factors impacting resident prescribing patterns as Grant et al. Ninety-five percent of residents surveyed noted their prescriptions were influenced by attending or senior resident preference, and 84% noted they had a standard prescribing habit for a certain operation regardless of other factors. Again, a minority noted any formal training on opioid prescribing (6%). Five different general surgery procedures were looked at, and for all procedures, except bedside incision and drainage (I&D), 97–100% of residents prescribed postoperative opioids. For bedside I&D, 76% of residents noted prescribing post-procedure opioids. Furthermore, when residents were asked how many pills of 5 mg of oxycodone the average patient would use after a laparoscopic cholecystectomy, residents reported 15 pills. Yet, the analysis showed that residents on average provided

patients with 22 pills of 5 mg of oxycodone after a laparoscopic cholecystectomy [10]. This indicates that residents are *knowingly overprescribing* opioids and that these habits are largely learned from their superiors. More concerning still, as seen with Grant et al., the study by Chiu et al. indicates that residents often develop a standardized practice of opioid prescription and do not take into account other factors such as patient age, comorbidities, or risk for opioid abuse.

More telling still is the fact that there may be a disconnect between perceived opioid prescription patterns and actual opioid prescriptions. A single-institution study looked at the opioid prescription patterns of general surgery residents and attendings. Their results demonstrated that both attendings and general surgery residents self-reported prescribing a lower quantity of opioids after certain surgical procedures than what was actually prescribed. Additionally, residents and attendings both prescribed similar amounts, but when surveyed, residents reported almost 70% of the time that they prescribed "too many" pills, while attendings reported the same amount of the time that they prescribed "just enough" [11]. Another study looking at perceptions was done as a multicenter randomized trial, and they showed that 73% of attending physicians and advanced practice providers in the emergency department underestimated their prescription amounts compared to their peers, while 27% of emergency medicine residents underestimated their prescribing rank compared to their peers [6]. There is clearly a disconnect between perceived ideas of opioid prescribing and actual opioid prescribing patterns.

The above studies highlight the strong need for formal education on opioid prescription, pain management, and postsurgical anesthesia among residents. Unfortunately, formal education is often lacking.

Steps to Improve Opioid Prescribing Education

Formal education in pain management has only been implemented in a limited fashion. Among physicians of all specialties surveyed in Michigan in 2001, only 10% of responders reported receiving

any education on this subject during medical school, residency training, or via continuing medical education. It is noteworthy that younger physicians were more likely to have received this education [13]. Residency is an important time to develop clinical practice habits. Implementing a comprehensive postoperative pain management strategy among surgical residents has been seen as a vital part of combating the opioid epidemic. This has led to the creation of educational sessions targeting surgical residents at multiple institutions, providing information on the opioid epidemic, non-opioid analgesics, and opioid analgesics. These education efforts have demonstrated a significant decrease in both the quantity of opioids residents perceived as warranted [16] and the total amount of opioids residents prescribed [12, 14–17]. In one study, a resident-led educational session was given to general surgery interns during their orientation prior to the start of clinical duties. Their prescription patterns for the next 2 months were monitored and compared to interns from the previous year. The study demonstrated a decrease on average of 80 oral morphine equivalents per postoperative prescription [16].

Many of initiatives to increase resident education have included didactic lectures. An interesting study looking at prescription patterns in hand surgeons went a different route. They analyzed opioid prescription patterns for four common hand surgeries. The Department of Plastic and Hand Surgery then determined official recommendations for multimodal pain management for each of the four surgeries. This information was distributed to residents, fellows, attendings, and nursing staff. Additionally, an educational assist device of a laminated card was provided as a memory aid. Results demonstrated a statistically significant decrease in opioid prescriptions in two of the four surgeries looked at 3 months after the implementation. A consistent downward trend of opioid prescriptions were seen at a year after the intervention, indicating some amount of long-term adherence and change [18].

A major concern posed with decreasing the amount of postoperative prescriptions is that patients will experience inadequately controlled pain, leading to an increase in refill requests. Yet, multiple studies have demonstrated that, after implementation of lower postoperative opioid prescriptions, numbers of refill

requests remain insignificant [17–19]. This finding is predicated on determining a reasonable amount of opioid for specific operations, and although studies have focused on specific procedures in opioid-naïve patients, there is limited information as to how a general implementation of decreased opioid amounts can be applied to all postoperative patients. Additionally, despite the perceived and reported benefits of resident opioid education, a recent survey to US surgical residency program directors demonstrated that only 20% of programs required opioid education during their residency program [20].

One of the significant limitations of resident education in opioid prescription is the lack of autonomy residents perceive. Surveys of resident prescription practices, including those that asked about practices after formal education, found that pressure by patients and or attending surgeons to prescribe a large amount of opioids was a significant driving force in their prescription habits [17, 21, 22]. This lack of autonomy presents three major challenges. First, it limits the impact that resident opioid prescription education can have by limiting actual implementation. Secondly, it limits a proper analysis of the effects of educational initiatives as results are skewed based on the biases of attending surgeons. Lastly, persistent outside pressure on residents can delay a change in opioid prescription culture and clinical judgment. Targeting both residents and attendings allows for a unified goal in standardized prescription practices and faster implementation of decreased postoperative opioid prescriptions. Education efforts which have targeted both residents and attendings have shown to significantly decrease the average amount of postoperative opioids prescribed [17, 18].

There are other concepts that would likely help change the culture of postoperative opioid prescriptions. Surgical residents and attending surgeons are acutely aware of the need for a thorough discussion regarding the risk and benefits of surgical procedures. However, discussions with patients and education regarding the risk of opioid prescriptions are often lacking [23]. Having these discussions prior to the perioperative period would help set realistic expectations. Many states have begun to implement prescription monitoring programs that will allow prescribers the ability to check recent opioid prescriptions given to a patient. Again, this is

an area lacking in formal resident education, and further instruction in this topic would help residents optimize their postoperative analgesic plan for every patient and develop a habit that would shape their future independent practice.

Medical School Opioid Education

Residency education is not the only area where pain management education is lacking. Medical school education also demonstrates inadequacies. A survey of North American medical schools between August 2009 and February 2010 demonstrated that only 3.8% of the 104 reporting US medical schools had a required pain course, and an additional 16.3% offered a designated elective course [24]. Given the increased awareness of the opioid epidemic, implementation of pain management education has increased at medical schools nationwide [7]. However, there is a lack of a broadly used curricula or consensus as to competency in pain management among US medical school [24]. Lawmakers in several states have worked with medical schools to require education and core competencies into curricula to establish some standardization to required education [23, 24]. There is, however, a paucity of information regarding the effects of these educational efforts due to the delay between education in medical school and when students become prescribers. There is also difficulty in tracking students after nationwide dispersion for residency. However, just as programs that target residents and attending education have been shown to decrease opioid prescriptions, targeting medical students will hopefully generate a culture of opioid prescription awareness as well as other potential postoperative analgesia methods.

Conclusions

The road to changing the culture around opioid prescriptions is a long one. It is worth noting that multiple factors are at play. Marketing campaigns by pharmaceutical manufacturers over the

years have encouraged the use of opioids for pain management while downplaying the risks associated with these medications. In recent years, these improper marketing campaigns have resulted in criminal charges and over a billion dollars in fines [24]. These campaigns illustrate the difficult road that lays ahead for combating the opioid epidemic. Efforts to educate surgical resident not only have to bring new medical information to the table but must also be focused on undoing the damage caused by false marketing information. While there is significant room for improvement in our residency education for opioid prescription patterns, these studies show that change is possible. Future studies need to investigate the change and potential benefit these educational initiatives have in the long term, as well as potentially create standardized opioid education tools throughout the country.

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Preoperative Optimization

5

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Introduction

Pain control is a prominent concern of patients undergoing surgical procedures [1]; however, less than half of patients report adequate postoperative analgesia [2]. Inadequate pain control is undesirable for multiple reasons, including poor patient satisfaction, worse quality of life, worse functional recovery, increased risk of postsurgical complications, and increased risk of chronic pain [2]. Planning for postoperative analgesia should begin preoperatively, so that patients are screened appropriately, realistic expectations are set, and there is opportunity to include a multidisciplinary approach, if necessary. The surgeon may need to

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consult with the anesthesiologist, outpatient opioid provider, pain management, addiction specialist, or pain psychologist for optimal planning.

Pain History

According to the 2016 clinical practice guideline on postoperative pain management by the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, optimal pain control begins in the preoperative period [2]. The surgeon should conduct a focused pain history (Table 5.1). Patients should be screened for any chronic pain conditions and baseline pain. It is important to know about chronic pain even if it is unrelated to the surgical site, as it will affect postoperative pain management. Understanding the patient's baseline pain score may help set realistic expectations for postoperative pain control. Pain medication history must be detailed, including the specific medications and doses that the patient is on. For an as needed "PRN" medication, it is important to know how many doses of the medication the patient actually takes on a daily basis. This can be confirmed via prescription drug monitoring systems for controlled substances and through discussion with the outpatient prescriber. If the patient is on nonsteroidal anti-inflammatory drugs (NSAIDs), the patient should be instructed whether these medications may be continued in the perioperative period. Anxiolytic therapy is important to note, as concurrent use of benzodiazepines and opioids increases risk of respiratory depression and death [3, 4]. Any adverse reactions to previous medications should be noted. In addition, patients may employ non-pharmacological treatments, such as transcutaneous electrical nerve stimulation (TENS) unit, heat/ice, exercise program, massage, or cognitive behavioral techniques in order to treat their pain, in which case an effort can be made to continue these modalities postoperatively. The social history is of paramount importance, as the surgeon must be aware of any history of substance use disorder. Recent substance use can make postoperative analgesia more challenging.

Table 5.1 Focused pain history

Pain history	Do you have a history of chronic pain? Where is the pain located? Baseline pain score
Medical history	Chronic pain conditions Medical conditions (see Table 5.2) If regional technique is anticipated, contraindications (see Table 5.4)
Surgical history	Previous experience with postoperative pain
Medications	Pain medications Anxiety medications Dose of pain medications Number of doses taken daily What pharmacological modalities are helpful? What non-pharmacological modalities are helpful? Are you on buprenorphine or methadone for pain? Who is managing pain provider?
Allergies	Allergies/adverse reactions to pain medications
Social history	Smoking Alcohol Illicit drug use Substance use disorder Which substance(s)? How long ago was last use? Are you on MAT with methadone, buprenorphine, or naltrexone*? Who is addiction specialist?
Psychiatric	Depression Anxiety
Miscellaneous	Expectations regarding postoperative pain management

**MAT* medication-assisted treatment

Patients on medication-assisted treatment (MAT) of substance use disorder require advanced planning. Whether prescribed for chronic pain or for substance use disorder, the surgeon should be aware of patients on methadone or buprenorphine, as they require special consideration, as discussed below.

The surgeon should be aware of how the patient's chronic medical conditions will affect postoperative analgesic choice (Table 5.2). Medications that need to be renally dosed include

Table 5.2 Chronic conditions affecting analgesic choice

Condition	Consideration
Renal dysfunction	NSAIDs contraindicated[a] Gabapentinoids renally dosed[b] Avoid duloxetine in severe renal dysfunction Tramadol renally dosed Avoid morphine with significant renal dysfunction Avoid meperidine – increased risk of toxicity
Hepatic dysfunction	Acetaminophen – if stable hepatic dysfunction, limit dose to 2000 mg total daily Tramadol – hepatically dosed in severe dysfunction
Gastritis or gastric ulcer	Avoid NSAIDs Selective COX-2 inhibitors safer than nonselective COX-1 and COX-2 inhibitors
Cardiac disease	NSAIDs increase thrombotic risk, except for aspirin
Cerebrovascular disease	NSAIDs increase stroke risk
Coagulopathy	Risk of bleeding with concurrent use of anticoagulants and NSAIDs Regional anesthesia may be contraindicated

[a]Do not discontinue aspirin without consultation with prescribing provider
[b]Gabapentinoids include gabapentin and pregabalin

gabapentinoids (gabapentin, pregabalin), as well as tramadol. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided in patients with renal dysfunction, gastritis, or gastric ulcers. Aspirin should not be discontinued without consultation with the prescribing provider as it is commonly prescribed as an antiplatelet agent. Selective COX-2 inhibitors, such as celecoxib, exhibit less gastrointestinal side effects than nonselective COX-1 and COX-2 inhibitors [5]. NSAIDs other than aspirin are prothrombotic and increase risk of acute coronary syndrome and stroke [5, 6]. Morphine should be avoided in severe renal dysfunction. Caution should be exercised for patients with renal dysfunction, as creatinine clearance may worsen postoperatively. For patients with stable liver dysfunction, maximum recommended dose of acetaminophen is 2000 mg from all sources. Take into consideration all sources of acetaminophen that the patient may be taking; common formulations of opioids that include acetaminophen include hydrocodone-acetaminophen (brand

names include Norco, Vicodin), oxycodone-acetaminophen (brand name includes Percocet), and codeine-acetaminophen (brand name includes Tylenol 3). It should be noted if patient is on anticoagulation or has history of coagulopathy. If regional anesthesia is being considered, contraindications should be noted.

Postoperative Respiratory Depression

Postoperative respiratory depression may lead to catastrophic morbidity and mortality. The surgeon should be aware of any factors that may increase risk of respiratory depression postoperatively (Table 5.3). Opioids are a contributing factor, and it is estimated that opioid-induced respiratory depression (OIRD) occurs following 5 out of 1000 anesthetics [3]. The pathophysiology of OIRD includes depression of respiratory drive, decreased level of consciousness, and decreased supraglottic muscle tone, which may contribute to hypoxia and hypercapnia [7]. The majority of OIRD develops within 24 hours of surgery, so patients are at risk beyond the close monitoring of the postanesthesia recovery unit [3, 8]. However, a significant 15% of OIRD occurs beyond the initial 24 hour postoperative period. Cardiac disease and pulmonary disease are risk factors for OIRD [3]. Concurrent administration of other sedating agents, including benzodiazepines and gabapentinoids, increases risk of OIRD [3]. A meta-analysis and systematic review by Gupta et al. revealed that opioid dose was higher in OIRD group versus control group, although the mean oral morphine equivalents over 24 hours were 24.7 mg in OIRD group versus 18.9 mg in control [3]. For comparison, 25 mg of oral morphine is approximately equivalent to five doses of 5 mg hydrocodone administered over a 24 hour period or less than four doses of 5 mg oxycodone over a 24 hour period.

Diagnosed obstructive sleep apnea (OSA) and high risk for OSA are risk factors as well [3, 8]. OSA patients have a decreased arousal response to hypoxia and prolonged airway obstruction [3]. The STOP-Bang questionnaire is a validated screening tool for OSA, with patients scoring ≥ 3 at higher risk for postoperative complications [9]. Early preoperative screening would allow the

Table 5.3 Risk factors for postoperative respiratory depression

Diagnosed obstructive sleep apnea
Suspected obstructive sleep apnea
Opioids
Concurrent use of sedatives – opioids, benzodiazepines, or gabapentinoids
Cardiac disease
Respiratory disease
Major organ failure
Smoking
Residual anesthesia
Residual muscle paralysis
Splinting secondary to pain
Continuous opioid infusion (as part of IV-PCA)

IV-PCA intravenous patient-controlled analgesia

surgeon to refer the patient to a sleep specialist if necessary. Patients on continuous positive airway pressure (CPAP) devices should be instructed on the importance of postoperative CPAP use if not contraindicated and to bring their home CPAP device based on hospital policy. Postoperatively, lack of appropriate monitoring was cited in litigation [8, 10]. Monitoring considerations include an appropriate level of care setting and duration. Continuous pulse oximetry has been shown to improve recognition of desaturation events over intermittent pulse oximetry checks [11]. Sedation should be recognized as a primary predictor of respiratory depression [8].

The surgical team should be aware of risk factors putting patients at increased risk for postoperative respiratory depression. Mitigation strategies for high-risk patients may include the use of opioid-sparing modalities, including regional anesthesia and multimodal analgesia [12]. Appropriate level of monitoring and duration of monitoring should be employed.

Patient on Chronic Opioids

Patients on chronic opioids require special consideration, as they may experience greater pain intensity and slower pain resolution postoperatively [13]. Preoperative opioid use is associated with

higher postoperative analgesic requirements [2]. Patients with repeated exposure to opioids can develop opioid tolerance. Tolerance occurs when the same opioid dose results in a lesser analgesic effect, or there is a need for higher opioid dose to achieve the same therapeutic effect [14]. Abrupt discontinuation of opioid can lead to withdrawal, which is a sign of physical dependence, and can occur without any relation to substance use disorder or abuse [14]. Patients may experience opioid-induced hyperalgesia, a neuropharmacological phenomenon of nociceptive sensitization caused by opioid exposure that results in a patient becoming more sensitive to painful stimuli [13]. A lower pain tolerance can be seen in such patients [15].

Patients with chronic opioid use preoperatively are at a higher risk for postoperative complications, longer hospital stays, hospital readmission, emergency department visits, additional surgical procedures, and worse outcomes [13, 15]. Some studies suggest that these patients are also at higher risk for infection, ileus, pneumonia, and wound healing [15]. In 2016, a clinical practice guideline from the American Pain Society, American Society of Regional Anesthesia and Pain Medicine, and American Society of Anesthesiologists' Committee on Regional Anesthesia concluded that there is insufficient evidence to routinely recommend opioid dose reduction or discontinuation prior to surgery [2]. The surgeon may discuss whether preoperative opioid reduction may be helpful for the specific patient with the prescribing physician. Preoperative reduction of opioids continues to be examined. A retrospective cohort study by Nguyen et al. examining patients undergoing total joint arthroplasty found that patients who successfully tapered their preoperative opioid dose, defined as 50% dose reduction, had improvement in outcomes based on activity and function scores comparable to opioid-naïve patients [13]. The study suggests that chronic opioid use can be viewed as a modifiable risk factor.

A potential reason for opioid wean is concern for opioid-induced respiratory depression, particularly if increased doses of opioids are anticipated postoperatively. Patients on chronic opioids develop less of a tolerance to respiratory depression than to the analgesic effects of opioids [16]. Thus, the chronic opioid

patient is at risk for respiratory depression postoperatively, especially when escalated doses of opioids are used for analgesia [16]. According to the Centers for Disease Control and Prevention, risk of overdose doubles for patients on 50 mg oral morphine milligram equivalents (MME) or higher and increases up to nine times for patients on 100 MME or more daily [17]. Numerous studies support that tapering of opioids in patients with chronic non-cancer pain results in lower or unchanged pain scores or improved function [18–20]. Barriers to tapering include time and patient's concurrence [21]. For chronic opioid use, dose decrease of 5–20% every 1–4 weeks has been suggested [22]. If the decision is made to taper, it should be done gradually and guided by the patient's prescribing provider.

In the perioperative period, patients on chronic opioids should be treated with multimodal analgesia, and regional anesthesia should be implemented if appropriate [2]. Abrupt discontinuation of the patient's baseline opioid requirement postoperatively should be avoided due to risk of withdrawal and worsening pain. A standardized way of thinking about the patient's opioid dose is calculating the oral morphine milligram equivalents (MME) that the patient uses over 24 hours. Table 5.4 can be used to calculate approximate MME, although difference in conversion factors exists in the literature and interindividual differences occur as well. Postoperatively, the patient will likely require at least their baseline MME. For surgeries with anticipated little to no pain, or for which regional anesthesia techniques can be employed, the patient may be treated with their baseline MME plus multimodal analgesia. For surgeries with anticipated moderate to severe pain, when adjuvant medications and/or regional anesthesia cannot be expected to provide adequate analgesia, the patient will likely require their baseline MME plus additional opioid, in addition to multimodal analgesia. Appropriate gauge for postoperative opioid requirement must begin preoperatively by recognizing and calculating the patient's baseline opioid use. In clinical practice, postoperative pain control is sometimes poor because the patient is receiving less opioid in the immediate postsurgical setting than their preoperative baseline. For example, oxycodone 5 mg every 4 hours as needed would be insufficient analgesia for a patient

Table 5.4 Equianalgesic table of commonly used oral opioids

	Equivalent dose orally[a, b, c]	Conversion factor
Morphine	30 mg	1
Hydromorphone (brand name Dilaudid)	7.5 mg	4
Hydrocodone (when combined with acetaminophen, brand name Norco or Vicodin)	30 mg	1
Oxycodone (brand name Roxicodone; when combined with acetaminophen, brand name Percocet)	20 mg	1.5
Tramadol	3 mg	0.1

[a]Fentanyl patch is dosed in micrograms per hour (mcg/hr.) and is exchanged every 72 hours. Multiply the mcg/hr. dose by conversion factor of 2.4 in order to calculate milligrams oral morphine equivalents over 24 hours. For example, a patient on 12mcg/hr. fentanyl patch *over 24 hours* receives approximately the equivalent of 28.8 mg oral morphine

[b]If opioid rotation is involved, decrease opioid dose by 25–50% to account for incomplete cross-tolerance

[c]Doses noted are for conversion purposes only and are not dose recommendations (https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-March-2015.pdf)

who was taking morphine 30 mg every 4 hours at home. In this example, it is important to elucidate how many times the patient actually takes morphine at home, especially since many pain medications are written for "as needed," so actual use may vary greatly.

If opioid rotation is employed postoperatively, meaning the patient receives a different opioid than their chronic preoperative opioid, the provider should take into consideration incomplete cross-tolerance [23]. This phenomenon suggests that if a patient is chronically on one opioid (e.g., morphine), they are tolerant to all opioids but have the highest tolerance for morphine and less tolerance to other opioids (e.g., oxycodone). Using a conversion table, morphine 30 mg would be equivalent to approximately oxycodone 20 mg. However, 25–50% dose reduction should occur to

account for incomplete cross-tolerance, and so the patient should actually receive 10–15 mg of oxycodone in practice to achieve the same analgesic effect. This would account for the patient's baseline opioid requirement, and supplemental opioid may be necessary in the postoperative period. Failure to account for incomplete cross-tolerance can result in overdose. Opioid conversion is an art as well as a science, clinical judgment should be employed as these are high-risk medications, and pain service consultation may be needed to ensure safety for patients on high-dose opioids.

The patient should be counseled on a plan for opioid tapering postoperatively. Following surgery unrelated to the patient's chronic pain, the end goal should be to taper to the patient's preoperative baseline. The outpatient provider should be aware of the patient's surgery ahead of time and may help formulate the postoperative plan. Appropriate follow-up with outpatient prescriber should be arranged.

Preoperative Medications

The patient should be counseled on which home medications to continue prior to surgery (Table 5.5). Because of the potential bleeding risk of NSAIDs and aspirin, the surgeon should weigh the consequences of bleeding, should it occur, versus the benefit of the medication. If it is necessary to discontinue aspirin, the patient should receive medical clearance to do so, as it is often prescribed for medical comorbidities such as cardiac conditions or stroke history. Acetaminophen is commonly continued in the perioperative period. Gabapentin or pregabalin should be continued preoperatively and postoperatively, if enteral administration is possible. Concurrent use of two agents in the gabapentinoid family should be avoided (i.e., a patient on home gabapentin receiving postoperative gabapentin plus pregabalin). The patient should be instructed to take their usual opioid dose, except for buprenorphine, which requires special consideration and is discussed below. Abruptly discontinuing the patient's chronic opioid may precipitate withdrawal symptoms. Fentanyl patch will lead to increased blood concentrations if heated, such as with a

Table 5.5 Home medications – preoperative management

NSAIDs	Hold or continue based on risk benefit analysis of anticipated bleeding risk[a]
Acetaminophen	Continue Monitor total dose from all sources
Gabapentinoids (gabapentin, pregabalin)	Continue Avoid adding a second gabapentinoid agent if patient is on home gabapentinoid
Antidepressant (SNRI, TCA)	Continue
Opioid	Generally continue[b]

SNRI serotonin norepinephrine reuptake inhibitor, *TCA* tricyclic antidepressant

[a]Do not discontinue aspirin without discussion with prescribing provider

[b] Read separate discussion for fentanyl patch and buprenorphine

forced air warming device, which leads to some providers removing it preoperatively [24]. If the fentanyl patch is removed preoperatively, the patient should be given their baseline opioid requirement through a different modality. Others advocate for continuation of fentanyl patch, in which case it should be kept away from any heat sources [25].

Multimodal analgesia can begin preoperatively. A dose of NSAIDs and/or acetaminophen is commonly given in the preoperative area, unless contraindicated. A clinical practice guideline on the management of postoperative pain by the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia recommends consideration of a single dose of celecoxib (a selective COX-2 inhibitor) preoperatively in patients undergoing major surgery, if there are no contraindications [2]. Common doses of celecoxib include 200 to 400 mg given 30 minutes to 1 hour preoperatively. NSAIDs administered in conjunction with acetaminophen may result in superior analgesia than either agent alone [2]. The guidelines also recommend consideration of gabapentin or pregabalin as part of multimodal analgesia in patients who undergo surgery, as they are associated with reduced opioid requirements after major or minor surgical procedures and sometimes lower pain scores [2]. A pre-

operative dose should be considered particularly in patients who undergo major surgery and surgery resulting in expected substantial pain or as part of multimodal analgesia for highly opioid-tolerant patients. Common preoperative dose of gabapentin was 600 or 1200 mg, and common preoperative dose of pregabalin was 150 or 300 mg, given 1–2 hours prior to surgery [2]. While the higher dose may be more effective, the risk of oversedation is also higher. The provider should be cautious of oversedation, especially in vulnerable populations, such as the elderly. Dose recommendations for gabapentin and pregabalin are lower for patients with renal dysfunction.

Methadone, Buprenorphine, and Naltrexone

Methadone and buprenorphine are unique opioid mediations that may be prescribed for chronic pain or for substance use disorder as part of MAT. The indication for the medication is important to elucidate. Patients on these medications are opioid tolerant and require special considerations in the perioperative period. Naltrexone is an opioid antagonist. The outpatient prescriber of these medications should be aware of surgery and may help formulate a perioperative analgesic plan.

Methadone is a mu opioid receptor agonist, NMDA antagonist, and also has serotonin and norepinephrine reuptake inhibitor properties [26]. The patient should be instructed to take their methadone dose as scheduled preoperatively. When used to treat addiction, patients often receive a single dose from a methadone clinic daily. When used to treat chronic pain, methadone is often dosed at 8 hour intervals. Methadone is a potent high-risk medication with a long plasma half-life [26]. Methadone obtained from a methadone clinic may not appear on prescription drug monitoring programs, and the patient's methadone dose should be verified with the methadone clinic preoperatively. It is important to note that many of these clinics are open for a short period of time in the morning only. If a patient reports a dose higher than prescribed, they are at risk for overdose. Conversely, if the patient recalls a dose lower than is prescribed, their pain may be difficult to control

postoperatively due to inadequate opioid dose. Methadone causes QT prolongation, so caution should be exercised with other QT-prolonging agents, such as numerous antiemetics used in the perioperative period [26]. Methadone conversion rates to morphine vary based on the dose. Dose adjustment or opioid rotation should only be performed by practitioners that are specifically trained to do so. Postoperatively, methadone is usually continued if enteral access is possible, and for procedures with anticipated moderate to severe pain, supplemental short-acting opioid may be necessary [26]. Multimodal analgesia and regional techniques should be considered. When used for substance use disorder, a DEA-X license is required for methadone prescription, for which follow-up with the outpatient provider is recommended.

Buprenorphine is a partial mu receptor agonist and kappa receptor antagonist [27]. Buprenorphine has a high affinity for the mu opioid receptor and binds tightly, displacing and preventing other opioids from binding [28]. It is often formulated with naloxone (brand name Suboxone or Zubsolv), although naloxone has poor absorption orally and is only active if injected as a deterrent for abuse [28]. Other common formulations include buccal film (brand name Belbuca), transdermal formulation (brand name Butrans), and sublingual formulation (brand name Subutex) [28]. The surgeon should discuss upcoming plans for surgery with the buprenorphine prescribing provider to formulate the optimal plan as early as possible once the procedure is scheduled [28]. Options for managing buprenorphine perioperatively include stopping the buprenorphine for a certain amount of time prior to surgery versus continuing buprenorphine throughout the perioperative period [28]. Because discontinuation of buprenorphine prescribed for substance use disorder may put the patient at risk for relapse in the preoperative period, some advocate for continuation of buprenorphine throughout the perioperative periods, and cases of successful analgesia have been reported with this strategy [29]. Discontinuation of buprenorphine prescribed for chronic pain may lead to patient discomfort in the time leading up to surgery. Discontinuation of buprenorphine should thus only be done in conjunction with the prescribing provider. Conversely, continuation of buprenorphine throughout the perioperative period may

make postoperative pain management challenging as the high binding affinity of buprenorphine makes other opioids less effective [28]. For procedures with anticipated little to no pain, buprenorphine may be continued, and pain can be controlled with non-opioid modalities including multimodal analgesia and regional anesthesia [30]. For example, this strategy can be employed for a colonoscopy. For surgeries with anticipated moderate to severe pain and a likely opioid requirement, discontinuation of buprenorphine may be considered. Some advocate for holding buprenorphine 72 hours prior to surgery, while others advocate a dose-based time approach for stopping buprenorphine (Table 5.6) [28, 30]. If buprenorphine has been stopped outside of the recommended time period for a surgery with anticipated moderate to severe pain, high-dose opioid requirement can be expected, possibly requiring intensive care unit monitoring [30]. As the buprenorphine dissociates from the mu receptor and allows other opioids to bind, the patient becomes at risk for respiratory depression. Buprenorphine transdermal patch results in lower plasma concentration than the sublingual formulation, and for this reason, discontinuation can be done 12 hours prior to surgery or not at all [30]. Whether buprenorphine is continued or stopped, multimodal analgesia and regional anesthesia techniques should be employed [28, 30]. If buprenorphine is discontinued perioperatively, the surgeon should coordinate a plan with prescribing provider to reinstitute this therapy. When used for substance use disorder, a DEA-X license is required for buprenorphine prescription, for which follow-up with the outpatient provider is recommended.

Table 5.6 Time-based discontinuation of sublingual buprenorphine

Total daily dose	Discontinuation time prior to surgery*
0–4 mg	24 hours
>4–8 mg	48 hours
>8–12 mg	72 hours

*There is no consensus on the best strategy for buprenorphine management perioperatively. Some advocate for continuation of buprenorphine throughout the perioperative period. Some advocate for cessation of all buprenorphine doses 72 hours prior to surgery

Naltrexone is a mu receptor opioid antagonist used to treat substance use disorder [26]. In preparation for elective surgery, oral naltrexone should be discontinued 2–3 days preoperatively [27]. Long-acting formulation of naltrexone (brand name Vivitrol) is available as an injection every 4 weeks. If opioid therapy is anticipated postoperatively, long-acting naltrexone injection should be stopped 30 days preoperatively in coordination with the prescribing provider, as discontinuation may put the patient at risk for relapse [27]. Patients may have high opioid requirements and must be monitored appropriately postoperatively. Lack of analgesia has been described within the first 2 weeks of treatment [27]. However, both increased and decreased sensitivity to opioids have been described, so patients must be monitored closely if receiving opioid therapy [27]. After naltrexone is discontinued, patients may have an increased sensitivity to opioids due to upregulation of central nervous system opioid receptors [26]. Restarting naltrexone should be done in conjunction with the prescribing provider, 7–10 days after the patients have been off opioids to avoid withdrawal [27].

For patients with a history of polysubstance abuse, the provider should consider a preoperative urine drug screen, complete blood count, liver function tests, renal function tests, and electrocardiogram [26].

Patient Education

Clear expectations and goals should be set regarding postoperative pain management. The patient should receive tailored education on the treatment options for pain control. This has been shown to reduce postoperative opioid consumption, less preoperative anxiety, and reduced length of stay postoperatively in complex patients [2]. Enhanced recovery after surgery protocols (ERAS) may help guide postoperative pain control. For the straightforward patient, the discussion may be a quick conversation between the surgeon and patient. Modalities other than in-person instruction include written materials, videos, and web-based materials. For the complex patient, a multidisciplinary

approach may be helpful, and the surgeon may consult the anesthesiologist, pain specialist, pain psychologist, or addiction specialist, depending on the situation. A multimodal analgesic approach is encouraged [2]. Children are a special population and should receive education and counseling on a developmentally appropriate level, in addition to the education provided to their parents.

Education regarding postoperative medication use is of growing importance with the increasing number of outpatient surgeries. Patients should be instructed on safe medication use and potential side effects. The patient should be counseled on the risk of accidental overdose and death if alcohol and illicit drugs are used in combination with sedating medications. Patients should be counseled on appropriate opioid tapering. Numerous studies have found that patients commonly have leftover opioid tablets postoperatively, so patients should be instructed on safe opioid disposal [31–33].

Special Considerations

Considerations for Regional Anesthesia

Numerous procedures are now performed under regional anesthesia, with or without general anesthesia or sedation. Peripheral nerve blocks, either single shot or with continuous infusion via catheter, as well as neuraxial anesthesia including spinal and epidural anesthesia can provide postoperative analgesia. The optimal anesthetic will be ultimately decided by the anesthesiologist; however, a discussion between the surgeon and anesthesiologist ensures concurrence. Table 5.7 details considerations for regional anesthesia. Patient refusal constitutes absolute contraindication for the procedure. Patient cooperation may also limit the anesthesiologist's ability to perform a regional technique. Coagulopathy, whether preexisting or if expected postoperatively, should be considered. American Society of Anesthesiology and Pain Medicine guidelines are commonly followed for regional anesthesia in a patient receiving anticoagulation [34]. If regional anesthesia is

Table 5.7 Considerations for regional anesthesia

Patient consent and cooperation
Coagulopathy
Anticipated postoperative coagulopathy
Perioperative anticoagulant use
Infection
Peripheral neuropathy
Central neuropathy
History of spine surgery
Requirement for neurologic examination intraoperatively
Requirement for neurologic examination postoperatively
Postoperative ambulation

planned, anticoagulation plan should be discussed with the prescribing provider. If clearance is obtained, anticoagulation can be held for an appropriate amount of time, if necessary. The surgeon should discuss plans for perioperative anticoagulation with the anesthesiologist. Infection at the skin entry site is an absolute contraindication, and any regional technique in a patient with systemic infection should involve a risk versus benefit analysis. Peripheral or central neuropathy may be a relative contraindication as it may predispose the patient to increased risk of nerve injury with regional technique [35]. History of spinal surgery may not preclude neuraxial anesthesia, but preexisting neurologic deficits should be considered [36]. As regional anesthesia commonly affects sensory and motor function, the need for postoperative neurologic examination may be a contraindication. In addition, any effect on postoperative ambulation should be considered, although many regional techniques may safely be employed while preserving ambulation. For example, thoracic epidural analgesia can be employed, and improved pain scores with walking activity have been noted [37].

Implanted Devices

Commonly used implanted devices for chronic pain include intrathecal pumps, spinal cord stimulators, and peripheral nerve stimulators. The provider should contact the outpatient managing

provider; it is important to ascertain the type and location of the specific device. There are multiple components to these devices, which may include leads, catheters, pumps, reservoirs, and/or internal pulse generators at different locations, so the entire course of the device should be known to avoid surgical or regional anesthetic trauma [25]. The anesthesiologist should be aware of any implanted devices as this can affect the decision to perform neuraxial or other regional anesthesia. If magnetic resonance imaging (MRI) is anticipated, the provider should note manufacturer recommendations regarding compatibility, as they differ for each device.

Intrathecal pumps commonly deliver opioids, local anesthetics, ziconotide, baclofen, or other medications into the intrathecal space. In general, the intrathecal infusion should be continued in the perioperative period if possible [25]. The provider should be aware when the pump was last interrogated and when the next refill of the pump reservoir is due to ensure that the medication does not run out and refill is not delayed by surgery [25, 38]. Baclofen withdrawal is life-threatening and must be avoided. Baclofen may produce a synergistic effect with opioids, resulting in a greater than expected effect [38]. Opioid withdrawal can occur with discontinuation of intrathecal opioid. The pump should be interrogated pre- and postoperatively to ensure it is functioning appropriately [25]. Supplemental intravenous or oral opioid may be necessary for analgesia. If supplemental opioids are indicated, continuous pulse oximetry may be reasonable due to possibility of respiratory depression. Electrocautery and computerized tomography may be used [38].

A spinal cord stimulator should be reprogrammed to the lowest possible amplitude and turned off prior to the induction of anesthesia [39]. Manufacturers recommend avoidance of monopolar electrocautery, although it is noted by Harned et al. that it is often used. If electrocautery is required, bipolar cautery is recommended. If monopolar cautery is unavoidable, the device should be interrogated preoperatively to ensure the insulating sheath of the device is functional [39]. Monopolar cautery should then be used on the lowest effective setting. The grounding pad should be placed on the side contralateral to the internal pulse generator and

as far away from the spinal cord stimulator as possible. Spinal cord stimulators can interfere with cardiovascular implanted electronic devices, such as pacemakers and defibrillators. Devices differ on MRI compatibility. Computerized tomography (CT) is generally the preferred imaging modality, and while there have been reports of patients reporting shocking sensations, the risk is considered to be extremely low. However, it is recommended that the spinal cord stimulator is turned off for the scan and that the lowest dose necessary is used to obtain CT imaging [39]. The device should be interrogated postoperatively, although this does not need to happen in the immediate postoperative period.

Conclusion

Formulating a plan for postoperative analgesia should begin early in the preoperative period. This should begin with a focused pain history to screen for patients who require more complex planning. The provider should be aware of history of chronic pain, chronic opioid use, substance use disorder, and conditions that will make the patient more susceptible to postoperative respiratory depression. The outpatient pain provider should be aware of upcoming surgery and may help formulate the optimal analgesic plan. For the complex patient, consultation with pain management, pain psychology, and/or addiction specialists may be helpful. Multimodal analgesia, including regional anesthesia when possible, should be employed.

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6 Non-opioid Adjuncts and Alternatives

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Introduction

Managing pain appropriately is an imperative aspect of perioperative surgical planning. The US healthcare system focuses on saving costs related to pain control practices utilized in the approximately 70 million surgical procedures performed each year [1]. Improving pain control saves costs by shortening hospital stays post surgery, reducing complications, and accelerating recovery time [1] and is a required element by health-system accrediting bodies [2]. Reliance on opioid analgesics for pain management, however, is associated with increased morbidity and

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mortality [2]. Moreover, pressure exists for healthcare providers to reduce opioid prescribing in order to combat the ongoing opioid crisis. Recommended for its ability to improve patient outcomes, multimodal analgesia (MMA) represents an alternative to perioperative unimodal systemic opioid use [1].

Multimodal Analgesia

The idea of targeting multiple receptors of the pain pathway by utilizing more than one pharmacological class of analgesic medication first appeared in the literature more than two decades ago [3]. Balanced analgesia, or what is today known as MMA, allows for individualized pain management and a reduced reliance on opioid-based agents [4]. The goal of MMA is to improve pain relief while minimizing the side effects of individual agents [3]. MMA is recommended in many clinical scenarios for postoperative pain management, and a joint clinical practice guideline was created in support of MMA by the American Pain Society, the American Society of Anesthesiologists, and the American Society of Regional Anesthesia and Pain Medicine [5]. Preoperative evaluation is strongly recommended to guide perioperative pain management [5]. The aforementioned guidelines state the exact components of an MMA regimen will vary based on patient factors, care setting, and type of surgical procedure [5].

Multiple pain subtypes exist perioperatively depending on the surgical procedure, including nociceptive, neuropathic, psychogenic, idiopathic, and mixed pain [6]. Individualized MMA regimens target multiple pain subtypes by combining various drug mechanisms that work in concert to deliver broad analgesia. Choice of analgesic agents for MMA regimens is dictated by patient factors such as age, medical comorbidities, allergies, concomitant medications, history of chronic pain, substance abuse potential, and previous postoperative treatment regimens [5]. This chapter will discuss the use of systemic non-opioid adjunct and alternative analgesic drug classes for the management of perioperative pain.

Systemic Analgesics

Building a successful perioperative MMA regimen should begin with non-opioid analgesics (Table 6.1). Many systemic agents are proven to reduce postoperative pain significantly and aid recovery by improving patient mobilization and attainment of healing milestones. A variety of drug forms allow for MMA therapy choices to be individualized by administration route and perioperative phase. Common dosing regimens can be found in Table 6.2.

Acetaminophen

With decades of safety and efficacy data, acetaminophen is one of the hallmark MMA agents included in many clinical pain management protocols [7–9]. High-quality evidence sparked a strong recommendation by consensus guidelines for acetaminophen's inclusion in postoperative MMA regimens, although it is often used across perioperative phases [5]. While there are concerns for liver injury associated with its use, appropriate doses of acetaminophen exhibit cost-effective, opioid-sparing effects. The maximum recommended dose for a patient without hepatic disease is commonly reported as 4 grams per day, although there are reports of hepatotoxicity at this dose, so some experts recommend a maximum of 3 grams per day [10]. For patients with stable liver disease, a maximum of 2 grams per day is recommended. The prescribing provider should take care to counsel the patient on the potential for livery injury and reconcile current medications to account for all sources of acetaminophen, as it is a common component of prescription and over-the-counter medications. Although acetaminophen alone is sufficient in treating postoperative pain after some procedures [11], it can be used as an adjunct perioperatively to reduce overall opioid consumption or combined with other non-opioid agents in an opioid-free MMA regimen. Several meta-analyses describe positive opioid-sparing effects of acetaminophen used adjunctively with an opioid analgesic but fail to identify a

Table 6.1 Non-opioid adjunct and alternative drug agents

Therapy class and example agents	Common administration route(s)	Perioperative phase(s) of use	Adverse considerations
Acetaminophen	PO, IV, PR	Preoperative, intraoperative, postoperative	Liver toxicity, cost (IV)
Nonsteroidal anti-inflammatory drugs Ibuprofen Ketorolac Celecoxib	PO, IV, PR	Preoperative, intraoperative, postoperative	Renal toxicity, cardiovascular thrombotic events, stroke risk, gastrointestinal bleeding/ulceration, platelet dysfunction Elderly may be at increased risk for adverse effects; lower dose may be necessary
Gabapentinoids Gabapentin Pregabalin	PO	Preoperative, postoperative	Sedation, dizziness, respiratory depression, suicidal ideation, peripheral edema
N-Methyl-D-aspartate antagonists Ketamine	PO, IV	Intraoperative, postoperative	Hallucinations, dissociative mental state, sialagogue, cardiac effects (sympathomimetic but may cause myocardial suppression)
Alpha-2 adrenergic agonists Clonidine Dexmedetomidine	PO, IV, TD	Preoperative, intraoperative, postoperative	Bradycardia, hypotension, CNS depression

PO oral; *IV* intravenous; *IM* intramuscular; *PR* per rectum; *TD* transdermal; *CNS* central nervous system

Table 6.2 Commonly used doses of perioperative systemic non-opioid agents by perioperative phase in adults

Class	Analgesic	Preoperative or postoperative phase	Example regimen
Analgesic	Acetaminophen	Pre	325–1000 mg PO or IV
		Post	1000 mg PO or IV every 8 hours scheduled[a]
NSAIDs	Celecoxib	Pre	200–400 mg 30 minutes to 1 hour preoperatively
		Post	200 mg every 12 hours
	Ibuprofen	Pre	600–800 mg PO or IV
		Post	600 mg PO or IV every 6 hours
	Ketorolac	Post	30 mg every 6 hours for a maximum of 5 days If age 65 or older, reduce dose to 15 mg every 6 hours for a maximum of 5 days

(continued)

Table 6.2 (continued)

Class	Analgesic	Preoperative or postoperative phase	Example regimen
Gabapentinoids	Gabapentin[b]	Pre	300–1200 mg 1–2 hours preoperatively
		Post	Common starting doses for inpatients range from 100 mg daily or every 8 hours (elderly, frail) to 300 mg every 8 hours (young, alert) May uptitrate every several days as tolerated
	Pregabalin[b]	Pre	75–300 mg 1–2 hours preoperatively
		Post	Common starting doses for inpatients range from 25 mg daily or every 12 hours (elderly, frail) to 50 mg every 12 hours (young, alert) May uptitrate every several days as tolerated

(continued)

Table 6.2 (continued)

Class	Analgesic	Preoperative or postoperative phase	Example regimen
Topical anesthetic	Lidocaine cream (4%, 5%)[c]	Post	Apply to affected area three times daily; use on intact skin only
	Lidocaine patch (4%, 5%)[c]	Post	Apply up to three patches to painful area; use on intact skin only. Use 12 hours on and 12 hours off in 24 hour period

PO oral, *IV* intravenous, *NSAIDs* nonsteroidal anti-inflammatory drug, *Pre* preoperative, *Post* postoperative

[a]For patients with normal liver function. Do not exceed acetaminophen 4000 mg over 24 hours from all sources

[b]Dose adjustment necessary in renal dysfunction

[c]Insurance often does not cover the 5% prescription formulation; the 4% over-the-counter formulation may be used as alternative

reduction of opioid side effects [2, 8, 12, 13]. Intravenous administration of acetaminophen is not superior to oral administration, but is appropriate in specific instances such as patients unable to take medications orally or rectally or during long surgical procedures [14–16]. Usual adult doses are 650 mg IV every 4 hours or 1000 mg IV every 6–8 hours, not to exceed 4000 mg over 24 hours from all sources. Intravenous acetaminophen was shown to reduce opioid consumption postoperatively in colorectal surgery when utilized as part of an enhanced recovery after surgery (ERAS) protocol [17]. Additionally, postoperative pain management that includes intravenous acetaminophen was shown to reduce length of stay and lower hospitalization costs after hysterectomy [18].

Nonsteroidal Anti-Inflammatory Drugs

Another class of analgesic agents that are highly effective in managing perioperative pain is the nonsteroidal anti-inflammatory drugs (NSAIDs). These agents inhibit cyclooxygenase (COX) enzymes, which results in decreased synthesis of prostaglandin precursors. Treatment with NSAIDs may be associated with increased risk of postoperative bleeding and renal toxicity, and black box warnings exist for cardiovascular thrombotic events and gastrointestinal events [7]. A meta-analysis by Gobble et al. concluded that ketorolac does not increase the risk of perioperative bleeding [19] for certain surgical procedures. The authors note that care should be taken when data is interpreted from other surgical specialties, and the risk of bleeding and consequences of bleeding should be considered. Although the sample size was 2314 patients, the study may have been insufficiently powered to detect a difference in bleeding with ketorolac. NSAIDs that are selective COX-2 inhibitors (e.g. celecoxib) are safer than nonselective NSAIDs for patients particularly at risk of developing gastrointestinal ulcers [19–21]. Recent studies have suggested that celecoxib has a similar, if not more desirable, cardiovascular risk profile than nonselective NSAIDs [22, 23]. It is a common misconception that COX-2-selective inhibitors increase cardiovascular risk more than nonselective NSAIDs, most likely due to the significantly increased risk of myocardial ischemia and stroke associated with rofecoxib, an agent taken off the market in 2004.

Consensus guidelines strongly recommend utilizing NSAIDs, with or without acetaminophen, in all postoperative MMA regimens, if not contraindicated [5]. Results of one study indicated a single-dose combination of ibuprofen and acetaminophen improved postoperative pain relief in 50% of patients with a number needed to treat of only 1.5 [24]. NSAIDs, including selective COX-2 inhibitors, provide enhanced analgesia when combined with opioid-based MMA regimens and result in opioid dose sparing and reduction of opioid side effects [8, 25, 26]. NSAIDs may also serve as the backbone component of non-opioid MMA regimens. Data suggests the combination of NSAID plus acetaminophen provides an analgesic benefit in non-opioid MMA regimens [27–30]. Adding a local anesthetic component to NSAID-based

MMA regimens can result in avoidance or sparing of opioids for procedures that normally require opioid therapy, and substantial data exists indicating a positive analgesic benefit [31–33]. For example, the following regimen has been suggested by plastic and reconstructive surgeons: preoperative celecoxib 400 mg and acetaminophen 1000 mg orally, with or without pregabalin 150 mg orally for increased analgesia requirements or major surgery; intraoperative localized anesthesia at the surgical site with the choice of agent dependent on the duration of anesthesia required; and postoperative celecoxib 200 mg every 12 hours orally and acetaminophen 1000 mg every 6 hours orally, both for 48–72 hours as needed, with the addition of a gabapentinoid for 2–5 days or short-acting opioid given only as needed [34].

Gabapentinoids

MMA regimens often include drugs of the gabapentinoid class, such as gabapentin and pregabalin, to prevent and treat perioperative neuropathic pain, as well as off label to decrease opioid requirements. These agents bind receptors on voltage-gated calcium ion channels in the central nervous system to inhibit the release of neurotransmitters that participate in epileptogenesis and nociception [35]. Two meta-analyses demonstrated improvement in postoperative pain when gabapentin [36] or pregabalin [37] was included as part of an MMA regimen. The literature has mixed results regarding the superiority of one gabapentinoid over the other, although some studies report better pain control and less postoperative opioid use with pregabalin [38, 39]. Gabapentin is commonly dosed orally 1–2 hours prior to surgery at 300–1200 mg and may be continued in the postoperative period [36]. Similarly, pregabalin is also administered 1–2 hours preoperatively but at doses of 75–300 mg orally [37]. Dirks et al. suggested that premedication with gabapentin significantly reduces analgesic requirements postoperatively without increasing the incidence of side effects, but perioperative administration was not shown to reduce overall incidence of chronic pain after radical mastectomy [40]. In general, gabapentinoids are medications that are initiated at a low dose to avoid side effects and are gradually uptitrated to

a target range as tolerated. One risk associated with the use of gabapentinoids is sedation, particularly in populations that are already at risk of experiencing this side effect, such as the elderly. Of note, the Food and Drug Administration (FDA) issued a warning that gabapentinoids may cause significant respiratory depression in patients with coexisting respiratory illness (e.g. chronic obstructive pulmonary disease), patients on concomitant opioid therapy (chronically or intraoperatively), and elderly patients [41]. Therefore, the prescriber should use caution and initiate therapy at a lower dose, such as gabapentin 100 mg or pregabalin 25–50 mg titrating based on tolerability, or consider avoiding agents in this class altogether in the aforementioned vulnerable patient populations. The risks of gabapentinoids should be weighed against the risks of opioids, which are also known to cause sedation and respiratory depression. Gabapentinoids at doses higher than the initiating dose should be weaned off and not discontinued abruptly. Gabapentinoids are renally cleared, so dosing must be adjusted for patients with renal insufficiency or those on dialysis. A rare adverse effect includes suicidal ideation [42]. Pregabalin is a controlled substance, and gabapentin has been reclassified as a controlled substance in some states. As with all sedating medications, patients should be instructed not to drive until they know how the medication affects them. Evidence is favorable for gabapentinoid use in MMA regimens but is insufficient to warrant recommendation for all patients.

N-Methyl-D-Aspartate Antagonists

Additional agents that may be considered in MMA protocols include the N-methyl-D-aspartate (NMDA) antagonists, which block the binding of glutamate to NMDA receptors and prevent the transmission of pain signals between neurons in the central nervous system. Small doses of adjuvant intravenous ketamine appear to provide opioid-sparing effects and reduce the frequency of opioid adverse events, and a recent systematic review found that perioperative administration of ketamine reduces postoperative pain and opioid consumption [43, 44]. However, a significant side effect profile prompts caution for use in MMA regimens [45].

Despite confirmed postoperative pain reduction, evidence of increased side effects (e.g., vivid dreaming) during ketamine- and morphine-containing MMA regimens warrants additional monitoring with use [46]. For these reasons, ketamine is often reserved for surgeries that result in significant postoperative pain or for opioid-tolerant patients. Ketamine may be administered intravenously intraoperatively by the anesthesiologist. For example, intraoperative ketamine infusion during spinal fusion surgery in patients with opioid dependency was associated with significant reductions in opioid consumption within the first 24 hours post surgery [47]. Low-dose ketamine infusion can also be used postoperatively to improve analgesia or reduce opioid requirements. Special monitoring, staff training, and expert consultation (e.g. pain service) may be necessary for postoperative ketamine infusion; institutional guidelines should be followed.

Alpha-2 Adrenergic Agonists

Use of opioids in perioperative pain management may also be reduced by incorporating an alpha-2 adrenergic agonist (e.g. clonidine, dexmedetomidine). This drug class prevents pain signal transmission by stimulating alpha-2 adrenoceptors that activate inhibitory pathways. One study found that the inclusion of oral and transdermal clonidine premedication in an MMA regimen decreased opioid patient-controlled analgesia requirements by 50% postoperatively [48]. Dexmedetomidine is an intravenous medication that can be administered perioperatively by the anesthesiologist to improve analgesia and reduce opioid use postoperatively [49–51] and also exhibits intraoperative opioid-sparing requirements with premedication [52]. An additional benefit of dexmedetomidine is that it can prevent postoperative delirium in children [53] and adults [54].

Side effects from agents in this class can be limiting. Adverse effects include sedation, bradycardia, hypotension, and dry mouth [50]. Patients on dexmedetomidine infusion are monitored in a high-level care setting, such as the postanesthesia recovery unit, the intensive care unit, or in the operating room under the care of an anesthesiologist. There are also several positive effects beyond reduced postoperative pain and opioid sparing seen with these

agents. Reduced postoperative nausea and vomiting [48, 55], decreased intraoperative blood loss [51], enhanced glycemic control [56], and reduced myocardial ischemia after surgery [57] represent benefits of alpha-2 adrenergic agonist use.

Antidepressants

Antidepressants are commonly used in the chronic pain setting for treatment of neuropathic pain [58, 59]. Common classes of antidepressants with an analgesic effect include serotonin-norepinephrine reuptake inhibitors (SNRI) and tricyclic antidepressants (TCA). There is mixed data on the effects of the SNRI duloxetine on postoperative pain [58, 59]. A meta-analysis by Zorrilla-Vaca et al. found that duloxetine was associated with reduced postoperative pain scores, decreases in postoperative opioid use, and reduction in postoperative nausea and vomiting, although the authors noted that the reduction in opioid use was more statistically significant than clinically significant [59]. The provider should be aware of drug-drug interactions, including other serotonergic medications the patient is taking, such as selective serotonin reuptake inhibitors or other antidepressants. The data is mixed regarding the perioperative analgesic effects of TCAs [58, 60]. Drug-drug interactions and adverse effects, such as sedation, orthostatic hypotension, dry mouth, and QT prolongation, make the TCA class of medications more cumbersome to use.

Miscellaneous Non-opioid Agents

Other unique non-opioid agents (e.g. magnesium, neostigmine, adenosine) may be utilized perioperatively as adjuncts to traditional opioid-based pain management protocols. The analgesic-sparing effects of these agents have not been extensively studied, but preliminary findings offer some insight into their use in practice. The divalent cation magnesium has shown opioid-sparing properties with continuous infusion and bolus dosing [61, 62]. A non-opioid MMA regimen containing magnesium was shown to produce comparable postoperative pain management and fewer

side effects than an opioid-based MMA regimen [63]. Neostigmine, a cholinesterase inhibitor, has been reported to enhance opioid and non-opioid analgesia via intrathecal administration, although it is not FDA approved for this use [64–66]. Infused adenosine, an antiarrhythmic agent, produced a significant opioid-sparing effect and improved postoperative pain scores compared to an infused opioid alternative [67]. Several other drug classes have limited data supporting their use as adjunctive analgesic agents in MMA regimens, including but not limited to glucocorticoids, antipsychotics, and beta-blockers [45].

Conclusion

There are many agents available for perioperative use adjunctively or as alternatives to opioid analgesia. Extended surgical procedures are being increasingly performed in the outpatient setting, and management of perioperative pain for these patients is paramount [45]. Use of non-opioid adjunct and alternative analgesic therapies as part of MMA regimens will likely continue to increase due to their ability to facilitate improved recovery time, reduce reliance on opioids, and minimize costs. Optimization of MMA regimens should be based on individual patient factors, and choice of agents will vary for different procedures. A discussion of additional therapies for use in MMA regimens, such as local and regional anesthetics, is included in subsequent chapters of this text.

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7 Postoperative Analgesia for the Chronic Pain Patient

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Introduction

Postoperative pain in patient on chronic opioids may be challenging to manage. To adequately manage pain in this patient population, anesthesiologists, surgeons, and other professionals involved in the care of this patient population must be aware of physiological changes that occur that increase analgesic requirements. This population has altered perception of pain and reports higher pain scores in the postoperative setting than patients without chronic pain [13]. Preoperative analgesic use and preexisting preoperative pain are both well-established risk factors for poor postoperative pain control [1]. This chapter will provide insight into the obstacles faced by

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providers when managing pain in chronic opioid users and will offer tools to help healthcare professionals optimize their care.

Physiology of Chronic Opioid Use

The physiological and pharmacological effects of prolonged opioid use contribute to the difficulty of adequately treating postoperative pain in the chronic opioid patient. Tolerance and dependence are widely studied pharmacologic phenomena associated with long-term usage or exposure to a substance. Tolerance, in short, is the reduced response to a drug following previous administration of the drug. In the case of opioids, it is a physiological response that may involve receptor desensitization, receptor downregulation, and increased metabolic activity [3]. This ultimately lowers the efficacy of the opioid, requiring a higher dosage to achieve the same therapeutic effect. Physical dependence occurs when the body adapts to the presence of drug as the normal baseline, upon which removal of the drug precipitates withdrawal symptoms. A unique opioid-centric phenomenon, opioid-induced hyperalgesia (OIH), is the paradoxical sensitization to acute pain occurring after opioid exposure [4]. For example, higher doses of intraoperative remifentanil were found to be associated with increased acute postoperative pain and morphine consumption as compared with lower doses [5]. While an abundance of studies have characterized OIH in both humans and animals, there is insufficient data to predict it with absolute certainty, so the best approach remains prevention [6]. Physical dependence and tolerance should be distinguished from addiction, which is described as "substance use disorder" in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders V* [7]. It is important to be aware of the difference between opioid use for chronic pain and opioid use due to substance use disorder and avoid bias.

Managing Bias During Treatment

Patients on chronic opioids may encounter prejudice and marginalization from healthcare professionals and are consequently at risk of receiving inadequate pain control [8, 9]. During the

Table 7.1 Differences between chronic pain patients and opioid abusers

Evaluation criterion	Chronic pain patient	Opioid abuser
General usage	Appropriate, as prescribed	Inappropriate, not controlled
Treatment plan and/or contract	Present	Unavailable
Shares opioid history	Fully declares	May try to hide
Insight into negative effects	Aware	Not concerned
Effect on quality of life	Improved	Impaired

preoperative evaluation, it should be determined whether a patient's opioid usage is due to chronic pain or illicit abuse. A list of differences between the two groups are shown in Table 7.1 [10, 11].

Chronic pain patients generally have documented opioid usage in their medical chart and are willing to fully discuss their opioid history during the consultation. In contrast, opioid abusers may provide an incomplete or false history due to fear of bias and stigmatization. A common misconception among providers is that patients who report pain may be drug seekers [9]. If there is mistrust between the patient and provider, the patient's legitimate questions and concerns may be perceived as demanding or manipulative [12]. It is vital to establish rapport with the patient, reassuring them that their history will be used to formulate the best treatment plan. Achieving adequate analgesia while minimizing risks is the goal.

General Recommendations for Treating Postoperative Pain

Chronic opioid users may require higher opioid doses, up to a fourfold increase [11], postoperatively to manage their pain compared to patients who are opioid-naïve. These patients have been shown to report higher pain ratings immediately after surgery and also experience a significantly slower decline of their daily pain rating over time [13]. The combination of increased initial pain, duration of pain, and opioid requirements creates difficult pain management scenarios. Multimodal analgesia (MMA) is therapy targeted at multiple pain pathway sites to meet postoperative

analgesic requirements. However, significantly reducing or eliminating opioids in an MMA regimen can be deleterious for chronic opioid users. Daily opioid consumption and baseline requirements should be calculated and incorporated into MMA regimens in order to prevent opioid withdrawal.

The guidelines on the management of postoperative pain set forth by the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia acknowledge the challenges of treating patients with a history of chronic opioid use [2]. When standard pharmacological regimens are inadequate or when treating patients at high risk of experiencing uncontrolled postoperative pain, it is recommended to consult a pain management specialist to assist in perioperative pain management [2]. The guidelines include numerous recommendations, and those based off of high-quality evidence will be highlighted here. First, they recommend multimodal analgesia (MMA) or a variety of analgesic medications and techniques combined to target different mechanisms of action of pain receptors in the peripheral and central nervous systems. In this MMA regimen, acetaminophen and/or nonsteroidal anti-inflammatory drugs (NSAIDs), in addition to opioids, is associated with less postoperative pain and opioid consumption versus opioids alone. They also recommend peripheral regional anesthetic techniques as part of the MMA regimen in addition to neuraxial analgesia for major thoracic and abdominal procedures especially for those with increased risk for cardiac and pulmonary comorbidities or prolonged ileus. Both are associated with decreased use of opioids and lower postoperative pain scores. The reader is referred to Chap. 6 (Non-Opioid Adjunct and Alternatives) for in-depth discussion on MMA. A framework incorporating the recommendations from the guidelines into the management of postoperative pain in chronic opioid users is outlined in Table 7.2 [2].

Patients should be instructed to take any scheduled doses of oral opioids the morning of surgery, and any additional scheduled doses later in the day should be administered prior to induction of anesthesia [11]. The surgeon should be aware of the patient's home opioid use to ensure that the patient's postoperative opioid

Table 7.2 Framework for the management of postoperative pain in chronic opioid users [2]

1) Preoperative evaluation (a) Determine if chronic pain patient or opioid abuser (b) Obtain opioid name, route of administration, dosage, and length of use (c) Establish trust and avoid bias and passing judgment
2) Educate patient and acknowledge concerns (a) Implications of chronic opioid use on postoperative pain (b) Patient's previous experiences with postoperative pain (c) Discuss pain control management goals and set realistic expectations
3) Consider specialist consultation (pain medicine, behavioral, and/or addiction)
4) Consider additional modalities: (a) Systemic non-opioids 1. Acetaminophen, NSAIDs, gabapentinoids, etc. (b) Local or regional anesthesia techniques (c) PCA with monitoring (d) Ketamine (e) Nonpharmacologic 1. Transcutaneous electrical nerve stimulation 2. Cognitive behavioral therapy
5) Educate patient and caregivers on proper tapering of opioids and potential side effects post-discharge, and arrange for appropriate follow-up

regimen appropriately covers baseline opioid requirement. Table 7.3 details equianalgesic doses of common opioid medications and administration routes. Morphine is the recommended reference opioid for ease of use and standardization purposes. The patient's daily opioid requirement is thought of in terms of oral morphine milligram equivalents over 24 hours. Conversion steps, doses, and ratios differ from institution to institution and even from provider to provider, so it is recommended to use conversion tables as a general guide and further adjust based on clinical factors.

When converting to a different opioid (morphine to oxycodone), dose should be reduced by 25–50% due to *incomplete cross-tolerance* between different opioids [24]. For example, 30 mg of total oral morphine is equivalent to 20 mg oxycodone if a conversion is calculated. However, a patient chronically on

Table 7.3 Equianalgesic doses of oral and intravenous opioids

Opioid	Oral dose (mg)	Intravenous dose (mg)
Morphine	30	10
Hydromorphone	7.5	1.5
Hydrocodone	30	–
Oxycodone	20	–
Tramadol	300	–

When converting between different opioids in a tolerant patient, 25–50% dose reduction should occur to account for incomplete cross tolerance
Doses listed are for conversion purposes only and are not standard or suggested treatment doses

morphine is tolerant to opioids but less tolerant to other opioids (oxycodone) than morphine. This means that the patient should receive a lower dose of 10 mg–15 mg of oxycodone, which will lead to the same analgesic effect as the 30 mg of morphine. This is the basis of opioid rotation in chronic pain. After any conversion, patients must be frequently monitored to prevent undertreatment or overdose.

Patient-Controlled Analgesia

A common method to providing postoperative pain control is patient-controlled analgesia (PCA).While different routes of medication can be administered via PCAs (epidural, peripheral nerve catheter), this discussion will focus on intravenous opioid PCA. PCAs allow the patient to self-administer opioid therapy by pushing a button that causes medication to be released through a preprogrammed infusion pump. PCA use has been shown to provide improved pain control and increase patient satisfaction as the patient is able to self-administer a preset dose of opioid without waiting for a healthcare provider to administer therapy [20]. This allows the patient to control their pain without fear of judgment and to have a sense of control [20]. Moreover, the PCA pump records the amount of opioid the patient received over a time period and the number of attempts to self-administer treatment. This information allows the healthcare provider to establish the

patient's opioid requirements for pain control and track the effects of MMA adjustment. As the patient's postoperative pain resolves over time, it is expected that their daily opioid use decreases. Conversely, opioid use decrease may reflect improving pain.

Through small, frequent doses, the PCA allows the patient to remain in the effective analgesia zone. Outside of the effective analgesia zone lies inadequate analgesia (too little opioid) and oversedation (risking respiratory depression and death). The settings on a PCA include the initial loading dose, demand dose, lockout time interval, background infusion, and 1- or 4-hour limits. The initial loading dose is a one-time dose administered by the provider (not the patient), commonly the postanesthesia care unit (PACU) nurse or postsurgical nurse, when the PCA is being initiated. The demand dose is the dose delivered to the patient via pump when the patient presses the demand button. For the PCA to be effective, the demand dose should provide a level of analgesia that is evident to the patient. If the dose is too high, the patient may be oversedated. The lockout time interval is the minimum time period that must pass before the PCA pump can administer another patient bolus if the demand button is pushed. For example, if the lockout time interval is 8 minutes and the patient pushes the button at 12:00 PM, they will receive a dose. If the patient again pushes the button at 12:04 PM, they will not receive a dose because only 4 minutes has passed. The lockout time interval is a safety feature that prevents the patient from administering too much medication within a short amount of time. The PCA also has limits to the amount of opioid administered per 1 hour or 4 hours. Some PCAs have a clinician bolus that the nurse may activate at certain time intervals for breakthrough pain.

Continuous basal rate is a continuous opioid infusion at a constant rate that the patient receives regardless of their activation of the demand dose. Continuous basal rates in opioid-naïve patients are frequently associated with respiratory depression [20]. They are not recommended as the initial setting and should only to be used after repeated complaints of inadequate pain relief despite attempts of increasing demand doses, adding non-opioid adjuvants, and reeducating the patient to push the button before the pain becomes severe [19]. Without a basal rate, the patient needs

to be awake enough to push the PCA button in order to receive medication. Therefore, no additional doses will be given if the patient is asleep or oversedated, allowing the patient to become more alert. With the use of basal continuous rate, this safety mechanism is eliminated because the sedated patient continues to receive opioid without activating the demand dose, putting the patient at risk for overdose. Because of the high risk of respiratory depression with continuous basal rates, the provider must have extensive training in safe opioid practices, and the authors recommend expert consultation if basal rate is believed to be necessary.

Morphine is commonly considered the first choice for IV-PCA; hydromorphone is commonly used; and other opioids, such as fentanyl, can be employed [21]. The patient will require a loading dose at the initiation of PCA, commonly 2–4 mg or morphine or equianalgesic equivalent if another opioid is used. If PCA is started in the postanesthesia care unit (PACU), the postoperative nurse can appropriately administer the loading dose while the patient is under close monitoring. For the opioid-naïve individual, common initial settings include morphine 1 mg every 6–8 minutes or hydromorphone 0.2 mg every 6–8 minutes. Morphine 1 mg/6 minutes would give the patient access to approximately 720 mg oral morphine equivalents over 24 hours, although it is unlikely the patient would press the button every 6 minutes as allowed. Hydromorphone 0.2 mg/6 minutes would give the patient access to approximately 960 mg oral morphine equivalents over 24 hours. Thus, in the chronic opioid patient, the PCA will generally cover both the patient's baseline opioid requirement plus supplemental opioid for postoperative analgesia. If the patient reports inadequate analgesia, the provider should ensure the patient is using the PCA appropriately and, if necessary, provide education to the patient, prior to increasing the demand dose. The opioid-tolerant individual may require higher demand dose, and common PCA settings are listed in Table 7.4 [20]. It is important to note that higher demand doses (morphine 1.5 mg or 2 mg) are more commonly associated with adverse respiratory events [20]. The demand dose can be reduced in opioid-naïve vulnerable patients, such as the elderly or frail patients, although a full dis-

Table 7.4 Common IV-PCA settings for postoperative pain

	Opioid-naïve patient initial demand dose	Common demand dose	Vulnerable patient decreased demand dose	Lockout interval
Morphine	1 mg	1–2 mg	0.5 mg	6–10 minutes
Hydromorphone	0.2 mg	0.2–0.4 mg	0.1 mg	6–10 minutes

cussion is outside the scope of this chapter. The authors suggest avoiding a basal opioid rate at PCA initiation, or, if it is believed to be necessary, seeking expert consultation.

The provider should be aware of potential adverse effects of the PCA. Side effects of the opioid include, but are not limited to, nausea, vomiting, pruritus, sedation, and confusion [20]. The patient may intentionally dose more frequently than necessary for pain control. PCAs are dangerous if anyone other than the patient pushes the button. The patient may also be at risk for respiratory depression if they receive opioids through another modality (i.e., oral) in addition to the PCA. Continuous basal rate increases risks of respiratory depression as described above.

Methadone and Buprenorphine

Methadone and buprenorphine are opioids that can be used to treat chronic pain or substance use disorder. The indication for the medication should be elucidated preoperatively. Prior to elective surgery, the surgeon should contact the prescribing provider to ensure that they are aware of upcoming surgery and to establish a plan for postoperative analgesia. These patient can be expected to be opioid tolerant [14].

The literature suggests that methadone should be taken orally the morning of surgery and throughout the entire perioperative period if oral intake is not restricted [11]. Methadone is metabo-

lized by the CYP450 family, which means not only does its metabolism exhibit interpersonal variation, but it is also affected by agents that induce or inhibit CYP3A4. Methadone for MAT is commonly dosed every 24 hours, while methadone for pain is more effective when dosed at shorter intervals, commonly every 8 hours [9]. For analgesic purposes, the patient's methadone dose can be divided into every 8 hour dosing postoperatively while the patient is inpatient. However, the total daily dose should not be changed. For example, a patient receiving 30 mg methadone daily may receive 10 mg every 8 hours instead, keeping the total daily dose at 30 mg. The conversion factor from methadone to morphine is dose-dependent, so if opioid conversion is required, expert consultation is suggested.

There is no clear consensus regarding the optimal perioperative management of patients being treated with buprenorphine. Buprenorphine binds tightly to the mu opioid receptor, such that other opioids are not able to bind. Some advocate that buprenorphine may be continued and that an additional short-acting opioid may be added and titrated for analgesic effect [11]. However, pain may be difficult to control. If only mild pain is expected, it is possible to treat with non-opioid adjuncts in addition to the baseline buprenorphine. An alternative is to stop the buprenorphine preoperatively. It is important to note that buprenorphine discontinuation prior to surgery may lead to relapse, so the risk versus benefit should be discussed with outpatient buprenorphine provider, and any discontinuation should only be done at the discretion of the outpatient provider. In situations where surgery is emergent and there is no time to properly wean off of buprenorphine, high doses of opioids will most likely be required [15]. Patients who have stopped buprenorphine (but not for long enough per the guidelines) and patients who have continued buprenorphine and are receiving high-dose opioids should be closely monitored for respiratory depression. Intensive care unit monitoring may be required. The reader is referred to Chap. 5 (Preoperative Optimization) for more in-depth discussion on buprenorphine.

Multimodal analgesia should be implemented, including the use of regional anesthesia, if possible. The surgeon should not provide an outpatient prescription for maintenance therapy using

methadone or buprenorphine, unless they have a DEA-X license. Instead, discharge and appropriate follow-up should be coordinated with the patient's methadone or buprenorphine provider.

Transdermal Patches

Transdermal opioids are an available treatment option for chronic pain, with the most commonly prescribed transdermal systems containing fentanyl or buprenorphine. If a patient is on a fentanyl patch preoperatively, it may be continued postoperatively. However, it is important to note that heat (such as from a forced air warming system) will increase the dose absorbed [16]. Therefore, external sources of heat should be kept away from the patch. If the fentanyl patch is removed, equivalent opioid should be provided to meet the patient's baseline analgesic requirement. Fentanyl patch is contraindicated for patients who are opioid-naïve, for use in mild, acute, postoperative, or intermittent pain. Evidence is mixed regarding buprenorphine patches. Buprenorphine administered transdermally generally results in plasma concentrations lower than sublingual buprenorphine. It may be removed 12 hours prior to surgery [22] or continued postoperatively [23].

Intrathecal Pumps

Intrathecal pumps are invasive devices used to deliver medication directly into the intrathecal space for the management of chronic pain. The provider who manages the pump should be made aware of any planned procedure, and the device should be thoroughly investigated to obtain the drug name, dosage, frequency, and last fill date [17]. Compatibility with magnetic resonance imaging (MRI) should be verified if diagnostic imaging is anticipated. The delivery of analgesic medications via pump should be maintained perioperatively when the pump does not physically interfere with the procedure. Conversion from intrathecal morphine dosing to oral dosing is impractical, so the administration of additional opi-

oids should be done slowly and carefully [18]. Pumps may contain baclofen, which has been reported to have a synergistic interaction with opioids, increasing their potency [17]. Baclofen withdrawal is life-threatening, so it is imperative that the pump is functional postoperatively. Interrogation of the pump ensures appropriate function.

Naloxone

Opioids are high-risk medications with potential to cause respiratory depression and overdose. Nonetheless, these medications are sometimes necessary to achieve adequate analgesia in the postoperative setting. Centers for Disease Control and Prevention guideline for prescribing opioids for chronic pain recommends risk mitigation with consideration of offering a prescription for naloxone [25]. Naloxone is an opioid antagonist that the patient and family can be taught to use in the outpatient setting in case of accidental opioid overdose. It is available in intravenous, intramuscular, subcutaneous, and intranasal formulations, with intranasal being an easy formulation to use for outpatient purposes. The chronic pain guidelines recommend consideration of naloxone when factors are present that increase risk for opioid overdose, including history of substance use disorder, higher opioid dosage (≥50 MME/day), or concurrent benzodiazepine use [25]. The postoperative setting is unique in that patients have acute on chronic pain, often requiring an increase from their baseline opioid dose. The surgeon should be aware of risk mitigation strategies, including prescription of naloxone upon discharge, for high-risk patients.

Conclusion

The perioperative management of chronic opioid users presents a unique challenge to providers. As opioid use continues to rise, there will be an increase in the number of these patients requiring acute postoperative analgesia. It is important to identify patients

with chronic opioid use early in the surgical planning stages, as these patients will have higher postoperative analgesic requirements, and a postoperative pain treatment plan should be formulated. A multidisciplinary pain management approach involving the primary team caring for the patient, in addition to the patient, should be utilized. In order to reduce opioid requirements while optimizing pain relief, multimodal analgesia and regional anesthesia should be employed when possible.

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8 Non-Enteral Pain Management

Erin Maggie Jones, Gregory L. Barinsky, and Andrew P. Johnson

Introduction

Perioperative pain management is complex and challenging, but providers have a professional and ethical responsibility to relieve pain for all persons. Procedure type, length of procedure, amount and type of pain, and specific patient factors should be accounted for in the creation of individualized perioperative pain management plans. Monotherapy analgesia may not provide satisfactory pain relief in all cases and is often associated with intolerable side effects. Therefore, combination analgesia that targets multiple pain mechanisms is now recommended in a clinical practice guideline jointly published by the American Pain Society, the American Society of Anesthesiologists, and the American Society of Regional Anesthesia and Pain Medicine [1]. This guideline provides 32 evidence-based recommendations for the manage-

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ment of postoperative pain, as informed by a systematic evidence-based review [1]. As one of only four recommendations backed by high-quality evidence, Recommendation 6 states that multimodal analgesia (MMA) should be offered for the treatment of postoperative pain in children and adults [1]. MMA, also known as balanced analgesia, offers a contemporary evidence-based alternative to unimodal perioperative pain control with opioids [2]. MMA regimens are highly valued by payers due to their ability to improve patient outcomes, increase the quality of healthcare services, and reduce procedure-related costs [2]. Moreover, the sparing of opioid analgesics has the potential to make a positive impact on the current opioid crisis. Any discussion of MMA with an emphasis on reducing or eliminating the use of opioids must include non-enteral pain management techniques. This chapter seeks to review evidence supporting the inclusion of non-enteral analgesia in perioperative MMA regimens.

Parenteral Analgesia

Non-enteral analgesia represents an important alternative to enteral analgesia and should be considered in patients who cannot receive oral intake, have contraindications to enteral analgesic agents, require an extended duration of analgesia, or require supplemental analgesia to manage their pain or when gastrointestinal absorption is limited or absent [3]. The term parenteral refers to any administration route that does not require absorption via the gastrointestinal tract. This includes the intravenous (IV), intramuscular (IM), rectal (PR), subcutaneous (SC), transdermal (TD), and transmucosal (TM) routes (Table 8.1). Choice of administration route is dependent on clinical factors, safety and efficacy, patient preference, drug pharmacokinetics, and pharmacoeconomics. For example, the majority of agents are formulated for IV injection, and this route provides the quickest onset of action and is easily titrated to effect. Safety and efficacy should be given primary consideration when choosing an administration route, with other factors as secondary considerations [4]. Patient preference should also be included in the choice of administration route to

Table 8.1 Pharmacokinetic properties and considerations of different routes of administration

Route of administration	Drug class	Example drugs	Onset of action	Duration of analgesia	Route benefits
Intravenous	Analgesic	Acetaminophen	5–10 minutes	4–6 hours	Standard access route Many classes of drugs available for intravenous administration Quick onset of analgesia Doses easily titrated to effect or to relieve side effects
	NSAID	Ketorolac	15–30 minutes	4–6 hours	
		Diclofenac	15 minutes	5 hours	
	Opioid	Morphine	5–10 minutes	3–5 hours	
		Fentanyl	Immediate	0.5–1 hour	
	A2 antagonist	Dexmedetomidine	10–30 minutes	1–2 hours	
	NMDA agonist	Ketamine	Immediate	5–10 minutes	
Intramuscular	NSAID	Ketorolac	30 minutes	4–6 hours	Alternate to IV in NPO patients
	NMDA agonist	Ketamine	3–4 minutes	15–30 minutes	
Rectal	Analgesic	Acetaminophen	1 hour	4–6 hours	Alternative route when NPO patient has no IV access Alternative route when patient is needle phobic
	NSAID	Indomethacin	30 minutes	4–6 hours	
	Opioid	Morphine	20–60 minutes	3–7 hours	
Subcutaneous/ infiltration	Local anesthetic	Lidocaine	45–90 seconds	10–20 minutes	Targets localized areas Minimal systemic effects when used correctly
		Bupivacaine	2–10 minutes	2–8 hours	
		Ropivacaine	3–15 minutes	3–15 hours	
Transdermal	Opioid	Fentanyl patch	6 hours	20–72 hours	Provides around-the-clock analgesia Alternative route when patient is needle phobic
	Local anesthetic	Lidocaine cream Lidocaine patch	3–5 minutes 4 hours	Varies	
Transmucosal	Opioid	Fentanyl lollipops	5–15 minutes	2–4 hours	Quicker onset of action than oral

NSAID nonsteroidal anti-inflammatory drug; *NMDA* N-methyl-D-aspartate; *IV* intravenous; *NPO* nothing by mouth

encourage treatment adherence, promote patient satisfaction, and motivate the patient to be involved with their care plan. Pharmacoeconomic considerations include a variety of factors, from drug acquisition costs to the nursing staff burden of drug administration.

One example highlighting how administration route decisions are impacted by the aforementioned factors is ketamine. A study of perioperative IV ketamine in appendectomies resulted in significantly lower postoperative pain scores compared to preincisional low-dose SC ketamine infiltration [5]. However, in peritoneal dialysis catheter placement, SC ketamine provided similar pain control but exhibited a superior side effect profile compared with IV ketamine [6]. The nature of the expected postprocedural pain and procedure-specific patient recovery factors play an important role in guiding analgesic drug administration decisions.

Total Intravenous Anesthesia

Parenteral agents can also be utilized for procedural anesthesia using a technique known as total intravenous anesthesia (TIVA). TIVA, as the name suggests, is the induction and maintenance of general anesthesia solely through the administration of IV agents, without the use of inhaled volatile anesthetics. Propofol, a positive modulator of the central nervous system inhibitory neurotransmitter GABA, is the cornerstone of TIVA, with short-acting opioids such as fentanyl or remifentanil commonly used in adjunct. TIVA can be used for most procedures but has particular value in certain surgeries (e.g. otolaryngologic or thoracic procedures where an endotracheal tube would obstruct the field) or in situations where volatile anesthetics may be contraindicated (e.g. long QT syndrome, risk of malignant hyperthermia, neurosurgery requiring low intracranial volume) [7]. A major benefit of TIVA that is well documented in the literature is the reduction of postoperative nausea and vomiting [8–10]. One systematic review found that TIVA with propofol was associated with lower pain scores after extubation and shorter stays in the postoperative anesthesia care unit compared to volatile agents [8]. Overall, there are no differences in hospital length of stay or incidence of

readmissions between TIVA and inhalational anesthesia [8–10], although propofol-based TIVA may incur slightly higher drug costs [10]. Propofol infusion syndrome is a life-threatening adverse event associated with larger doses and longer infusion times and can present as cardiovascular dysfunction, acute kidney injury, rhabdomyolysis, hyperkalemia, hepatic dysfunction, or anion gap metabolic acidosis [11].

Opioids

In light of the opioid epidemic and our greater understanding of opioid-related adverse events, recommendations for MMA regimens have shifted to encourage the use of non-opioid analgesia backbones. However, opioids remain an important and useful class of analgesic agents for perioperative use. Opioid-naive patients may not be able to tolerate oral opioids due to side effects, thus making them candidates for IV opioids as part of their MMA regimen [12]. A joint consensus statement by the American Society for Enhanced Recovery and Perioperative Quality Initiative recommends utilizing short-acting IV opioids for rescue analgesia in this patient population only after a comprehensive non-opioid MMA regimen that includes local anesthetic agents is in use [12]. Enhanced recovery pathways are sets of intraoperative protocols that may be utilized to reduce the surgical stress response, optimize physiological function, and facilitate patient recovery through a multidisciplinary approach [13]. Implementation of an enhanced recovery pathway reduced overall opioid use by approximately 80% in one study, lowering use of opioid-based patient-controlled analgesia (PCA) from 90% to less than 5% [12].

PCA is an established modality that consists of IV or epidural analgesics controlled by the patient as needed for postoperative pain. PCAs offer a convenient way for the patient to get adequate pain relief without involving nursing staff when a bolus dose is required. Although PCAs may be managed by pain or anesthesia services at many institutions, it is still vital for the surgeon to understand their role and how they function. Compared to a traditional opioid order, there are additional parameters that must be set when ordering a PCA. All of the components of a PCA order

Table 8.2 Patient-controlled analgesia parameters and examples

Parameter	Description	Example order[a]
Analgesic medication	Opioids: morphine, hydromorphone, fentanyl, meperidine Local anesthetics: bupivacaine, ropivacaine Other: clonidine, baclofen	Morphine sulfate
Concentration	The amount of drug per mL of solution	5 mg/ml
Total solution volume	The package size of the drug product	30 mL (150 mg in 30 mL)
Loading dose	Initial bolus dosing to achieve analgesia, generally given in PACU	2–4 mg every 5 minutes until pain ≤4/10, max 20 mg
Demand dose	The dose given when the PCA button is pressed	2 mg
Lockout interval	The minimum time interval between demand doses	10 minutes (i.e. a demand dose will not be delivered until 10 minutes have passed from the previous dose)
Basal rate[b]	A continuous infusion of analgesic per hour. Should not be initially used in naive patients. May be helpful in tolerant patients and for nighttime analgesia	2 mg/hour
1 or 4 hour limit[c]	A maximum limit for the total amount of drug that can be administered per 1 or 4 hour period, including both demand and basal doses	50 mg in 4 hours

PACU postanesthesia care unit; *PCA* patient-controlled analgesia
[a]Individual institutional guidelines and protocols should be consulted
[b]May be considered for opioid-tolerant patients or severe uncontrolled pain
[c]May not be appropriate for opioid-tolerant patients or severe uncontrolled pain

are displayed in Table 8.2 using morphine as an example, although most institutions will have protocols in place to facilitate order entry of preferred agents and doses. All patients for whom a PCA

is planned should be initially loaded with opioid via short interval bolus dosing to reach an effective plasma concentration while in the postanesthesia care unit. The demand dose is the dose delivered when the patient activates the device by pressing the button. The lockout period prevents the delivery of continuous demand doses by enforcing a minimum time between doses. The basal rate provides a continuous infusion of analgesic, independently of demand doses, and is useful in opioid-tolerant patients or those with higher opioid requirements. The final parameter is a limit placed on the total amount of drug that can be administered in a given time interval, usually 1 or 4 hours.

PCAs should always be tailored to the individual patient, taking into account factors such as patient age, comorbidities, opioid tolerance, history of chronic pain, and expected amount of pain from the procedure. It is important to note that if the demand dose is too low, patients may become frustrated with the PCA and cease pressing the button, further exacerbating inadequate pain control [14]. Furthermore, the purpose of a limit is to provide an additional layer of safety, though it may inadvertently prevent the delivery of enough drug to achieve pain control. Morphine is the most commonly used opioid, although other agents can be used, such as hydromorphone in opioid-tolerant patients so that the reservoir does not have to be changed frequently, or meperidine in patients allergic or intolerant to all other opioids [14].

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) decrease the body's inflammatory response to surgical trauma. Specifically, inhibition of the cyclooxygenase (COX) isozymes by NSAIDs results in the blockade of prostaglandin synthesis and subsequent reduction in the production of inflammatory mediators [15]. Reduction of nociception without opioid-like side effects has made agents in this class backbone components of MMA regimens [12]. Several NSAIDs, such as ketorolac and diclofenac, are available in IV formulations and widely utilized in the management of perioperative pain [3]. Evidence suggests that parenteral

ketorolac and diclofenac possess analgesic properties that are comparable to fentanyl [16–18] and superior to the partial opioid agonist tramadol [19].

Perioperative IV ketorolac has been highly studied and is associated with reduced postoperative pain, opioid consumption, and side effects (e.g. nausea/vomiting) [18, 20–27]. Ketorolac is dosed postoperatively at 10–30 mg IV every 6 hours, not to exceed 5 days of use. The usual dose of diclofenac is 37.5 mg IV every 6 hours for postoperative analgesia. One study comparing IV ketorolac with IV diclofenac as elements of perioperative MMA regimens in total hip and knee arthroplasty found no difference in postoperative pain intensity or length of stay, but patients who received IV diclofenac had lower opioid consumption and greater satisfaction postoperatively [28]. A systematic review reported a 9–66% reduction in opioid use with ketorolac as part of a MMA regimen and a 17–50% reduction with diclofenac [29]. Concerns exist regarding the potential for bleeding and gastric ulcers, the hallmark adverse events associated with NSAID use. However, a meta-analysis of 2314 patients across 27 randomized controlled studies found that there was no statistically significant difference in postoperative bleeding and other adverse events in patients receiving ketorolac compared with controls [30]. Additionally, doses of 30 mg or less of ketorolac were found to have a lower incidence of adverse events than doses greater than 30 mg [30]. Still, patients who are at high risk of developing gastric ulcers present a challenge in the perioperative setting due to a lack of available parenteral COX-2-selective NSAID preparations [31]. Therefore, alternative MMA regimen backbone agents should be explored in this patient population.

Acetaminophen

An alternative to NSAIDs in MMA regimens is the safe and cost-effective analgesic acetaminophen, also known as paracetamol. In two meta-analyses, preoperative single-dose IV acetaminophen resulted in significantly reduced postoperative pain, opioid consumption, and nausea and vomiting [32, 33]. Additionally, there is evidence suggesting superior postoperative analgesia is achieved

when acetaminophen is given in combination with an NSAID versus either agent alone [34–36]. Moreover, parenteral acetaminophen has been shown to produce opioid-sparing effects compared to placebo [37, 38]. Since there appears to be no difference in efficacy between oral and parenteral acetaminophen, cost and institutional protocol should guide provider decision-making when including acetaminophen in an MMA regimen [39].

N-Methyl-D-Aspartate Antagonists

Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) glutamate receptor antagonist that may be incorporated into perioperative MMA regimens. When bound by the excitatory neurotransmitter glutamate, the NMDA receptor allows the propagation of electrical impulses along the central nervous system. Ketamine antagonizes NMDA receptors in dorsal horn neurons of the spinal cord, inhibiting pain signal transmission. In addition to its action on NMDA receptors, ketamine also has activity at opioid receptors, voltage-dependent ion channels, and nicotinic and muscarinic cholinergic receptors. It was originally developed to exhibit less emergence delirium than phencyclidine while having a similar anesthetic profile [40]. The commercially available ketamine preparation consists of a racemic mixture of S(+) and R(−) enantiomers, each of which individually contributes to its physiological and psychoactive effects. Relative to the R(−) isomer, the S(+) isomer is associated with greater analgesia, decreased spontaneous motor activity, lower incidence of emergence delirium, and fewer psychotomimetic side effects [41]. The psychoactive properties of ketamine limit its use to patient populations without active psychosis. Additionally, ketamine use is contraindicated in patients with severe hepatic disease or high-risk coronary artery disease [42].

Five recent systematic reviews and meta-analyses examined the efficacy of ketamine for analgesia in the perioperative setting when given as a bolus or infusion and as an adjunct to opioids in PCA [43–47]. Four of these reviews found that ketamine significantly lowered postoperative pain scores and decreased postop-

erative opioid consumption [42–46]. Ketamine was also associated with a decreased incidence of postoperative nausea and vomiting in these reviews. There were no significant adverse effects found to be associated with ketamine, although one review reported an increased incidence of neuropsychiatric events [43]. Two randomized studies reported decreased pain scores, nausea and vomiting, and morphine use in patients receiving morphine plus ketamine via PCA versus morphine alone [48, 49]. Recent consensus guidelines conclude, with a moderate level of certainty, that ketamine should be considered for patients undergoing painful surgery and opioid-tolerant patients undergoing any surgery [42]. Although ketamine use for analgesia is currently off label and dosing regimens reported in the literature are varied, these guidelines suggest using bolus doses of up to 0.35 mg/kg and infusions up to 1 mg/kg/hour [42].

Alpha-2 Adrenergic Agonists

Alpha-2 adrenergic agonists (e.g. dexmedetomidine, clonidine) are also available for parenteral administration and have been shown to reduce opioid consumption when used as part of an MMA regimen [50]. These agents exert their analgesic effects through two primary mechanisms in the nervous system, although the full extent of their involvement in physiological pathways is not completely understood. First, activation of G_i-protein-gated potassium channels triggers the influx of potassium and membrane hyperpolarization, which decreases neuronal excitability [51]. Second, calcium influx into cells is reduced, inhibiting excitatory neurotransmitter release [51]. Together, these mechanisms inhibit neuronal excitation and impede impulse propagation to adjacent neurons. Dexmedetomidine's primary site of action is hypothesized to be the locus coeruleus, which is associated with the reticular activating system and arousal [52]. This agent is associated with increased sedation, bradycardia, and hypotension but may reduce intraoperative opioid usage [53] and postoperative pain scores [54]. Moreover, dexmedetomidine has demonstrated the ability to prolong nerve blocks when administered perineurally and intravenously [55, 56].

In order to mitigate cardiovascular side effects, dexmedetomidine loading doses of 0.5–1 mcg/kg/hour are routinely infused over 10 minutes, followed by maintenance infusions titrated to effect, usually in the range of 0.2–1 mcg/kg/hour [57].

Another alpha-2 adrenergic agonist, clonidine, also exerts analgesic effects when administered parenterally [58–60]. In contrast to dexmedetomidine, clonidine's primary site of analgesic action in the central nervous system is the dorsal horn of the spinal cord, where it binds alpha-2 receptors and inhibits the afferent transmission of pain signals [61]. Available non-enteral formulations of clonidine include transdermal patches and vials for epidural infusion. A systematic review examining the effect of perioperative clonidine on postoperative pain and opioid use found that administration of clonidine did not reduce opioid usage at 2 hours post procedure, but significant reduction was reported at 12 and 24 hours [62]. Concordantly, clonidine was not associated with reduced pain scores at 4 hours post procedure, but lower pain scores were observed at 12 and 24 hours [62]. However, this review did not differentiate between enteral and non-enteral formulations, making it difficult to draw conclusions specifically for one route of administration. The role of transdermal clonidine is unclear as the majority of studies examine epidural or oral routes of administration. However, one recent study found no difference in pain scores or opioid consumption in patients receiving preoperative oral clonidine and postoperative transdermal clonidine compared to placebo [63].

Local Anesthesia

Surgical incision infiltration with local anesthetic is a reliable pain control technique that should be a part of MMA regimens when appropriate [64, 65]. Local anesthetics exert their effect by inhibiting sodium influx into neurons, preventing an action potential from arising and transmitting sensory information. Lidocaine and bupivacaine are local anesthetics commonly utilized at the site of incision that are proven to reduce postoperative pain [66, 67]. Some studies have reported that the addition of local anesthetic at the end of laparoscopic surgery provides improved pain relief

compared to preincisional infiltration alone [68–71]. Another study of sternotomies found postoperative pain and opioid analgesic requirements were reduced by continuous postoperative localized infusion of bupivacaine [72]. Similarly, one study reported using a continuous infusion of ropivacaine, a long-acting local anesthetic, which resulted in improved pain control after spinal fusion surgery [73].

There are several considerations with the use of local anesthetics based on patient-specific comorbidities. Systemic absorption may cause significant adverse events in patients with cardiovascular instability or in patients taking alpha agonists or beta-blockers. With proper infiltration technique, however, these side effects are minimized. Due to class-wide hepatic metabolism, patients with liver dysfunction are more likely to experience systemic side effects, most commonly hypotension and bradycardia [74].

Regional Anesthesia

Regional anesthesia, consisting of peripheral nerve blocks and neuraxial anesthesia, is a unique modality that should be considered for use in MMA regimens. Peripheral nerve blocks have been consistently reported to reduce postoperative opioid consumption and decrease pain scores in appropriate procedures, such as upper and lower extremity surgery [2, 75–78]. Recent advances in ultrasound-guided regional anesthesia technology have led to improved patient outcomes and quality of analgesia [79]. Local anesthetic can be administered as a single injection, or a perineural catheter can be placed to provide continuous infusion when longer durations of analgesia are desired. Single dosing and continuous infusion were compared in total knee arthroplasty, and outcomes such as postoperative opioid consumption were similar between the two modalities [80, 81]. Bupivacaine has the longest duration of analgesia, followed by ropivacaine, mepivacaine, and lidocaine, although duration varies depending on the site of injection. These agents have a relatively quick onset of action, ranging from 10–30 minutes. Anesthesia goals such as desired block duration and degree of block inform the choice of agent. To avoid systemic

toxicity, the volume and concentration of anesthetic should also be determined based on the site of injection.

Local anesthetics and opioids may also be utilized to provide neuraxial anesthesia via a catheter that is inserted transcutaneously to deliver medication into the epidural space. Epidural analgesia can be administered as regular interval bolus dosing, continuous infusion, or as needed with PCA. Some agents used in regional blocks, such as bupivacaine and ropivacaine, can also be administered epidurally, though in significantly smaller doses. Opioids may be administered neuraxially alone or in combination with local anesthetics. The advantages of combining epidural opioids and local anesthetics include greater pain control, decreased dose requirements of both agents, and potentially lower incidence of side effects [82–84]. For opioids, drug molecule lipophilicity determines the onset and duration of action when administered neuraxially (Table 8.3). Morphine is the least lipophilic with an onset of approximately 45 minutes and a duration of action of up to 24 hours. Fentanyl and sufentanil, in comparison, have the fastest onset of about 15 minutes with a much shorter duration of action. Additionally, intrathecal administration of opioids into the subarachnoid space of the spinal cord is an option for patients who are chronically reliant on opioids for pain relief.

Adverse events and complications should be considered when incorporating regional anesthesia into an MMA regimen. Regional blockade can cause local anesthetic systemic toxicity,

Table 8.3 Epidural opioid lipophilicity

Degree of lipophilicity (LogP)[a]	Drug	Onset of action	Duration of analgesia
4.05	Fentanyl	5–15 minutes	1–2 hours
3.95	Sufentanil	10–15 minutes	1–2 hours
1.06	Hydromorphone	15–30 minutes	Up to 18 hours
0.87	Morphine	30–60 minutes	Up to 24 hours

[a]A higher LogP value correlates with greater lipophilicity. LogP is the logarithm of the partition coefficient P, the ratio of a substance's concentration in octanol over water

manifesting with neurological symptoms such as dizziness, tinnitus, or oral numbness. Systemic toxicity can be avoided by aspirating prior to injection, using the lowest effective dose required, and administering larger doses as multiple injections. One of the most common complications of neuraxial anesthesia is post-dural puncture headache, with a reported incidence rate of up to 7% [85]. It presents up to 72 hours after dural puncture with a dull headache and may be accompanied by nuchal stiffness or spinal muscle tenderness [85]. Meningitis, epidural hematoma, and epidural abscess are extremely rare but serious complications of epidural anesthesia that can have disastrous neurological sequelae.

Conclusion

Non-enteral analgesia options make up a significant portion of the available agents for inclusion in MMA regimens. The variety of mechanisms of the agents reviewed in this chapter allow for individualized analgesic and anesthetic requirements to be taken into account based on patient-specific factors, procedural requirements, and cost-effectiveness. Evidence supports use of parenteral analgesics across procedure types with benefits such as reduced pain, decreased postoperative opioid use, and improved recovery speed.

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9 Pain Psychology and Perioperative Pain Management

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Introduction

The occurrence of acute postsurgical pain is almost ubiquitous and is often discussed with patients in the perioperative setting. However, the development of persistent chronic pain after surgery is a potential risk that is difficult to predict and frequently a challenge to control. The discussion of the transition from acute pain to chronic pain has been a topic of great interest, as it has created

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an enormous burden on the healthcare system. This has in part led to the current opioid epidemic and a shift to treating patients with a multimodal therapeutic approach. In recent years, the focus has been to better identify the risk factors that contribute to the development of persistent postsurgical pain and utilize methods to prevent these pain symptoms from developing. Similar to chronic pain that is not related to surgery, psychological and social factors are important to recognize as potential influencers in the development of persistent postsurgical pain.

Definition

The International Association for the Study of Pain (IASP) previously defined chronic postsurgical pain as pain that develops after surgery and lasts at least 2 months, with other causes of pain being excluded [1]. Due to an oversimplification, this definition has often been criticized and revised. More recently, the "International Classification of Diseases defined chronic postsurgical pain as pain developing or increasing in intensity after a surgical procedure, in the area of the surgery, persisting beyond the healing process (i.e., at least 3 months) and not better explained by another cause such as infection, malignancy, or a pre-existing pain condition" [2].

Epidemiology

The true incidence and prevalence of chronic postsurgical pain are difficult to accurately quantify. However, it has been estimated that there are over 300 million surgical interventions that occur globally every year, and approximately 10% of these patients go on to develop debilitating chronic postsurgical pain [3]. Thus, chronic postsurgical pain has been recognized as a public health issue requiring special attention.

The development of chronic postsurgical pain may occur after any type of surgery. However, thoracic, breast, lumbar spine, inguinal hernia, and hip or knee arthroplasty have a particularly higher prevalence (>20%) [3]. It has been postulated that these types of surgeries often have an increased risk of nerve injury, which may be a risk factor.

Pathophysiological Changes During the Transition from Acute to Chronic Pain

Pain physiology is a complex interaction involving various systemic processes and contribution from the immune, sensory, hormonal, and inflammatory pathways. There are changes that occur in both the peripheral nervous system and the central nervous system (i.e., the brain and spinal cord).

Generally, with the termination of an acute nociceptive signal and with an adequate recovery time, there is a restoration of homeostasis that ends the pain process. However, in the transition from acute to chronic pain, these nociceptive signals often continue to fire and stimulate the pain pathways. In the periphery, these prolonged pain signals lead to chronic inflammation and a reduction in the pain threshold, often leading to peripheral sensitization. These continued nociceptive signals in turn lead to central stimulation within the spinal cord and brain and the development of the "wind-up" phenomenon. The structural changes that occur enhance signal transduction and the release of additional neurotransmitters, inflammatory markers, and chemokines. The combination of these changes leads to the development of central sensitization. Functional magnetic resonance imaging and positron emission tomography have identified structural changes in the brain once central sensitization has occurred as well. These changes can often create psychological and mental health problems, such as depression, anxiety, poor pain-coping strategies, and substance use disorders. These stressors can often times worsen a patient's pain symptoms [4].

General Risk Factors

Currently, there is no way to predict with certainty which patients will develop chronic pain symptoms after surgery. However, there are a number of risks factors which have been identified that can help determine which patient populations may be at higher risk (Table 9.1). Appropriate steps can be taken to potentially identify and treat these patients earlier in the process. These predictive factors can be patient related or surgery related. Patient-related factors may include medical comorbidities, a genetic predisposition,

Table 9.1 Risk factors for developing chronic postsurgical pain

Patient factors
Genetic predisposition
Medical comorbidities
Chronic pain prior to surgery
Female gender
Younger age
Depression
Anxiety
Stress
Hypervigilance
Catastrophization
Rate of return to work
Surgical and perioperative factors
Type of surgery[a]
Surgical technique[b]
Duration of surgery
Severity of postoperative pain
Analgesic regimen
Type of anesthesia

[a]Thoracic, breast, lumbar spine, inguinal hernia, hip, and knee arthroplasty have high prevalence of chronic postsurgical pain
[b]Open (high risk factor) versus laparoscopic (low risk factor)

the presence of chronic pain before surgery, female gender, and younger age. Psychosocial factors include depression, anxiety, stress, hypervigilance, catastrophizing, and rate of return to work. Surgical factors include type of surgery, surgical technique, duration of surgery, severity of postoperative pain, analgesic regimen, and type of anesthesia [1, 3–5].

Psychological Risk Factors

"The question of transition from acute to chronic pain is one of the most fundamental and enduring challenges in the field… we lack consensus on what the mechanisms are likely to be" [6]. Fundamental to this knowledge is answers to two key questions: (1) who will develop chronic pain, and (2) what makes a person vulnerable to developing chronic pain? Extant research has identified numerous risk factors including demographics, mood disor-

ders, lifestyle, and comorbidities [7], but these account for only 10–20% of the variance in chronic pain [8]. It is only recently, because of neuroimaging, that we have been able to study brain mechanisms and processes that explain how these factors mediate the development of chronic pain. From this body of research, the identified brain structures and physiological processes predict the development of chronic pain with an 80–100% accuracy [9]. Brain imaging studies show that brain anatomy and function are altered in patients with chronic pain [10]. A longitudinal study tracking persistent low back pain demonstrated that "the neural representation of spontaneous pain was dominated by somatosensory activity that shifted toward the limbic representation as the pain became chronic" [11]. The corticolimbic system has been found to control or amplify pain states and has been documented in orofacial pain states. Additionally, if pain is an ongoing stressor and changes an individual's nervous system, then it is possible that early life adversities including chronic sociodemographic and environmental stresses can prime the individual by reorganizing the mesolimbic circuitry and increasing their risk for developing chronic pain [12].

Hruschak and Cochran [13] conducted a systematic review to study psychosocial predictors in the transition from acute to chronic pain. Of the 18 articles that met inclusion criteria, 83% reported an association between psychosocial factors and chronic pain. Twenty-nine percent demonstrated that depression was a possible predictor, and 35% found chronicity to be associated with fear avoidance. Similarly, higher distress levels were predictive of increased likelihood of transitioning to chronic pain in musculoskeletal pain [14]. More recently, in a fact sheet, IASP documented the following risk factors for chronicity after surgery: preoperative mood disorders such as depression, anxiety, and PTSD symptoms, preoperative pain catastrophizing and fear of surgery, and postsurgical kinesiophobia in the acute phase of recovery [15].

Linton [16] highlights the following psychological factors associated with the development of chronic pain:

1. *Pain behaviors* which overtly communicate the experience of pain (rubbing, grimacing, bracing), low levels of activity, and an avoidance of those pain-aggravating behaviors which are "learned" though operant or classical conditioning.

2. *Pain cognitions* which are strongly held beliefs about pain and illness and are often influenced by social and cultural factors. They may include catastrophization, cognitive distortions, locus of control, hypervigilance, and avoidant coping strategies.
3. *Emotions* which include distressed mood states such as fear, anxiety, depression, anger, and low frustration tolerance associated with pain.
4. *Social factors* may serve both, as a risk (vulnerability factor) or as a resiliency resource. Social isolation, limited options to return to work or ability to return to work in a modified capacity, financial hardship, and disparities in access to quality care may prolong the presence of pain and contribute to disability. As a resiliency resource, it may buffer the effects of pain on function.

There are a few mechanism-specific models that have been proposed to better explain the development of chronic pain. They are as follows.

The fear-avoidance model, first described by Letham in 1983 [17] and further discussed by Vlaeyen in 2016 [18], proposes that the fear of pain leads to a "deleterious effect" when avoidance rather than confrontation is the behavioral response [19]. In this model, fear which is a normal anticipatory response to imminent threat becomes conditioned, through experiential or observational learning, to nonthreatening or painful stimuli. The fear of these stimuli results in avoidance and generalizes to closely related stimuli. This avoidance leads to further reinforcement of the fear resulting in the development of a fear and avoidance loop. Two factors, anxiety sensitivity (AS) and experiential avoidance (EA), have been identified as vulnerability factors in the fear-avoidance model, to explain individual differences in the fear of pain [20]. AS is defined as the fear of bodily sensations due to beliefs that these sensations will have negative somatic, cognitive, or social consequences [21]. EA is the unwillingness to tolerate upsetting emotions, thoughts, and memories leading to a maladaptive attempt to escape such experiences. Individuals with higher EA have lower pain tolerance and higher pain catastrophizing [22].

The cumulative risk load model emphasizes the importance of the cumulative interactions over time among overlapping factors such as catastrophizing, fear, and depression. The advantage of this model over the fear-avoidance model is that it has a greater ability to predict pain outcome than the combination of individual severity measures. Recent evidence suggests that global risk indices are better predictors and may be better targets for treatment [19].

The avoidance-endurance model (AEM) hypothesizes that some patients will become fearful and avoidant, while others will show an endurance response. "The core component of the AEM is the assumption that people who experience pain reveal characteristic patterns of cognitive, affective, and behavioral responses to that pain, which influence maintenance of pain and disability" [p. 366]. Affective and cognitive factors will determine the type of endurance response [19, 23].

In summary, the neuroanatomical basis of the psychological factors which facilitate the transition of acute to chronic pain is now better understood and promotes a comprehensive and early intervention of pain.

Evidence-Based Psychological Approaches

While there is significant evidence regarding the utility of cognitive behavioral therapy (CBT) for chronic pain, less evidence has been found for managing acute pain, particularly perioperative pain. Common postoperative approaches include mindfulness-based stress reduction (MBSR), cognitive behavioral therapy (CBT), acceptance and commitment therapy (ACT), mindfulness-based approaches, pain education, relaxation, and hypnosis, which typically require multiple sessions (Table 9.2) [24]. Psychological interventions targeting acute pain have been less widely studied, though pain-specific distress has been shown to predict outcomes including chronic pain intensity, postsurgical pain intensity, disability, response to opioids, use of opioids, and postsurgical pain at 4-month follow-up [24].

Both pre- and postoperative psychological interventions have been suggested. Several original studies and subsequent reviews

Table 9.2 Commonly used psychological interventions postoperatively

Cognitive behavioral therapy
Mindfulness-based stress reduction
Acceptance and commitment therapy
Mindfulness-based approaches
Pain education
Relaxation
Hypnosis

have attempted to examine the effectiveness of these interventions on short- and long-term outcomes such as analgesic use, pain ratings, pain-related anxiety, and chronic pain among different patient populations. Relaxation, hypnosis, mindfulness, cognitive behavioral strategies, and acceptance and commitment are among the most well-known interventions for acute pain.

While psychological factors can serve as predictors for perioperative pain [25], pain catastrophizing, specifically, may play a significant role in patients' perceptions of pain, pain severity, and development of chronic pain [26–28]. Therefore, some researchers have attempted to evaluate the effectiveness of interventions that target pain catastrophizing and pain expectations prior to and following surgical procedures. An experimental study induced pain using a thermode (inducts thermal heat on the skin surface) among undergraduate female students [29]. Those with acute or chronic pain were excluded from the sample. Authors stated that women were studied due to the greater prevalence of pain conditions in women and differences in pain sensitivity. Participants were assigned to conditions and provided instructions to use acceptance, cognitive restructuring, or distraction in response to heat-related pain, and their tolerance (measured by amount of heat applied before they asked researchers to stop) was recorded, as well as pain intensity, measured by visual analog scale. Results found that while the relationship between acceptance and greater pain tolerance was stronger than that of cognitive restructuring (a CBT-based strategy) and pain tolerance, there was no significant difference between acceptance and distraction regarding potential impact on pain intensity. This may offer basic information regarding the role of psychological interventions on acute pain experiences.

Reichart and colleagues attempted to reduce perioperative pain and necessary treatment following spinal neurosurgery using a short psychological intervention [30]. Their intervention was developed to address preoperatively increased fear levels as they found that this has been shown to impact postoperative outcomes. Their short psychological intervention (SPI) focused on reducing fear avoidance beliefs through increase of self-efficacy and locus of control and increase of patients' motivation to adopt new behaviors. They utilized a mental contrasting intervention with implementation intentions. Mental contrasting is suggested as a method for achieving goals independently of an individual's expectations. In the first session of the intervention, participants were asked their most important goal following their hospitalization and were then asked to name positive aspects of achieving set goal and potential barriers. During the second session, they reviewed these goals and included implementation intentions ("if-then" plans) to further identify ways to overcome obstacles and achieve stated goals. Outcomes suggested lower pain intensity among patients in the treatment group, and authors hypothesized that this was due to them learning a method for coping with their illness. Though it has limitations, this study offers support for brief psychological interventions and their role in improving postoperative pain.

Results of a Cochrane Review of psychological interventions for acute pain after open heart surgery [31] found moderate-quality evidence that psychological interventions can help reduce mental distress in patients undergoing open heart surgeries. Authors concluded that there is a lack of evidence available to support or refute the impact of psychological interventions on postoperative pain or other outcomes, such as analgesic use or mobility. However, their review focused only on psychoeducation, cognitive behavioral interventions, and relaxation techniques. An updated review incorporating more psychological interventions will provide a more comprehensive understanding regarding efficacy and effectiveness.

As noted across studies, there is a dearth of literature regarding psychological interventions for acute pain, and as Darnall suggested in her review [24], evaluating effectiveness of combined

approaches, such as relaxation and cognitive strategies, may provide more comprehensive treatment. Additionally, mind-body interventions may supplement an important element of managing and treating acute pain, as it may address the interaction between psychological and biological experiences. Specifically, brief mindfulness interventions have been shown to reduce experimentally induced pain intensity [32, 33]. A randomized controlled trial completed with hospitalized patients who reported significant pain evaluated the effectiveness of mindfulness training, hypnotic suggestion, and psychoeducation [34]. Their study found both mindfulness and hypnotic suggestion had significant changes in reported pain intensity following intervention. A systematic review by Nelson and colleagues [35] found that guided imagery was effective in reducing postoperative pain levels and had moderate support for reducing analgesic intake. Their review found partial support for efficacy of hypnosis on postoperative anxiety or pain. Overall, there were inconsistent results regarding the impact of mind-body therapies on physiological measures, including vital signs and endocrine measures.

Based on the available, though limited, scientific evidence, it appears that psychological interventions could play a role in reducing perioperative pain experiences. These interventions appear to be most effective, when effective, if implemented prior to surgery, providing patients with sufficient time to practice learned skills. Across studies, it appears that patients may benefit from strategies aimed at reducing pain catastrophizing and/or pain-related anxiety, as well as acute coping skills. As mindfulness entails purposeful, nonjudgmental, present-moment awareness [36], it can be implemented as a foundational strategy to promote more effective use of additional skills. This preoperative "training" could provide patients an opportunity to learn effective coping skills that challenge pain catastrophizing, help to manage expectations, and increase abilities in self-regulation. Further research is needed regarding the effectiveness of these interventions, the patient populations for which they are effective, and the feasibility of implementing and disseminating these interventions.

Clinical Case Examples

Case 1: Lori Collaborative Intervention

Lori was a 25-year-old female patient with a history of complex regional pain syndrome (CRPS) in her right lower extremity resulting from a fall on the ice. During pain exacerbations, she will seek out emergency pain management and at times would be admitted to the hospital. While in the hospital, general medicine, acute pain, psychiatry, and nursing care were involved in her treatment. Medical pain management included imaging and diagnostic tests, intravenous opioid pain medication, and intravenous ketamine. Outpatient treatment for CRPS included oral anti-inflammatory and anxiety medications. Monthly ketamine infusion treatments mitigated ongoing pain symptoms. Lori reported a strong belief that intravenous medications were the only treatments that could provide relief for severe pain exacerbations. Intravenous opioid and ketamine medications were recommended only on an intermittent basis with the acute pain service strongly advising against this approach. Lori was open and receptive to psychiatric follow-up that mostly involved psychotherapy while in the hospital and emergency department. She was hopeful during each admission and emergency visit that intravenous opioids or ketamine would be provided to her. Psychological treatment involved individual psychotherapy with a psychologist on the consultation and liaison service. The psychologist reviewed coping strategies with Lori such as eliciting the relaxation response, self-soothing, problem-solving, expression of emotions, and cognitive coping. The psychologist also worked on actively managing expectations for treatment and conflicts that emerged with the patient and the treatment team that lead to expression of suicidal thoughts and self-injurious behavior, i.e., pulling her intravenous catheter out. A team approach was used to manage expectations and provide education about oral versus intravenous pain medications and development of tolerance. Lori was able to express her feelings with the psychologist, such as feeling misunderstood and invalidated. This helped to develop a rapport with the psychologist and, however, also leads to her

feeling betrayed when the psychologist aligned with the medical team. This was eventually resolved with ongoing follow-up while in the hospital. Lori continued with outpatient pain management and amelioration of pain on an emergency basis. Her ability to cope with pain and exacerbations improved over time with a multidisciplinary approach and family support that reinforced the belief that intravenous pain medications should be avoided when possible.

A comprehensive psychiatric team approach was required in this case to help resolve conflicts that arose during hospitalization, as well as outpatient mental health support. Ongoing communication and follow-up while reinforcing a consistent pain management treatment plan with inpatient and outpatient services were crucial. Psychological interventions focused on creating a supportive environment through rapport building. Psychoeducation and cognitive reframing approaches were helpful in managing expectations for acute pain management. She was seen daily while in the hospital for 3–7 day stays. She was seen for outpatient psychotherapy at least once per week, approximately 4 months after the development of chronic pain. This patient had a history of chronic pain, anxiety, bipolar disorder, and attention deficit hyperactivity disorder prior to hospital admissions.

Case 2: Carrie Individual Intervention

Carrie was a 23-year-old female patient who sustained a severe de-gloving injury to the right knee that required multiple reconstructive surgeries. This injury was sustained during a train derailment that resulted in over fifty passengers who were injured and four fatalities. Carrie required medical follow-up and hospitalizations over several years with orthopedics, plastic surgery, and infectious disease. She also suffered from post-traumatic stress symptoms. Carrie was referred for individual psychotherapy while in the hospital 11 days after the injury. Treatment initially entailed rapport building, post-traumatic stress disorder education, processing memories from the traumatic event, and learning cognitive behavioral skills to manage pain and anxious mood. CBT involved learning to elicit the relaxation response, attention diversion, sleep management, goal setting, and behavioral activa-

tion. Mindfulness meditation was practiced during sessions. Carrie was also interested in learning how nutrition could be used to facilitate wound healing and pursued this independently. Learning to adjust and adapt to changes associated with loss of independence and decreased ability to function as she was able to in the past and manage interpersonal conflict that arose from conflicting points of view regarding her treatment and litigation was a key component of psychotherapy treatment. Over time, Carrie had an increase in self-efficacy as evidenced by her confidence to live a full life despite her injuries. Her strong motivation to utilize non-pharmacological approaches and minimize use of medications was an important factor to consider when approaching her pain management.

In the second case, a team approach was not necessary. Individual psychotherapy and inherent personality characteristics may have helped reduce subsequent disability and adaptation to her circumstances. Management of anxiety and depression symptoms was an important component of her treatment plan. She was seen for two sessions in the hospital and thirteen sessions on an outpatient basis. This patient had no prior history of mental health disorders.

Future Directions for Investigation

The practice and pressures on healthcare providers caring for patients in pain have changed over the past several years. Much of this has been the result of the individual and societal damage that has occurred with the opioid epidemic due to unintended consequences of excessive opioid prescribing over the past several decades.

Psychological approaches have the opportunity to make an impact in the management of postoperative pain. The narrow focus on pain intensity or opioid reduction reduces a complex human experience, pain, down to a single number. Multimodal approaches focus on the treatment of the nociceptive component of pain. Psychological ones are perhaps better suited to address the entire patient experience as it relates pain. Pain is a perception,

both sensory and emotional. There is a need to develop outcome measures that go beyond pain intensity scales and reductions in opioid consumption and capture the overall patient experience. Each patient in pain, even if they have had the same surgery, may respond better or worse to different treatment approaches depending on the other variables that they bring to the table. The patient's qualitative experience may provide insight into how to improve postoperative pain management.

A major limitation in improving the patient's perioperative experience is time. Surgical settings are very time-pressure-intensive environments. Good pain management done well takes time. Investigating a combined outpatient and inpatient psychotherapy and/or psychoeducational program prior to and after surgery will help us understand whether this will facilitate better pain outcomes. Skills learned in the outpatient setting can be reinforced and adapted for the inpatient setting. Another area for investigation may include the use and training of allied healthcare workers and volunteers to aid with some of the more humanistic but time-consuming aspects of proposed treatment strategies. This may have the additional benefit of allowing harried staff to feel more connected to their patients and profession.

Chronic outpatient pain clinics have for some time now known the benefits of having access to psychology services for the co-management of their patients. Psychological care in this setting can help patients function and thrive with residual pain that has reached the limits of medical treatment to improve. Surgical and inpatient acute pain services should look to this model as a guide for future research and an inspiration to improve the perioperative experience of their patients.

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Part II

Specialty-Specific Chapters

10

Perioperative Analgesia in General Abdominal, Vascular, and Thoracic Surgery

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General Abdominal Surgery

The topic of perioperative anesthesia for general abdominal surgery has been dominated over the last several years by the increased uptake of enhanced recovery after surgery (ERAS) protocols. ERAS is a comprehensive perioperative protocol that includes both opioids and opioid alternatives (Table 10.1). While the bulk of this chapter will focus on opioid alternatives, we will first discuss the current role of opioids in modern perioperative analgesia.

Opioid analgesia remains as the mainstay for perioperative analgesia despite the rising interest in alternative pain control. Anything other than a cursory insight into the past and present

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Table 10.1 Multimodal approach to perioperative analgesia

Preoperative
Counseling
Gabapentinoids
NSAIDs
Intraoperative
Regional blocks
Epidural anesthesia
Lidocaine infusion
Liposomal bupivacaine
Opioids
Gabapentinoids
NSAIDs/acetaminophen
Postoperative
Opioids
Gabapentinoids
NSAIDs/acetaminophen

role of opioids is beyond the scope of this chapter. Decades of data exist about the role, dosing, and safety profile of opioids, but with the recent epidemic of opioid deaths, much of this data is now viewed with significant skepticism. Much of the research that has since surfaced concerns the use of narcotics for chronic pain control, but there are some guidelines for management of acute pain. The CDC released guidelines in 2016 that act as our baseline. These guidelines recommend initiation of nonpharmacological (i.e., discussions about alternative therapies and expectations) and nonopioid pharmaceuticals prior to or in addition to narcotic initiation. They further recommend minimizing the initial dose, with some data suggesting that daily doses of >50 morphine milligram equivalents (MME) lead to both increased long-term use and complications such as overdose [47]. Similar harm was found when the use of long-acting or extended release formulations was initiated without demonstration of failure of immediate-acting narcotics for at least 1 week. Similarly, prescribers should only prescribe for the expected duration of severe pain; 3 days is usually sufficient, while longer than 7 days should be rarely required [48]. The safety profile of narcotics is well described and includes most notably the potential for profound respiratory depression,

narcotic dependence and abuse, onset of delirium, postoperative nausea, and tolerance.

For the vast majority of our practice's surgeries, a short duration of 5/325 mg acetaminophen-oxycodone prescribed every 6 hours is most commonly used. We employ a minimally invasive approach for virtually all of our abdominal operations and have found that with a robotic approach, the need for narcotics has greatly diminished compared to previous approaches. In addition to preoperative counseling, we take advantage of liberal use of local and regional blocks and both intraoperative and postoperative use of nonnarcotic medications such as acetaminophen and ketorolac. For routine inguinal hernias, we often recommend only Tylenol and have found that of the patients that require narcotics, the vast majority uses them only for the first 24 hours. For cholecystectomies, appendectomies, and related operations, a course of 5–8 tablets is almost always sufficient. More painful operations such as ventral hernia repairs still suffice with a course of 10–12 tablets. Using a similar approach to inpatient operations such as colectomies has led to hospital stays of 24–48 hours with discharge prescriptions of 10–15 tablets that are generally sufficient with satisfied pain scores. For those few patients who need more than a second short course of narcotic pain control, we refer them to a pain control specialist for further management, but this is rarely required.

For much of the history of surgery, a preoperative component of surgical analgesia was largely neglected. Research has demonstrated that preoperative education can greatly improve postoperative pain management. Indeed, the idea of preoperative pain education dates back at least to 1964, when Egbert et al. published a single-blinded study with remarkable results. In this study, an anesthetist counseled the patient prior to the operation regarding the type and degree of pain expected and described methods of pain control, including both self-relaxation and narcotics. This counseling was continued in the postoperative period as well. Over the first five postoperative days, the study arm requested half the amount of morphine, was discharged 2.7 days sooner, and had a significantly lower perception of pain than the control group [1]. While this study is now over 50 years old, its premise has been

Table 10.2 Commonly used perioperative analgesia medications

Medication	Class	Associated adverse effects
Ketorolac	NSAID	Renal dysfunction, colorectal anastomotic leaks
Liposomal bupivacaine	Local anesthetic	LOST
IV lidocaine	Local anesthetic	LOST, arrhythmias
Oxycodone, Dilaudid, hydrocodone	Opioids	Respiratory depression, tolerance, dependence
Gabapentin, pregabalin	Gabapentinoids	Respiratory depression, sedation

tested over the years and found to have lasting significance [2]. Further studies have also found a reduction in fatigue, wound infections, and stress response with similar preoperative counseling [3, 4].

Preoperative medication administration has also been evaluated extensively for use in preventing postoperative pain and narcotic usage. While the data on this subject is rather controversial, many ERAS protocols include various combinations of medications as their use generally appears to have minimal significant side effects [5] (Table 10.2).

Gabapentinoids

A recent exception to these guidelines is the use of gabapentinoids. Gabapentin is a gabapentinoid released in 1993 for its antiepileptic properties but has since been used in a myriad of clinical cases in an off-label fashion. Studies related to the efficacy of both gabapentin and pregabalin as a preoperative element of perioperative analgesia in general abdominal surgery have been mixed and significantly different for various surgical subspecialties [50]. A perusal of available data suggests the efficacy of gabapentin vs pregabalin in abdominal surgery appears to be roughly equivalent without definitive research delineating their differences. While several randomized control studies and meta-analyses have shown a modest decrease in postoperative narcotic use [6–8], other

studies have failed to replicate this property consistently [9, 10]. Overall, an overview of the plethora of studies on gabapentinoids appears to suggest a small decrease in postoperative narcotic usage with similar pain scores and varying levels of increased sedation and visual disturbances. While there is a large body of research regarding these medications, they span a large variety of surgical subspecialties, pre- and/or postoperative administration, and different dosages, making definitive conclusion difficult. As efforts to combat the opioid epidemic increase, rates of prescriptions for both gabapentin and pregabalin have increased dramatically. With such increased exposure, significant side effects such as sedation and dizziness have surfaced. It is also associated with increasing rates of abuse for its euphoric effects [49]. Most importantly, several case reports of respiratory depression after perioperative administration of both gabapentin and pregabalin [11–14] have led the FDA to require the use of additional warnings related to this potential adverse effect. The incidence of respiratory depression is also present for pregabalin and appears to be highest in patients with preexisting respiratory conditions such as COPD, in the elderly population, and when combined with other CNS depressants such as opioids, benzodiazepines, and antihistamines [15]. Further studies will need to be conducted to delineate its role in these cases. Given this warning, strong caution is warranted when considering the use of gabapentinoids despite their apparent utility in a multimodal pain control program.

NSAIDs and Acetaminophen

The use of NSAIDs and acetaminophen has also been documented extensively both individually and in combination. A meta-analysis by Straube et al. is among several studies regarding preoperative Cox-2-selective NSAIDs that have demonstrated significant postoperative pain relief with decreased postoperative narcotic use [16]. This analysis compiled 22 randomized trials with a total of 2246 patients and found that 15/20 trials concluded with reduced postoperative pain and reduced narcotic use. Further studies have shown a similar result with the use of ketorolac, in addition to a decreasing incidence of postoperative ileus [17]. Indeed,

ketorolac-specific studies have demonstrated strong evidence of decreased postoperative narcotic use, pain scores, nausea/vomiting, length of stay, and even decreased rates of overall adverse effects over the use of narcotics alone. Unfortunately, few studies have delineated the efficacy of intraoperative vs postoperative administration of ketorolac in general surgery. It appears to be most commonly used in the immediate perioperative setting with well-documented success, but the few related studies to show its use in the postoperative setting also demonstrate improved outcomes with decreased narcotic use [51–53].

A prevailing barrier to the increased use of ketorolac is a theoretical risk of increased bleeding due to its status as a Cox-2 inhibitor. A substantial amount of research has been performed to investigate this in several surgical specialties, including abdominal surgeries. This data almost universally denies a clinical link between the perioperative use of ketorolac and postoperative complications from bleeding, including hematomas, blood transfusions, and returns to the operating room [51, 54, 55].

Lastly, it should be noted that limited studies on NSAIDs have shown a trend toward increased anastomotic leaks that have failed to be consistently demonstrated. A comprehensive analysis of these trials individually can be found in the ERAS guidelines published by the University of Toronto on the SAGES website [18]. Further research into the use of NSAIDs in colorectal cases should be entertained.

The use of acetaminophen with or without the use of an NSAID has been extensively surveyed as well. A systematic review of study by Maund et al. showed a significant decrease in opioid consumption with the use of acetaminophen alone that was similar to the decrease found in the use of NSAIDs or Cox-2 inhibitors alone [19]. Building off of this, an analysis by Ong et al. demonstrated a synergistic effect of acetaminophen with NSAIDs, showing that a combination of the two was more effective than either drug alone in 85% and 64% of studies [20]. In our practice, we have found a strong synergistic relationship between NSAIDs and acetaminophen that greatly decreases postoperative narcotic usage.

The use of acetaminophen in the postoperative setting also has the added potential benefit of decreasing opioid use. Valentine

et al. demonstrated that scheduled postoperative acetaminophen decreased opioid use without compromising analgesia [33]. A randomized control study by Aryaie et al. looked at the role of IV acetaminophen vs placebo in the postoperative setting. This found the postoperative IV acetaminophen decreased opioid consumption by nearly 50%, decreased pain scores, decreased return of GI function, and reduced hospital length of stay. Furthermore, it decreased rate of ileus from 22% to 2.1% [34].

Local and Regional Anesthetics

Intraoperative pain management continues to evolve as well. A great deal of research has been performed investigating the merits of epidural analgesia vs transversus abdominis plane (TAP) block in abdominal general surgery. An early study of TAP block compared it to local anesthetic infiltration. This meta-analysis, by Yu et al., looked at four randomized control studies and found that while 2- and 4-hour post-op pain scores were equivalent, the 24-hour pain scores were significantly lower for the TAP block arm [23]. The efficacy of TAP blocks has been shown by many other studies and has been effectively compared to alternative analgesic measures [26, 27].

The Americas Hernia Society compiles a database of hernia outcomes and related data, known as the Americas Hernia Society Quality Collaborative database. A study by Warren et al. used this data to compare these analgesia techniques and found that the use of TAP block significantly reduced length of stay (2.4 vs 4.5 days) and postoperative narcotic usage [21]. Similarly, a retrospective study by Ris et al. compared postoperative patient-controlled analgesia (PCA) usage alone or with TAP block usage against intraoperative epidural analgesia. The TAP/PCA block arm experienced significantly lower pain scores and morphine requirements at both 12 and 24 hours post-op. This was accompanied by earlier passage of flatus and stool as well as a shorter hospital length of stay than either opposing arm [22].

While TAP blocks are traditionally performed with conventional local anesthetics such as lidocaine or bupivacaine, the

release of a liposomal bupivacaine formulation has promised prolonged perioperative analgesia (48–72 hours) [31]. This formulation was originally FDA approved for use in hemorrhoids and podiatric surgery but has since been used in a wide variety of methods. Torgeson et al. demonstrated that the use of liposomal bupivacaine in TAP blocks for both open and laparoscopic colorectal surgery decreased length of stay and urinary retention over epidurals [24]. A similar study by Felling et al. also studied liposomal bupivacaine TAP blocks vs epidural analgesia in a randomized clinical trial. In this study of 179 patients, TAP block with liposomal bupivacaine was shown to be non-inferior to epidural in time to return of bowel function, hospital length of stay, and postoperative complications but was associated with significantly lower overall cost and lower opioid usage [25].

In our practice, we liberally utilize laparoscopic TAP blocks with liposomal bupivacaine with great success. The laparoscope allows for quick visual confirmation of the block. We visually identify the transversalis muscle and its aponeurosis (Fig. 10.1) and then inject a diluted mixture of liposomal bupivacaine in normal saline in three boluses on each lateral side of the patient for a

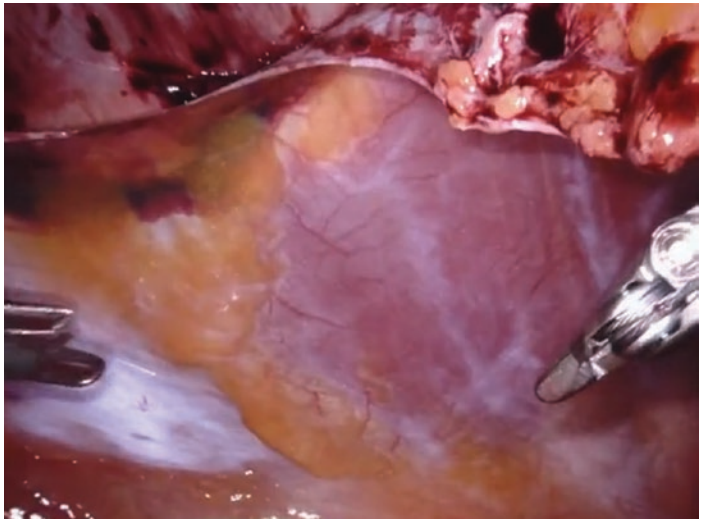

Fig. 10.1 Pre-TAP block view of transversalis muscle

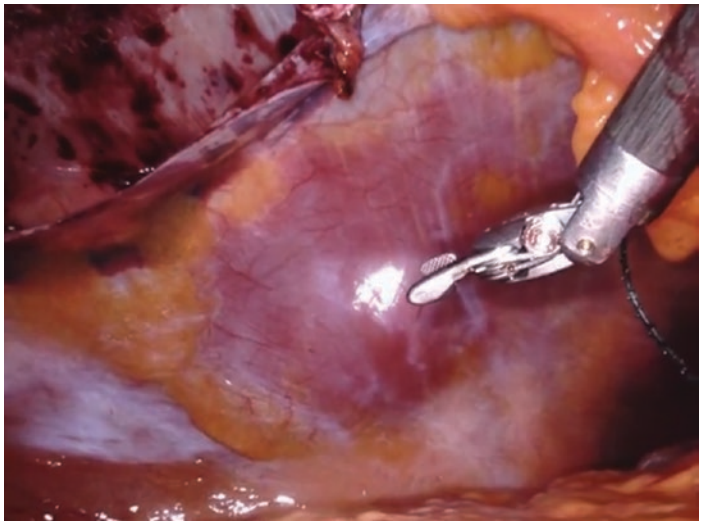

Fig. 10.2 Post-TAP block view of transversalis muscle with bulge

total of six boluses. The needle is inserted into the abdomen under direct visualization and retracted until it is just superficial to the transversalis. The bolus is then administered. When injected into the appropriate plane, the transversalis will usually bulge out significantly (Fig. 10.2). This procedure takes approximately 2–3 minutes total, minimizing additional OR time.

Local Anesthetic Systemic Toxicity

A discussion of local and regional anesthetics would not be complete without mention of local anesthetic systemic toxicity (LAST). This refers to systemic symptoms after administration of local anesthetics. This is a rare occurrence, occurring approximately 1–10 out of 10,000 epidurals and 1 out of 1000 peripheral nerve blocks. It is less common in local infiltration secondary to decreased systemic adsorption over time and is most commonly associated with bupivacaine over other amides and esters. The most severe complications tend to be neurologic, with seizures accounting for most mortalities [28]. Cardiovascular

symptoms are less common and can include hypotension and bradycardia. To help minimize the chances of LAST, the manufacturer of Exparel, the only FDA-approved liposomal bupivacaine product available in the USA, has made several recommendations for its use. Specifically, one should avoid additional use of local anesthetics for 96 hours and should not use for any analgesia other than local infiltration and interscalene plexus blocks. They further state that the use of non-bupivacaine local anesthetics at the same site can induce immediate release of bupivacaine, increasing the risk of LAST and decreasing the duration of action of the medication [29]. As the use of regional and depot injections increases, the rate of delayed presentation of LAST has increased. Any concern for LAST should prompt quick treatment with a lipid emulsion intravenous therapy [30].

IV Lidocaine Infusion

There has been interest also in the use of intraoperative IV lidocaine infusion for analgesia. This concept has been the focus of many studies, but the results thereof have been inconsistent at best. A Cochrane Review published in 2018 by Weibel et al. reviewed 68 trials, including 23 after 2015. In the vast majority of these studies, IV lidocaine was compared to placebo or no treatment. The approach for surgery, i.e., open vs minimally invasive, was fairly even between studies. Despite the bounty of research, the authors were unable to draw conclusions as to its efficacy in postoperative pain scores, GI recovery, postoperative nausea, or opioid consumption. A lack of high-quality data and comparative data to epidurals and TAP blocks prevented them from drawing more definitive statements [32]. Further research is warranted prior to any recommendations.

Vascular Surgery

One of the major difficulties in vascular-surgery-related analgesia is the management of pain secondary to critical limb ischemia. As this pain is thought to be largely neuropathic in nature, it can be very difficult to manage. Laoire et al. conducted a review of all accessible articles regarding this topic and found no therapy that could consistently relieve this pain. There were several novel

approaches, such as lumbar sympathectomy, ketamine infusions, and IV lidocaine, that are promising but have yet to demonstrate consistent evidence of efficacy [35].

Among the most common of vascular operations is the creation and revision of arteriovenous anastomoses for dialysis access. Two of the most common complications of the operation are thrombosis and a failure to mature. As such, understanding the relationship between perioperative analgesia and complication rates is vital. This was investigated by Malinzak et al. who performed a retrospective review and concluded that regional blocks "may improve the success of vascular access" through a variety of mechanisms, such as increased vasodilation, greater fistula blood flow, "sympathectomy-like effects," and an associated decreased time to fistula maturation [44]. These findings were confirmed by Macfarlane et al., who also added that there is minimal long-term data regarding the use of regional vs alternative analgesia with regard to fistula patency rates [45]. It is imperative to understand, however, that the systemic benefits of regional analgesia over general anesthesia are often profound in a patient population as morbid as renal dysfunction patients regardless of fistula patency rates. Indeed, a review by Hausman et al. showed that regional anesthesia in patients with COPD led to lower rates of pneumonia, prolonged ventilator dependence, postoperative intubation, and composite morbidity [46].

While the same principle of minimizing general anesthesia holds for other procedures such as carotid endarterectomies, endovascular procedures, and lower extremity revascularization, there are times when a patient will require general anesthesia. Under these circumstances, surgeons should follow the same principles outlined in the prior sections: use of a multimodal analgesia profile including local anesthetics, NSAIDs where appropriate, acetaminophen, and similar approaches.

Thoracic Surgery

Over the last several years, video-assisted thoracoscopic surgery (VATS) has become the standard of care for many thoracic surgeries. As such, here, we will focus on perioperative analgesia for

VATS operations. Among the simplest methods for analgesia is the use of the intercostal nerve block. This had been shown for many years to be an effective strategy for thoracotomy, and it remains so for VATS. An intercostal nerve block alone improves postoperative tachycardia, respiratory rates, pain scores, and opioid usage over systemic perioperative analgesics [38, 39].

A regional approach to thoracic surgery analgesia usually is composed of a paravertebral block. This has historically been performed as an injection at the onset or conclusion of the surgery. A traditional paravertebral block with immediate release local anesthetic is effective through the immediate post-op period but suffers from limited efficacy after 6 hours [40]. Given the lack of persistent pain relief in select patients, many surgeons now employ a continuous catheter-based paravertebral block. This method appears to provide superior pain control outside of the immediate postoperative period without additional significant adverse effects [41].

Since its release in 2012, liposomal bupivacaine has become a staple for many surgeons and is now used in both local (intercostal nerve block) and regional analgesia (predominantly paravertebral blocks) in thoracic surgery despite a lack of clear evidence of its utility. When used in intercostal blocks, some studies, such as Kelly et al., demonstrate slightly lower opioid usage immediately after surgery. These benefits, however, tend to disappear after 24 hours [36]. Other studies that demonstrate decreased opioid usage fail to consistently show improved outcomes in related areas such as hospital length of stay [37]. While the use of liposomal bupivacaine in intercostal nerve blocks may improve perioperative analgesia, its effect is likely minimal.

Epidural analgesia should also be discussed as an additional modality for VATS operations. Epidural analgesia was well established as an effective mediator of perioperative pain in the setting of thoracotomies, but its utility in the era of VATS is significantly more controversial. Studies such as that of Harky et al. demonstrate that while epidural analgesia provides effective pain control, its efficacy is eclipsed by paravertebral blocks in both pain control and side effect profile [42, 43]. While still used in several centers, it is used more sparingly than in previous years.

Conclusion

Just as the techniques of surgery have progressed to the art we see today, so has the art of perioperative analgesia. And just as the art of surgery continues to evolve, so does the art of analgesia. With proper pain control, both short-term and long-term patient outcomes are improving, but the revolution in perioperative care is just beginning. Continued research into this field is rapidly advancing with novel techniques and medications promising to transform the field. Surgeons of all varieties will need to continue to take advantage of these modalities to provide the best care for their patients.

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11

Perioperative Analgesia for Thyroid and Parathyroid Surgery

Brandon K. Nguyen
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Introduction

Thyroidectomy and parathyroidectomy are among the most commonly performed endocrine surgeries and have been demonstrated to be safe outpatient procedures [1–4]. While the potentially same-day nature of these procedures is cost-effective and convenient for both the patients and healthcare system, patient comfort and pain should be prioritized as well [1, 4]. Up to 80% of surgical patients experience significant postoperative pain, and inadequate perioperative pain management may negatively impact a patient's health, recovery, and overall experience, ultimately leading to chronic postsurgical pain [5]. In general, thyroidectomy and parathyroidectomy patients report postoperative pain levels between three and seven out of ten on a visual analog scale, characterizing

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the procedure as mild to moderate in severity [6–10]. Despite this intermediate level of pain, opioids are frequently overprescribed, leaving the possibility for diversion, misuse, and abuse. The authors hope that this chapter provides practical, evidence-based approaches for pain management and non-opioid alternatives for thyroidectomy and parathyroidectomy patients.

Opioid Epidemic

In the mid-1990s, the American Pain Society aggressively pushed the concept of pain as the "fifth vital sign" [11]. With this connotation, physicians were to regularly assess patient's pain levels. Concurrent with this emphasis was also the promotion of pain medications and the prescription of opioids as analgesics [11–13]. Surgeons have played a large role in this epidemic with over 36% of prescription opioids originating from surgical specialties [14]. In 2015, with regard to Medicare beneficiaries alone, otolaryngologists wrote nearly 1,000,000 days worth of opioid prescriptions [15]. As opioid prescriptions increased, deaths from opioid overdoses rose as well. Over the last two decades, more than 700,000 people have died from a drug overdose [16, 17]. In 2017 alone, over 70,000 people died from drug overdoses, making accidental overdose a leading cause of injury-related death in the United States [17, 18]. Thus, it is extremely important that physicians regularly evaluate their prescribing habits and strive to utilize non-opioid alternatives whenever feasible.

Preoperative Discussion and Opioid Disposal

The preoperative discussion remains a cornerstone of patient pain management. These dialogues with the patient and their families should consist of expected postoperative pain, likely timeline, medications, and side effects. The American Pain Society (APS) and American Society of Anesthesiologists (ASA) both recommend an individualized, patient-centered dialogue around pain management, as this education has been shown to reduce

postoperative opioid consumption, pain anxiety, and length of stay [19, 20]. As patients are further educated on the negative effects of narcotics, a vast majority will decline opioids in favor of non-opioid alternatives [19, 21, 22]. Additionally, when possible, verbal and written communication should be used in conjunction in order to encourage patient participation in their own care [23]. In these discussions, providers should take careful note of medical and psychiatric comorbidities, medications, histories of chronic pain or substance abuse, and past postoperative pain regimens if available. If there is a concern for misuse or abuse, prescription drug monitoring programs (PDMPs) should be queried to ensure that patients are not "doctor shopping" and to avoid polypharmacy.

Prescribers should also use this time to educate patients on proper medication disposal for unused opioids as many of these may be diverted for nonmedical use [24]. The Federal Drug Administration (FDA) recommends disposal at approved collection programs and sites [25]. If there are no programs or locations nearby, patients may flush approved medications down the toilet or dispose of them in the trash. Lists of approved drug disposal sites as well as approved flush medications can be found on the FDA website [25].

Opioids

Opioids, when prescribed appropriately, are an invaluable tool for perioperative pain control. Clinical opioids are agonists to mu opioid receptors, with additional activity at delta and kappa opioid receptors. These receptors are distributed throughout the central nervous system and, when bound, inhibit the nociceptive pathways to the brain and produce the classic analgesic effects [26, 27]. In general, opioids should be used orally and as an adjunct in multimodal regimens. Additionally, these medications should be prescribed at the lowest effective dose for the shortest duration possible as misuse and overdose have been linked with increasing opioid doses [28–30]. Lastly, clinicians should be wary of common side effects including respiratory depression, constipation, nausea, vomiting, sedation, and miosis.

No specific regimens have been specified for thyroid and parathyroid surgery. However, in evaluating postoperative pain following these endocrine surgeries, a vast majority of patients required less than twenty oral morphine equivalents [31]. The Centers for Disease Control and Prevention (CDC), APS, ASA, and AAFP are easily accessible sites for determining opioid conversions and morphine equivalent (OME) doses [19, 20, 32, 33]. Due to the potential for addiction and diversion, as well as low OME requirement, *opioids should be used sparingly in thyroidectomy and parathyroidectomy and should primarily act as a rescue medication for breakthrough pain*. Tramadol is an effective opioid medication shown to have low potential for dependence and abuse with low side effects [34, 35]. This medication may be an appropriate choice following thyroid and parathyroid surgery.

Non-opioid Alternatives

Non-opioid alternatives have been shown to be very effective for perioperative pain control with minimal side effects. As part of the multimodal approach as recommended by the ASA and APS, these regimens have been shown to decrease the prescription and consumption of opioids [19, 20, 36]. Acetaminophen, NSAIDs, and local anesthetics in particular have a large amount of evidence advocating for their use. Ketamine and gabapentinoids are also options for pain control. Figure 11.1 demonstrates a proposed multimodal regimen for patients undergoing thyroidectomy and parathyroidectomy. Common dosing and adverse reactions for these medications are listed in Table 11.1.

Acetaminophen

Acetaminophen has been shown to be exceedingly efficacious as a perioperative analgesic across many different specialties and various procedures [37–39]. The exact mechanism for acetaminophen is unclear although it is generally considered to be a weak prostaglandin antagonist with minor interaction with sero-

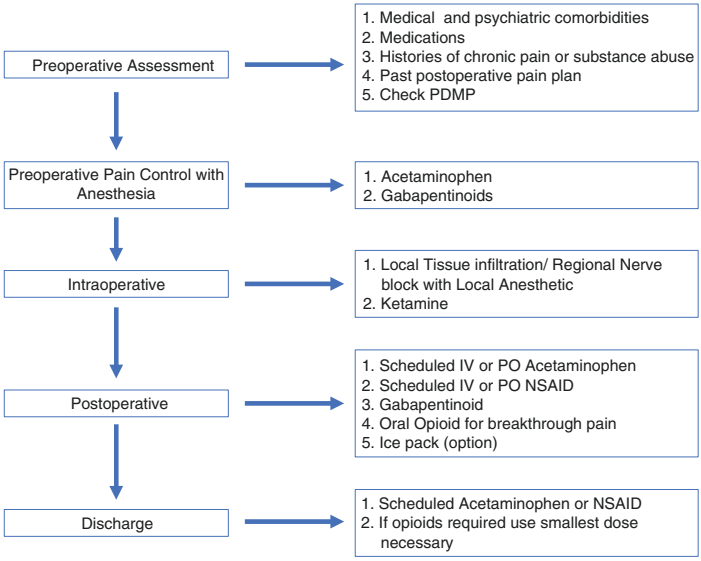

Fig. 11.1 Proposed multimodal analgesic algorithm for patients undergoing thyroid and parathyroid surgery

tonergic pathways. Although acetaminophen lacks anti-inflammatory properties, it has been shown to be effective in thyroid and parathyroid surgery [9, 40, 41]. It is one of the most frequently prescribed postoperative medications and remains a consistent recommendation from both the American Society of Anesthesiologists and the American Pain Society [19, 20]. Of note, timing of administration may also play a role in acetaminophen use. Studies have demonstrated that when prescribed preoperatively, acetaminophen reduces the consumption of opioids and other pain medications [9, 40]. Perioperative pain scores are also reduced compared to controls [9, 40, 41]. Postoperatively, the ASA and APS both recommend that acetaminophen be scheduled as opposed to on an "as needed" basis [19, 20]. Both intravenous and oral routes of administration have been shown to be practical courses following surgery [42, 43]. Effective dosing is 500–1000 mg every 4 to 6 hours with a maximum of 4000 mg daily as to limit the risk for hepatic dysfunction.

Table 11.1 Common dosing and adverse reactions of non-opioid alternatives

Type		Dose	Frequency	Route	Adverse reactions
Acetaminophen		500–1000 mg	q6h	PO/IV	Nausea, headache, hepatotoxicity
NSAID	Ibuprofen	400–800 mg	q6h	PO	Renal dysfunction, bleeding, GI ulcers, tinnitus, allergic reactions
	Ketorolac	10–20 mg	q4–6h	PO	
	Celecoxib	400 mg postoperative; 200 mg daily	qd	PO	
Local anesthetics	Lidocaine	1–2%	Intraoperative	Local infiltration	Dizziness, headache, blurred vision, twitching muscles, prolonged numbness
	Bupivacaine	0.25–0.5%	Intraoperative	Local infiltration	
	Levobupivacaine	0.5%	Intraoperative	Local infiltration	
Ketamine		0.1–0.2 mg/kg bolus, 0.3 μg/kg infusion	Varies	IV	Agitation, anxiety, dysphoria, hallucinations, sedation, nausea, vomiting, bradycardia, hypotension
Gabapentin		600–1200 mg preoperative; 600 mg postoperative	Once preoperatively; TID postoperatively	PO	Drowsiness, unsteadiness, nausea, anxiety, confusion, dry mouth

h = hour; *IV* = intravenous; *kg* = kilogram; *mg* = milligram; *PO* = by mouth; *q* = every; *qd* = daily

NSAIDs

Nonsteroidal anti-inflammatory drugs (NSAIDS) are an equally efficacious option for postoperative analgesia management following thyroid and parathyroid surgery. This class of medications works through reversible inhibition of cyclooxygenase enzymes (COX-1 and COX-2), thereby reducing the formation of thromboxane and the prostaglandins that mediate inflammation (Fig. 11.2) [44, 45]. The use of NSAIDs in thyroid and parathyroid surgery has been compared against placebo, opioids, and local anesthetics and was found to reduce the amount of consumption of rescue analgesics against all controls [8, 46, 47]. Against placebos, NSAIDs decreased postoperative pain scores and time to rescue analgesics as well [8, 47–49].

Despite their proven value, NSAIDs have historically been avoided by surgeons due to the perceived risk of bleeding as well as gastrointestinal and renal complications. Recent studies have examined this risk and found that this fear may be unwarranted as

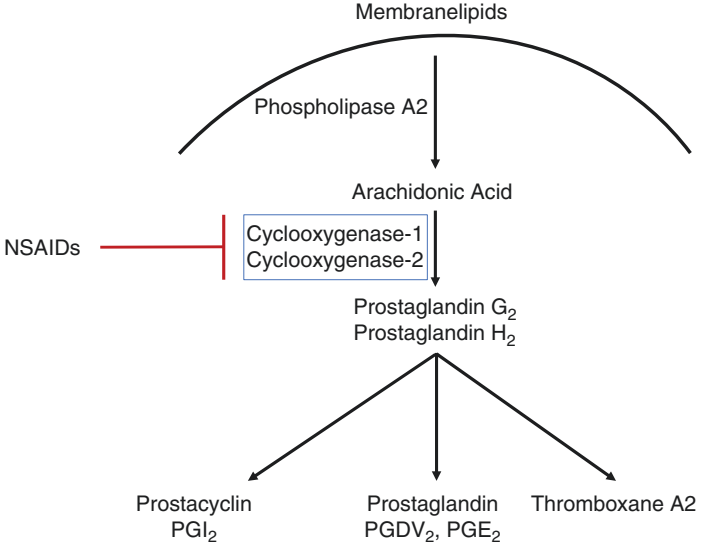

Fig. 11.2 Mechanism of action for NSAIDs

available evidence has shown exceedingly low levels of excessive bleeding with NSAID use post thyroid and parathyroid surgery [36]. Controversy still remains however; one NSAID, ketorolac, has been demonstrated to provide appropriate perioperative analgesia, but there is evidence that its use may elongate bleeding time and reduce platelet aggregation [40, 50]. A study by Lee et al. demonstrated that more than two doses of ketorolac were an independent risk factor for post-thyroidectomy hemorrhage [51]. Thus, when using ketorolac, consider low doses (10–20 mg PO q4–6hr PRN) for no longer than 5 days, or consider alternative NSAIDs. In cases where gastric complications and bleeding are feared, COX-2-selective inhibitors may prove to be a suitable alternative. While there have been no endocrine surgery-specific trials examining the relationship between COX-2 inhibitors and bleeding, Schop et al. and Smirnov et al. both demonstrated the value of etoricoxib in the preoperative and postoperative periods as both demonstrated decreased postoperative pain scores and rescue analgesic consumption [47, 48]. There have been no studies evaluating oral compared to intravenous routes of administration specifically for endocrine surgery. In general, both routes have been shown to be effective and can be considered postoperatively [52].

Local Anesthetics

Local anesthetic injection improves postoperative pain and analgesic consumption following thyroid and parathyroid surgery. Many different local anesthetics have been evaluated for viability for pain control; however, bupivacaine, ropivacaine, and lidocaine were most frequently studied for thyroid and parathyroid surgery [53–69]. Local anesthetics reversibly inhibit sodium influx through voltage-gated sodium channels, thereby blocking nerve conduction, suppressing central sensitization, and decreasing release of peripheral inflammatory mediators (Fig. 11.3). When used intraoperatively, numerous studies have demonstrated local anesthetics to be effective in decreasing postoperative pain scores and analgesic requirements [53–55, 57–70].

Although understanding the value of local anesthetics is significant, knowledge of the techniques in which to use this

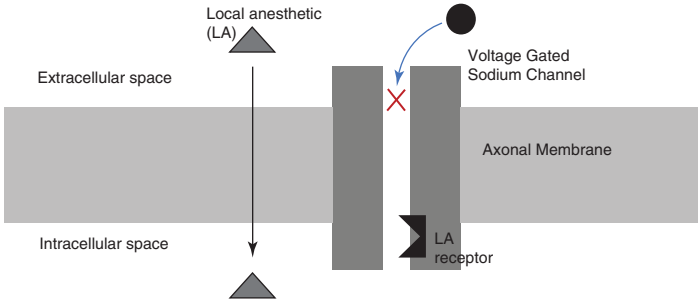

Fig. 11.3 Mechanism of action for local anesthetics

medication is equally important. There are two main regional techniques performed to provide postoperative analgesia following thyroid surgery, bilateral superficial cervical plexus block (BSCPB) and local wound infiltration (LWI) [71]. LWI is performed by injecting the anesthetic along the planned incision line. BSCPB, as compared to LWI and the other pain modalities previously mentioned, requires some anatomical knowledge and skill to be successful. BSCPB is typically placed at Erb's point along the posterior edge of the sternocleidomastoid muscle [71]. Both of these techniques block superficial innervation to the skin, and previous studies have demonstrated that both methods reduce postoperative opioid requirements, making them effective techniques for perioperative analgesia [53, 54, 59, 60]. While both techniques are comparable and have low risks of complications (local pain, infection, bleeding, and changes in blood pressure), BSCPB may subject patients to further potential complications such as nerve blockade, hematoma, or local anesthetic toxicity, and thus, image-guided placement should be considered [71]. Overall, local anesthetic use is safe, effective, and efficient with the current evidence and available literature citing this class as invaluable agents for perioperative pain.

Gabapentinoids

Gabapentinoid use has been extensively studied with current guidelines recommending the use of gabapentinoid as a

preoperative component to multimodal analgesia [72–74]. Gabapentinoids interact at the binding site of the alpha-2 delta subunit of voltage-gated calcium channels [75]. This interaction decreases the calcium influx, thereby reducing neurotransmitter release and neuronal excitability (Fig. 11.4) [76]. This class of medication has become increasingly popular over the last decade, and in 2016, gabapentin was the tenth most prescribed pain medication with over 64 million prescriptions dispensed [77]. Despite its value as an analgesic, gabapentinoids pose the risk of abuse, especially to those with a history of opioid abuse [78, 79]. Clinicians should be cautious of prescribing these medications to high-risk populations and should continually monitor patients (through PDMP and follow-up appointments) for signs of abuse [78, 80]. The most common side effects reported for gabapentinoids are somnolence, dizziness, fatigue, headache, and ataxia [76, 77, 81, 82]. Optimal dosing for gabapentin lacks consensus and varies between institutions; however, 600–1200 mg 1–2 hours preoperatively has been met with favorable results. Alternatively, 150–300 mg of pregabalin is generally accepted dosing for thyroidectomy patients.

Ketamine

Ketamine was originally synthesized in the 1960s as an anesthetic agent with minimal cardiorespiratory effects. In the 1980s, interest spurred around ketamine as an analgesic with many studies supporting ketamine use in the perioperative period [83, 84]. Ketamine acts as an N-methyl-d-aspartate (NMDA) receptor antagonist. The NMDA receptor is abundant in the central nervous system and is critical to many CNS functions including synaptic plasticity, memory function, and nociceptive transmission [85, 86]. By binding to these receptors, ketamine is thus able to attenuate centrally mediated pain processes [87]. While there have been only a few studies examining the use of ketamine for thyroid and parathyroid surgery, there is evidence that ketamine may be a reliable perioperative option for both pain and nausea control for endocrine surgeries [88–91].

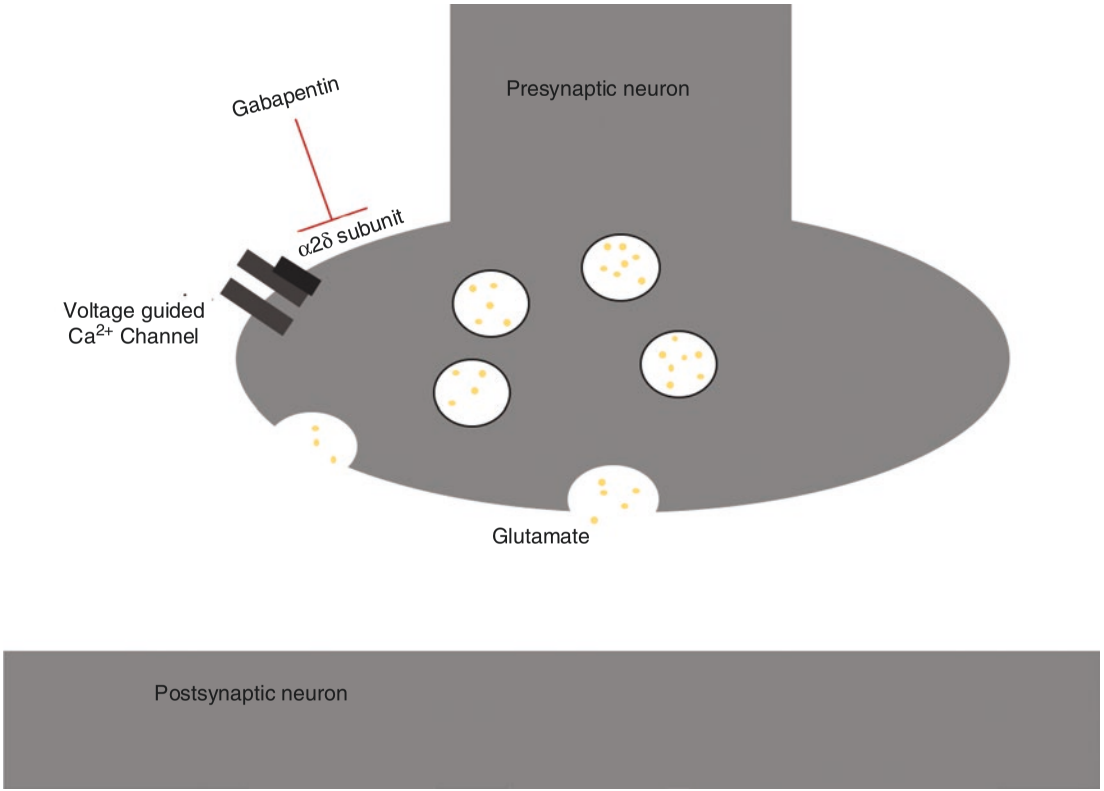

Fig. 11.4 Mechanism of action for gabapentinoids

This medication is not without risks. A majority of ketamine's adverse effects affect the psyche, including agitation, anxiety, dysphoria, and hallucinations, although dizziness, nausea, sedation, and tachycardia are common as well [87, 92]. These adverse effects are dose dependent, and thus, prescribers should be cognizant of these potentials and monitor patients closely [90, 93]. Dosing should consist of a 0.1–0.2 mg/kg bolus followed by 0.3 μg/kg infusion [87]. These considerations should be discussed preoperatively with the patient and anesthesiology care team.

Nontraditional Pain Control

As the opioid epidemic continues, more research has been conducted evaluating the efficacy of nontraditional pain control. Cognitive-based therapies, such as music, hypnosis, or guided imagery, have been studied with no clear benefits or adverse results [19, 20]. Physical modalities including acupuncture, massage therapy, and cold therapy have reported varying results as well [19, 20, 94–98]. One such study, evaluating the use of ice packs following midline abdominal surgeries, reported significantly decreased postoperative pain scores and opioid consumption as compared to controls [99]. While no specific study has been performed for thyroid and parathyroid surgeries, innocuous supplements such as ice packs may represent a simple and cost-effective adjuvant analgesic therapy. As of today, there is direct evidence for cognitive- or physical-based pain control directed at thyroid and parathyroid surgery.

Summary

Thyroid and parathyroid surgery are safe outpatient procedures resulting in mild to moderate postoperative pain. An individualized approach should be taken toward pain control for patients. Preoperative discussions including postoperative pain expectations, medications, and past medical and surgical history should be completed for every patient. Multimodal approaches to pain

focusing on non-opioid alternatives including NSAIDs, acetaminophen, and local anesthetics have demonstrated decreases in postoperative pain, opioid consumption, and opioid prescription.

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12

Evidence-Based Perioperative Analgesia for Otolaryngology: Head and Neck Surgery

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Head and Neck Surgery

Adequate perioperative analgesia following general otolaryngologic and head and neck surgery is an important consideration. It is well known that improved pain control contributes to faster

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recovery by encouraging earlier mobilization and participation in functional rehabilitation. Control may be difficult to achieve in head and neck cancer patients, whom often have unique pain management issues such as the inability to swallow oral medications as a direct manifestation of disease or subsequent consequence of surgical management. As the number of prescriptions for opioids and associated opioid-related deaths in the last two decades has been rapidly increasing, the role of opioids in the management of pain in head and neck cancer patients has come under question. In addition to the risk of dependence in a patient population with widespread nicotine and alcohol abuse, the use of opioids is known to be associated with a number of adverse effects, such as constipation, nausea, vomiting, sedation, respiratory depression, and potential for abuse [1].

In a 2017 consensus statement, the Enhanced Recovery after Surgery (ERAS) Society recommended opioid-sparing analgesia for major head and neck cancer surgery involving free flap reconstruction [2]. Pain management strategies involving a multimodal approach involve the use of a combination of local anesthetics and perioperative administration of acetaminophen, NSAIDs, and gabapentin to facilitate rapid recovery and decrease postoperative opioid requirements. Regional anesthesia, involving the use of blocks, may be an effective alternative but depends on a number of factors including the donor site. One retrospective study by Oltman et al. looked at the feasibility and safety of multimodal analgesia in patients undergoing outpatient otolaryngologic procedures (thyroid, parathyroid, and parotid surgery) with same-day discharge [3]. In the study, a single dose of oral acetaminophen (1000 mg), gabapentin (100–300 mg), and meloxicam (7.5 mg) or celecoxib (200 mg) was administered 1 hour before surgery. Incisions were infiltrated with 1% lidocaine with 1:100,000 epinephrine solution or 0.25% bupivacaine with 1:200,000 epinephrine solution, and patients were given intravenous fentanyl postoperatively. Following resumption of oral intake, patients were given oral ibuprofen (600 mg) and acetaminophen (500 mg) every 6 hours on an alternate staggered schedule. Of the 69 patients included, 39 (61%) were able to avoid postoperative narcotic use upon discharge, while 56 patients (88%) reported high or very high satisfaction with multimodal analgesia.

An analysis by Du et al. evaluated multimodal analgesia after non-aerodigestive procedures with subsequent inpatient admission [4]. Surgeries were subcategorized into minor (thyroidectomy, parathyroidectomy, parotidectomy, lymph node excision, and neck mass excision) and major (glossectomy, partial or total pharyngectomy, mandibulectomy, total laryngectomy, and modified or radical neck dissection) head and neck procedures. Postoperative analgesic protocol involved the use of acetaminophen (1000 mg IV or 650 mg PO every 4–6 hours) and ketorolac (15 mg IV every 6 hours for 48 hours). Preoperative analgesia included pregabalin (100 mg PO) for major head and neck surgeries which continued as a dose of 50 mg BID for 10 days. The findings of the study revealed an overall one-third reduction in the postoperative opioid requirements used in the first 24 hours after implementation of the multimodal analgesia protocol. However, this reduction in opioid use did not carry throughout the hospital course. The authors attributed this result to the fact that ketorolac was limited to the first 48 hours after surgery, as well as differences in cumulative opioid use which may have been missed when averaged over the length of hospitalization.

Understandably, the use of NSAIDs in the perioperative setting to control pain is often met with skepticism due to the perceived risk of bleeding as a result of antiplatelet effect. There is growing evidence that ketorolac, celecoxib, and other NSAIDs appear to provide effective analgesia without a significant risk of bleeding within head and neck patient populations when combined with meticulous intraoperative hemostasis (19). In another study, Chin et al. studied the use of ketorolac after thyroid surgery and found no difference in the rate of bleeding complications (21). However, in patient undergoing free-tissue transfer, the threshold for return to the operating room to control postoperative bleeding is lower due to concern of flap failure and microvascular thrombosis. In fact, one large retrospective cohort study of 3498 patients admitted for otolaryngologic surgery found that bleeding complications were associated with concomitant use of antiplatelet medications and venous thromboembolism prophylaxis [5]. The study noted bleeding incidence was significantly higher in the chemoprophylaxis group (11.9%) and more likely to occur when intraoperative ketorolac and prophylactic heparin were administered together.

Another study found no evidence to suggest a higher likelihood of bleeding after ketorolac administration in head and neck free-tissue transfer patients, although they also found no perceived analgesic benefit and subsequently no reduction in narcotic requirements [6]. As a result, the use of NSAIDs in the perioperative setting should be individualized, and further study is needed to justify the analgesic benefit in light of potential risk of bleeding within the head and neck population, particularly for "major" head and neck procedures.

Smith et al. investigated the postoperative use of intravenous acetaminophen (1 g every 6 hours for 24 hours after surgery) in a prospective study of 48 patients who underwent surgical resection for head and neck cancers [7]. They reported comparable low pain scores (0.8 vs. 1.0, $p = 0.408$) when compared to a retrospective cohort that only received opioid patient-controlled analgesia and breakthrough narcotics, respectively. In addition, they found a significant reduction in total narcotic requirements in the first 8 hours after surgery (13.5 vs. 22.5, $p = 0.014$) and significantly decreased length of stay (7.8 vs. 10.6 days, $p = 0.03$) when using intravenous acetaminophen. These findings suggest that intravenous acetaminophen is an efficacious non-opioid alternative that may be used to decrease postoperative opioid requirements while adequately controlling pain. A summary of common analgesics including benefits, adverse effects, and dosing can be found in Table 12.1.

Free Flap Reconstruction

There are a wide of array of free flap techniques available for microvascular reconstruction of head and neck cancer resections. The most common ones in the authors' training and practice include radial forearm, fibula, scapula, and anterolateral thigh (ALT) flaps. While most of these patients tend to have successful outcomes, it is important to recognize factors which can prolong hospitalizations and delay recovery, as these can cause significant complications and patient harm. Such complications include nosocomial infections, venous thrombosis, and atelectasis and have

Table 12.1 Summary of analgesics

Analgesic type	Mechanism of action	Benefit	Adverse effects	Common dosing	Cost
Acetaminophen	Unclear although considered to be a weak inhibitor of prostaglandins with possible interaction of serotonergic pathways	Excellent safety profile, may adequately control postoperative pain while reducing the immediate need for opioid use as a rescue analgesic after surgery. Safe to use in asthmatic and aspirin-intolerant patients	Nausea, vomiting, constipation, hepatotoxicity	325–650 mg PO/IV q4hr PRN	Low for oral tablets; moderate-high for intravenous formulation
Alpha-2 agonists	Inhibit adenylyl cyclase activity, preventing calcium ions from entering the nerve terminal, leading to a suppression of neural firing	Associated with reduced anesthetic requirements, attenuated heart rate, and blood pressure. Can also help with anxiolysis, sedation, attenuation of sympathoadrenal response to laryngoscopy and intubation, and postoperative analgesia	Sedation, dry mouth, nausea, vomiting, bradycardia, hypotension, loss of smell	Clonidine: 2–5 μg/kg bolus, 0.3 μg/kg infusion Dexmedetomidine: 1 μg/kg bolus, 0.2 μg/kg/h infusion Frequency determined by symptom severity	Low for oral tablets; moderate-high for intravenous formulation

(continued)

Table 12.1 (continued)

Analgesic type	Mechanism of action	Benefit	Adverse effects	Common dosing	Cost
Gabapentinoids	Binds at site of the alpha-2 delta subunit of voltage-gated calcium channels leading to decreases in calcium influx, thereby reducing neurotransmitter release and neuronal excitability	Known role in management of chronic pain (neuropathic, postherpetic, diabetic). Potential for controlled postoperative pain and a delay or reduction in opioid analgesic consumption	Dizziness, drowsiness, headache	600–1200 mg preoperative once; 600 mg postoperative TID	Moderate-high
Local anesthesia	Reversibly inhibit sodium influx through voltage-gated sodium channels, thereby preventing the conduction of action potentials	Regional analgesia via peripheral nerve block may permit adequate postoperative analgesia and reduce the need for any additional rescue analgesia. Quick onset of action. Simple to administer	Minimal risk, local irritation, edema. Lidocaine toxicity at concentrations above 5 μg/ml	Lidocaine 1–2%, bupivacaine 0.25–0.5%, levobupivacaine 0.5%	Low

NSAIDs	Inhibit the action of cyclooxygenase enzymes (COX-1 and COX-2), thereby reducing the formation of thromboxane and the prostaglandins that mediate inflammation	A known, safe analgesic. May reduce postoperative opioid consumption while providing adequate short-term management of mild to moderate pain	Renal dysfunction, bleeding, GI ulcers, tinnitus, allergic reactions	Ibuprofen 400800 mg q6h Ketorolac 10–20 mg q4–6h Celecoxib 400 mg postoperative; 200 mg qd	Low
Opioids	G-protein-coupled receptors inhibit adenylate cyclase, thereby reducing calcium influx and decreasing neuronal transmission	Effective analgesic, multiple routes of administration, hemodynamic stability, multiple forms (long vs. short acting)	Respiratory depression, sedation, nausea, vomiting, constipation, pruritus	Codeine 15–60 mg PO q4hr PRN Oxycodone 5–15 mg PO q4–6hr PRN Tramadol 25–50 mg PO q4–6hr PRN	Low-moderate

IV intravenous, *QD* daily, *PO* by mouth, *PRN* as needed, *TID* three times daily

been part of the impetus for development and implementation of ERAS protocols throughout the surgical community [8–10]. Surgical recovery of free flap patients also requires therapeutic activities, such as physical therapy to regain donor limb strength and mobility in cases of fibula, ALT and scapula flaps, and speech/swallow therapy in oral/oropharyngeal reconstructions, and earlier participation in such activities has been shown to improve patient functional capacities and decrease healthcare costs [11–13]. A significant factor in enhancing patient free flap surgery recovery is by optimizing patient analgesia.

One method of postoperative analgesia in free flap patients is with the use of a patient-controlled analgesia (PCA) pump, typically with opioid-derived medications. PCAs have the benefit of being patient controlled; however, this also presents problems when the patient is not consistent with their dosing and can also be difficult to wean off. Furthermore, opiates can themselves prolong hospital stays due to their side effects of constipation, altered mental effects, and possible dependence, all reasons for which there has been a significant effort to minimize opioid consumption.

As such, recent literature has studied the potential for other methods of analgesia to improve pain and recovery outcomes in free flap patients. One study by Lee et al. found better outcomes in patients treated with multimodal ketamine and gabapentin, and similar outcomes were discovered using preoperative gabapentin in patients undergoing ALT flap reconstruction [14, 15]. A few studies have also investigated the benefits of donor site blocks in fibula free flaps. Zhang et al. found decreased postoperative analgesic requirements using a regional block, while several studies have found benefit in combining epidural with general anesthesia [16–18].

In our experience, most of the pain experienced in free flap surgery stems from composite resections and is typically best treated with scheduled IV acetaminophen and an opioid along with a course of steroids to facilitate edema resolution. After the first postoperative day, most patients require only scheduled oral/enteral Tylenol and occasional opiate assistance, such as with Tylenol-codeine elixir or Roxicodone liquid, although those with

prior opioid use may require significantly more medication and possibly even a PCA. In some patients, the numbing sensation from disrupted nerves, such as a greater auricular sacrifice causing ear numbness, can be just as distressful as actual pain. In these cases, as well as in patients who are opioid intolerant, we often supplement with scheduled doses of gabapentin, typically between 500 and 1000 mg daily, for up to 1 week. Our practice has not used any particular regional or epidural blocks in the past, but these represent exciting strategies, particularly as an epidural infusion may be able to limit the required general anesthetic in patients at increased hemodynamic and cardiac risk from general anesthetics, and can be left in vivo for postoperative pain control as well.

Otology

As the majority of otologic surgeries are performed on an outpatient basis, adequate perioperative control of pain is important in potentially reducing postoperative opioid requirements. Data from the US Department of Health and Human Services identified over 11 million estimated cases of opioid misuse, over two million individuals diagnosed with opioid use disorder, and over 110 opioid-related deaths every day [19]. Therefore, knowledge of alternative perioperative pain management modalities, consideration of individualized patient pain tolerance, complete safety profiles, and the type of surgical procedure are all essential for reducing unnecessary opioid prescription.

Myringotomy and tympanostomy tube placement is the most common pediatric ambulatory procedure performed in the United States and one of the most common procedures performed by otolaryngologists [20]. Up to 70% of all patients are reported to require some form of postoperative analgesia. Current studies compare a wide range of medication doses and employ the use of various pain scores including the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS); Face, Legs, Activity, Cry, Consolability (FLACC) scale; Wong-Baker Faces Pain Rating Scale (WBS); visual analog scale (VAS); and Objective Pain Scale

(OPS); this lack of uniformity makes interpretation and establishment of validated perioperative guidelines for analgesia difficult. However, studies do suggest that low-dose monotherapy of non-opioid pain alternatives, particularly acetaminophen, may be **inadequate** for perioperative myringotomy and tube placement [21]. One study by Watcha et al. found that preoperative administration of oral ketorolac when compared to acetaminophen results in better postoperative pain control than placebo in children undergoing bilateral myringotomy [22]. Here, OPS scores for ketorolac were 1 (0–9), while those for placebo and acetaminophen were 5 (0–9) and 4 (0–7), respectively. In another study, Bean-Lijewski et al. reported lower median pain scores using ketorolac at 5 and 10 minutes but no difference of pain scores at discharge nor in post-discharge analgesic requirements [23]. They concluded the use of ketorolac in light of its slight analgesic benefit does not justify its cost in bilateral myringotomy and tympanostomy tube placement. Tobias et al. compared the effect of acetaminophen with codeine and acetaminophen alone [24]. Pain scores in the postanesthesia care unit revealed superiority of acetaminophen with codeine in the setting of tympanostomy tube placement. However, it should be noted that the efficacy of codeine is limited by its variable metabolism secondary to allelic variation of the CYP26D enzyme. There are reports of alternative pain control modalities, such as acupuncture, 4% topical lidocaine, and auricular nerve blocks; however, more studies are needed before they can be recommended. One study done by Lin et al. did report a significant reduction in median CHEOPS pain scores when comparing acupuncture to the control group (7 vs. 11 at arrival and at 5 minutes, 7 vs. 10 at 10 minutes, 6 vs. 9 at 15 minutes and 20 minutes, and 6 vs. 8 at 25 minutes and 30 minutes ($P < 0.005$)) [25].

Analgesia after tympanomastoid surgery may often be achieved with local anesthetic plus fentanyl infiltration at the surgical site or NSAIDs such as lornoxicam. In one study, Bhandari et al. found that the combination of 100 μg fentanyl with bupivacaine for field infiltration at the operative site was associated with better postoperative pain control than the combination with 50 μg fentanyl [26]. Following radical mastoidectomies, Nalini et al.

compared the difference between intramuscular lornoxicam 8 mg BID with diclofenac 75 mg BID [27]. They found that pain scores 3 days after injection of lornoxicam and diclofenac were 0.47 +/− 0.75 and 2.65 +/− 1.16, favoring the use of lornoxicam 8 mg to diclofenac 75 mg in this setting. Although support is growing for the use of greater auricular nerve blocks in the management of postmastoidectomy analgesia, evidence is conflicting. A single intraoperative greater auricular nerve block (reported as 1 hour prior to the end of the procedure) was found to provide superior analgesia when compared to intravenous morphine and subsequently reduce the need for opioids in children following tympanomastoid surgery [28]. However, in a later study, Suresh et al. reported no significant advantage for postoperative pain control when the greater auricular nerve block was performed preoperatively when compared to a sham block [29].

During a staged microtia reconstruction, most patients complain of pain at the costal cartilage donor site. As a result, local anesthetic injection as well as intercostal nerve blocks has been evaluated as potential treatments. Intercostal nerve blocks have been shown to be superior to intravenous analgesia alone when infusions of local anesthetic (0.2% ropivacaine) are injected into the operative field [30]. However, intercostal nerve blocks without continuous infusion were shown to not be as effective as blocks with continuous wound infusion.

Finally, studies involving perioperative pain alternatives for middle ear surgeries, including tympanoplasties and stapedectomies, are limited. Currently, only the use of alpha agonists such as dexmedetomidine and intravenous opioid administration has been studied at this time. In one randomized control trial, Mesolella et al. reported a decrease in adverse reactions and overall pain when using remifentanil when compared to local anesthetic [31]. The use of dexmedetomidine for pain control has been demonstrated in two randomized control trials [32, 33]. These studies found that dexmedetomidine was as effective as midazolam plus fentanyl in tympanoplasty surgeries and was superior to nalbuphine plus propofol when used with nalbuphine in middle ear surgery.

Laryngology

Anatomic site is a known significant predictor for postoperative pain [34–36]. In regard to otolaryngologic anatomy, the risk of pain in the oral cavity, pharynx, and larynx has been reported to be four to ten times higher when compared to otologic surgery [34]. However, there is a paucity of evidence for perioperative pain control in laryngeal procedures. Part of the explanation may be due to the wide variation in pain levels across laryngeal surgeries. Generally, endoscopic cases such as laryngoscopy and esophagoscopy are considered to result in "mild" postoperative pain, while major oncologic surgeries like laryngectomies result in the highest levels of postoperative pain [36]. As such, it is important to consider each laryngologic procedure on a case-by-case basis, taking into consideration patient age, gender, preoperative pain, expected pain, and surgical fear, as these have all been shown to be validated predictors of postoperative pain [34, 37–39].

In general, for minimally invasive procedures, monotherapy with non-opioids such as acetaminophen and nonsteroidal anti-inflammatory drugs can be used effectively for postoperative analgesia [36]. In practice however, many physicians prescribe additional narcotic medications. A survey of physicians noted that over 90% of otolaryngologists prescribe opioids following micro-direct laryngoscopy [40]. This same survey reported that 25% of prescribers were unaware of their patient's opioid use patterns postoperatively indicating that patients may be receiving a surplus of medications. It has been shown that overprescription of opioids leads to abuse and diversion [41, 42]. Thus, prescribers should discuss pain management with their patients prior to surgery and provide instruction for proper storage and disposal of excess medication. On the other end of the spectrum, physicians may be inadequately prescribing analgesics for laryngologic surgeries considered to cause "high" pain levels (pharyngeal surgery, laryngectomy, etc.) [36]. To ensure that patients are receiving adequate pain control, Orgill et al. recommend educating both physicians and nursing staff on adequate dosing of narcotics postoperatively, scheduling medications as opposed to "PRN," prescribing a set dose, and using patient-controlled analgesia when appropriate

[43]. The US Department of Health and Human Services (USDHHS) recommendations indicate that for moderate postsurgical pain, an adequate dose is considered to be 60 mg/d of morphine sulfate [44, 45].

Recently, the advancement of technology has allowed for new opportunities for the diagnosis and management of laryngologic procedures. Physicians now have access to high-powered, high-definition scopes, fiber-based lasers, and new injection materials among a myriad of new tools. These advances have led to a resurgence in in-office, awake procedures, including laryngoscopy, vocal fold injections, and laser procedures that provide benefit for both the physician and the patient. In-office procedures offer the advantage of cost, time, and the avoidance of general anesthesia [46, 47]. Additionally, as the patient is awake, the physician is able to observe real-time phonation before, during, and after the procedure, thereby providing more precise management and more favorable patient outcomes [47].

In-office procedures, while convenient, do pose the hurdle of managing patient anxiety and pain. Adequate anesthesia is of the utmost importance, and for many laryngeal procedures, this can be achieved via topical anesthetics and local anesthesia to the superior laryngeal nerve. In general, 2–4 ml of 4% lidocaine is efficacious for laryngeal procedures [48, 49]. Topical anesthesia may be applied in a few different methods. Transtracheal injection of lidocaine has been shown to be tolerable, effective, and straightforward to perform. For direct visualization and anesthesia, a flexible or rigid scope can be used in conjunction with a long cannula or syringe to apply local anesthetic. Lastly, nebulization of local anesthetic (4% lidocaine) may be used; however, this method may also require an adjunct anesthesia method [50]. With all of these methods, a laryngeal gargle should be employed to ensure that the local anesthetic is able to coat the entire laryngeal mucosa [51].

Adequate pre-procedure anesthesia results in many patients requiring very little to no postoperative analgesia. However, physicians should be cognizant that patients can still experience non-insignificant pain and discomfort post procedure [52]. In some cases, patients experience pain for up to a week following in-

office procedures [52]. As such, it is important to discuss pain expectations and pain control options with the patient prior to the procedure. Postoperative pain management for in-office procedures should be multimodal with the use of non-opioids such as acetaminophen and NSAIDs as the crux of the regimen. Opioids should be used in the cases of breakthrough pain [35].

Pediatrics

Assessment and management of pain in the pediatric population are a difficult task. Although children experience the same perioperative pain that adults face, quantifying extent is a challenge, and acute pain in this population is often undertreated [53]. In the pediatric population, there are three general methods to characterize pain: self-reporting, behavioral, and physiologic. Of these three, self-reporting is the most reliable and the closest to an objective measure [54]. Standardized pain scores have improved the physicians' ability to treat postoperative pain in children [55]. However, this method still depends on the child's ability to communicate and describe their pain. This capacity for communication changes with the child's experience level and stage of development and generally increases as the patient gets older [56]. Behavioral manners are more often seen in younger populations and consist of crying, body movements, facial expressions, and verbalizations. Physiologic measures refer to increases in heart rate, blood pressure, oxygen saturation, and diaphoresis. These have been shown to correlate with self-reported pain and however are often multifactorial and can be difficult to interpret on their own [57, 58].

There are a variety of factors that may affect the level of postoperative pain, the foremost being type of surgery. In the pediatric population, however, there is a lack of available literature on perioperative pain for otolaryngologic procedures, with the exception of tonsillectomy [59–63]. Emotional factors, such as anxiety, fear, and lack of social support, have also been shown to be factors that may exaggerate physical pain in children and adolescents [64, 65].

As for pain management strategies, current guidelines for the pediatric population are based on generally low-level evidence –

due to the ethical implications of randomized control trials in children. However, a majority of prescribers agree that a multimodal approach should be taken with emphasis on non-opioid alternatives whenever feasible [66, 67]. NSAIDs and acetaminophen have been shown to be effective perioperative pain control options in the pediatric population [59–61]. Opioids, when used appropriately, are also extremely effective at managing perioperative pain. In general, opioids should be prescribed as a "rescue" medication for breakthrough pain. Additionally, children who are prescribed opioids should be monitored closely for adverse events. Of note, the FDA released new guidelines in 2017 regarding the use of codeine and tramadol for children. It is now recommended to avoid codeine in children younger than 12 years regardless of indication and up to the age of 18 in patients undergoing tonsillectomy and/or adenoidectomy for obstructive sleep apnea. Tramadol recommendations include avoidance in children younger than 12 years and in children younger than 18 years after ENT surgeries. In the pediatric population, opioid consent should be discussed with both the patient and their family [68]. During this discussion, families should also be educated on the storage and disposal of unused medications as to prevent misuse, abuse, and diversion [69]. In general, opioids should be kept separate from normal medications and out of the reach of children in a locked container [69, 70].

Medication dosing should be based on the patient's age, weight, and past regimens (if applicable) [35]. Appropriate route of administration for analgesics should be considered such that additional discomfort is avoided. For most pediatric otolaryngologic cases, oral or rectal administration is appropriate for postoperative pain. Intravenous routes may be appropriate for intraoperative management, with acetaminophen or ketamine, for example, and should be discussed with the anesthesia team prior to surgery. Additionally, doses of analgesics should be scheduled as opposed to given on an "as needed" basis [35].

Nonpharmacological strategies may also be considered in the pediatric population. Although there are no ENT-specific studies evaluating the efficacy of these adjuvant treatments, distraction methods, patient support, and cold/heat therapy have been shown to be effective in reducing perceived pain in children [71–73].

Sleep Surgery

Obstructive sleep apnea is a disease characterized by intermittent and repetitive narrowing of the airway during sleep [74]. Surgical procedures for treatment of this disease are aimed at addressing specific sites of obstruction. In sleep surgery, perioperative pain control is an important consideration as these procedures may cause severe postoperative pain [75]. Intolerable pain can lead to increased hospital stays, dehydration, and poor patient outcomes [36]. Thus, many physicians prescribe increasing amounts of opioids in a preemptive attempt to reduce postoperative pain [42, 76]. However, as the authors have mentioned, while this tactic may lead to well-managed pain, it also lends to the risk of the overprescription of narcotics and subsequent misuse and abuse. Therefore, it is important for physicians to understand effective, evidence-based, non-opioid alternatives for sleep therapy.

In many cases, non-opioid regimens provide adequate analgesia without the use of additional narcotics. For tonsillectomy and adenoidectomy, which are known to be notoriously painful otolaryngologic procedures, NSAIDs, acetaminophen, and alpha-2 agonists have been shown to be efficacious at managing pain without increasing complications or length of stay [59–61]. Despite the fear that NSAID use may lead to postoperative bleeding, recent studies have refuted the concern. McClain demonstrated that NSAID use (ketorolac) following tonsillectomy and uvulopalatopharyngoplasty led to no increase in postoperative hemorrhage as compared to morphine. [77]

Uvulopalatopharyngoplasty (UPPP) has been the most common sleep apnea surgical procedure performed in the past 25 years [78, 79]. By rearranging the tonsils, palate, and uvula, UPPP increases the size of the airway and decreases potential tissue collapse. Multiple studies focusing on UPPP have shown the efficacy of local anesthetics in the perioperative period [80–82]. Li et al. demonstrated significantly reduced visual analog scores in patients receiving preoperative ropivacaine compared to control groups [82]. Intraoperatively, liposomal bupivacaine, a long-acting local anesthetic, reduced the consumption of postoperative opioids and allowed for shortened time to first oral intake [81]. An

active area of ongoing research, local anesthetics may also prove to be efficacious in the postoperative period as well. Ponstein et al. presented early experience with continuous lesser palatine nerve blocks and demonstrated the additional role of local anesthetics in multimodal analgesic regimens.

Multiple procedures have been established to address airway obstruction originating from the tongue. These procedures, namely, hyoid myotomy, genioglossal advancement, and hypoglossal stimulation, aim to relieve upper airway collapse by increasing retrolingual space. Unfortunately, there is a lack of evidence regarding analgesic guidelines for these procedures. However, these authors' experiences suggest that the utilization of non-opioids such as local anesthetics preoperatively and NSAIDs postoperatively are effective options for primary analgesia. Of note, a physician in Thailand demonstrated that hyoid myotomy with suspension as well as genioglossus advancement procedures may be done solely under local anesthesia with low probabilities of complications [83]. While this method has shown effective in one cohort, further study needs to be done to elucidate the feasibility of this technique.

Overall, pain control in sleep surgery is similar to that of other head and neck procedures. Pain should be addressed in a multimodal fashion, favoring non-opioid alternatives prior to opioids. These authors suggest a regimen of preoperative local anesthetics paired with postoperative scheduled NSAIDS and acetaminophen. Opioids should be utilized as a rescue medication should there be breakthrough pain.

Sinonasal Surgery

Sinonasal surgeries, including septoplasty, rhinoplasty, and endoscopic sinus procedures, offer a range of evidence-based analgesic strategies based on the extent of surgery required and surgeon experience. The vast majority of these are ambulatory procedures, and opiate derivatives have long been prescribed as postoperative analgesics. In fact, studies have shown that opiates are often overprescribed for these procedures and thereby increase the risk of

diversion [84]. However, as more focus is turned to ERAS protocols as well as the attempt to limit opioid prescriptions, recent studies have sought to determine the optimal combinations of analgesic agents in both the operative and postoperative setting to maximize patient comfort while minimizing opioid use.

Local Anesthetic Blockade in Sinonasal Surgery

Perhaps the most important factor in optimizing pain management for sinonasal surgery is the quality of local anesthetic blockade. A consensus of studies and meta-analysis has determined that local anesthetic is one of the biggest factors in reducing postoperative pain for such procedures [85–90]. Anesthetics studied included bupivacaine, levobupivacaine, and lidocaine, although no agent was found to be significantly more efficacious [91, 92]. Frequent methods of local anesthetic introduction include via local anesthetic-soaked nasal sponges, whose postoperative analgesic benefits can last long after their duration of action [73], as well as locoregional blocks of the infraorbital nerve [87, 93] and sphenopalatine ganglion (SPG), all of which have proven significantly effective in the appropriate setting [86, 88, 92, 93].

The SPG (Meckel's ganglion or pterygopalatine ganglion) is a parasympathetic ganglion found within the pterygopalatine fossa which also provides sensation to the nose, palate, orbit, and buccal mucosa and is also a target in patients with migraines, cluster headaches, and facial neuralgias [94, 95]. Blockade of the SPG is among the most cited and useful locoregional blockades in sinonasal surgery, with Scott et al. even describing a series of 55 patients who underwent in-office maxillary antrostomies and ethmoidectomies with or without sphenoidotomies, all of whom were satisfied with the analgesia provided and none of whom required postoperative pain medication [96].

The authors have had success with a similar blockade targeting the SPG and its sensory branches (Fig. 12.1). After decongesting and anesthetizing the nasal cavity with pledgets soaked in 1:1000 epinephrine and 1% lidocaine, a 25 gauge spinal needle is bent at

a 45° angle 1–2 cm from its tip and used to first infiltrate the area of the SPG at the attachment of the middle turbinate, near the sphenopalatine foramen (Fig. 12.2a), followed by above and below the tail of the inferior turbinate, at the level of the crista ethmoidalis and transitional zone. This anesthetizes the sphenopalatine and nasopalatine nerves as well as the superior and inferior lateral nasal nerves. By including a 1:100,000 concentration of epinephrine, this also provides excellent hemostasis, although it is important to draw back on the needle to avoid injecting directly into a branch of the sphenopalatine artery. Next, the uncinate, head, and axilla of the middle turbinate are injected (Fig. 12.2b), followed by the lateral nasal wall to anesthetize the anterior ethmoid nerve (Fig. 12.2c), and then the inferior turbinate.

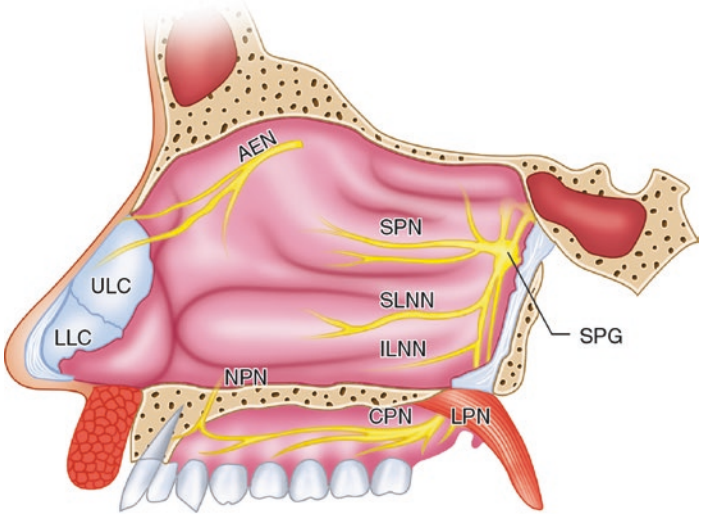

Fig. 12.1 Sagittal cross section of nasal cavity showing the lateral nasal wall and sensory branches of the sphenopalatine ganglion. Cutaway of sphenopalatine foramen and portion of pterygoid bone. *AEN* anterior ethmoid nerve, *GPN* greater palatine nerve, *ILNN* inferior lateral nasal nerve, *LLC* lower lateral cartilage, *LPN* lesser palatine nerve, *NPN* nasopalatine nerve, *SLNN* superior lateral nasal nerve, *SPG* sphenopalatine ganglion, *SPN* sphenopalatine nerve, *V2* maxillary branch of trigeminal nerve

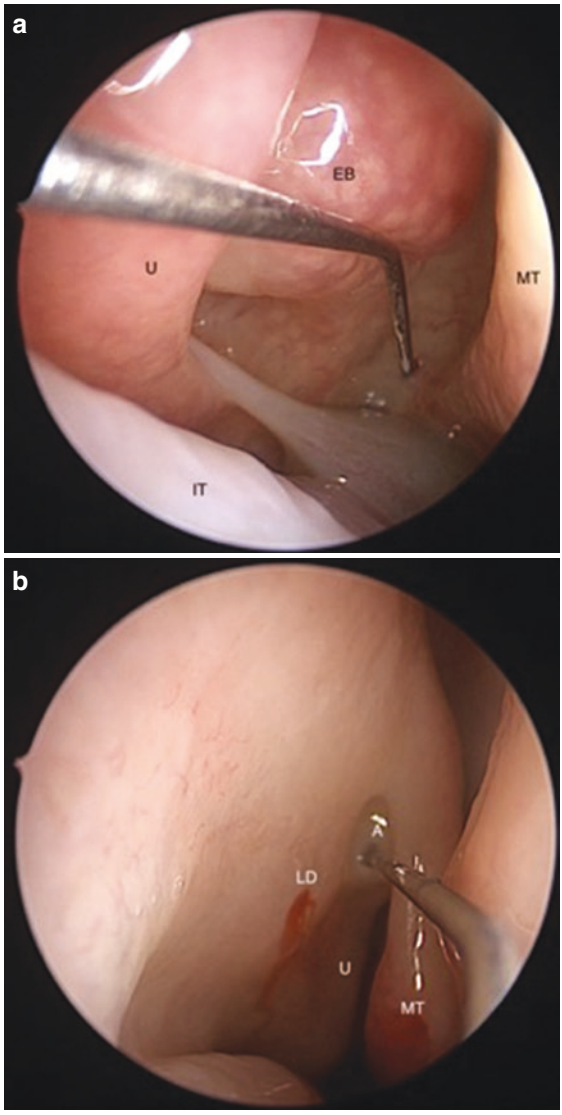

Fig. 12.2 **a**. Injection into the posterior attachment of the middle turbinate near the sphenopalatine foramen. **b**. Injection into axilla of the middle turbinate. **c**. Injection targeting the anterior ethmoid nerve along the lateral nasal wall, anterior to middle turbinate and above inferior turbinate, typically near the lacrimal system. *A* axilla of middle turbinate, *EB* ethmoid bulla, *IT* inferior turbinate, *LD* lacrimal duct/sac, *MT* middle turbinate, *U* uncinate process

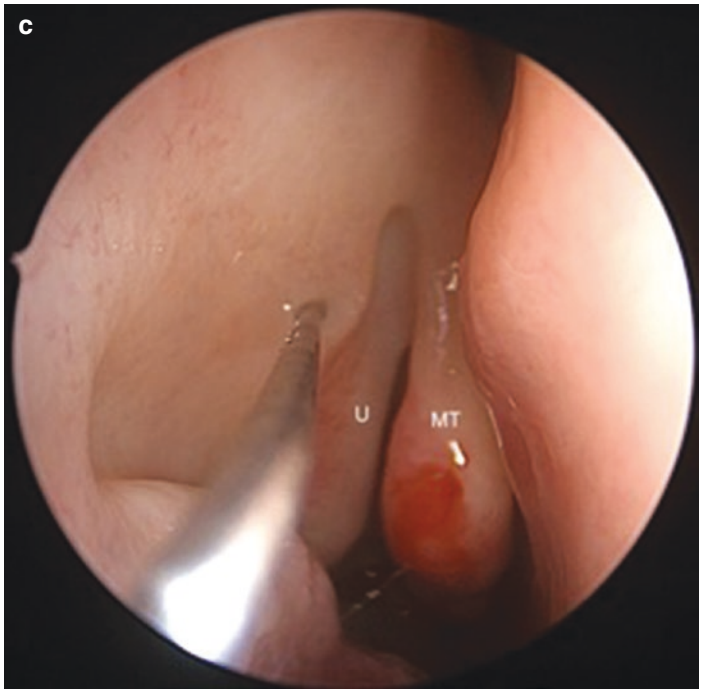

Fig. 12.2 (continued)

Perioperative Analgesia in Sinonasal Surgery

Among intravenous agents, acetaminophen has the largest body of evidence in optimizing analgesic outcomes for sinonasal surgery. The addition of acetaminophen during preinduction has been shown to improve postoperative pain scores and lower analgesic requirements [89, 97–100]. The preponderance of benefit with minimal risk makes acetaminophen an excellent perioperative agent, though it should be given at least 10 minutes prior to induction.

Perioperative administration of nonsteroidal anti-inflammatory drugs (NSAIDs) has also proven to be effective option in reducing postoperative pain, although most studies also emphasize the importance of quality local anesthetic blockade when considering using an

NSAID as a single agent [90, 101–104]. While increased bleeding risk is a concern when using NSAIDs, intraoperative Toradol had not been shown to significantly increase bleeding risk, and none of the studies analyzed in recent meta-analysis listed severe bleeding or hematomas as complications [89, 90, 103]. Another concern with using NSAIDs in patients undergoing sinus surgery is potential intolerance, particularly in patients with polyposis. Nausea and vomiting are also seen at higher rates than other analgesics, in over 20% of patients, so antiemetics should be prophylactically prescribed for the immediate postoperative period [89, 90].

Although alpha agonists, such as clonidine, have previously been reported as potential analgesics for nasal procedures, the majority of studies show they are not superior to standard sedatives and opiates and do not provide significant analgesic benefit [105–108]. However, intraoperative alpha agonists have shown significant benefit in providing optimal hemodynamic stability [105, 109].

Postoperative Analgesia in Sinonasal Surgery

It is important to anticipate the stresses a patient can face in the postoperative setting, as these increase anxiety and can further contribute to patient pain [110]. For this reason, it is important to review the postoperative expectations beforehand, such as the potential for soreness, numbness, nasal congestion, and nasal packing or splints. Surgeons are often tempted to prescribe opiates to help alleviate stress and anxiety, but this often leads to overprescribing and possible distraction [109, 111].

Acetaminophen in particular has been shown to be a standalone option for postoperative pain control in lieu of opioids, with minimal dosing requirements particularly when prescribed as a scheduled dose as opposed to as needed [97, 99]. The quantitative analgesic benefits combined with its minimal side effect profile make it the first-line choice of postoperative analgesia. Postoperative gabapentin has also been shown to significantly decrease analgesic requirements and pain scores in multiple studies and meta-analysis at doses of at least 600 mg, although dizziness and drowsiness have been recorded in 6.3% of patients and may limit its utility for certain patients [89, 90, 104, 112].

The authors typically prescribe a regimen of Tylenol alone for smaller cases such as septoplasty or limited sinus cases, scheduled for the first 1–2 days, followed by its use as needed. Gabapentin at 600 mg daily for up to 5 days is also used as a supplement, particularly in patients who either react poorly to opiates but for whom acetaminophen alone is not enough. A combination drug of acetaminophen and opiate, such as Tylenol 3, can also be used as a replacement or supplemented in patients when required for the first 2 days, although it is important to keep in mind the total daily doses of acetaminophen, particularly in children, elderly patients, or those with liver disease. For more complex sinus cases, a scheduled regimen of acetaminophen is still recommended, although the patient is also prescribed a combination drug such as Tylenol 3 or Percocet as a potential replacement for up to 5 days, followed by acetaminophen as needed, with the addition of gabapentin 600 mg daily in some cases. Postoperative pain requirements can vary significantly between patients due to differences in the extent of surgery, age, and sensitivity to pain/analgesics, and each regimen should be tailored to best suit each patient.

Conclusion

The systematic review presented in this chapter will hopefully provide a useful resource to both surgeons and anesthesiologists in managing perioperative analgesia for otolaryngology patients. The most recent evidence was analyzed to provide optimal analgesic guidelines for each subspecialty, which we hope will minimize patient pain while limiting side effects as well as opioid use in a targeted and systematic approach. Among the focuses of this chapter which can readily aid in this goal are guidelines for often overlooked drugs and thereby to widen a practitioner's arsenal while also giving recommendations for often used drugs such as narcotics which can often be reduced. While these guidelines are evidence-based, practitioners should be familiar with the mechanisms and potential side effects, as described, of the medications and therefore tailor analgesia on an individual basis.

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13

Perioperative Analgesia in Cranial and Skull Base Surgery

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This chapter focuses on the current status of perioperative analgesia with regard to cranial and skull base surgeries. As this chapter will demonstrate, perioperative pain control varies drastically between subspecialties and even specific procedures. This calls forth the need for subspecialty-level guidelines for perioperative pain management. In addition, this chapter will also exemplify the use of non-opioid analgesics in the current atmosphere of opioid overprescription.

The practice of cranial surgeries is deeply rooted in the historic record. In fact, there is archeologic evidence of trepanning, whereby a hole was created in the skull, dating back to as early as the Neolithic age of the prehistoric period [1]. Today, the breadth

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and level of invasiveness of cranial surgery are vast, ranging from biopsies to craniectomies. Craniotomies also vary in approach, including but not limited to extended bifrontal, supraorbital, retrosigmoid, orbitozygomatic, and translabrynthine. More recently, less invasive approaches to intracranial procedures have emerged including image-guided laser ablation and neuroendoscopy. Importantly, the emergence of minimally invasive endoscopic approaches to the skull base has led to a drastic decrease in high-morbidity procedures previously necessary to approach the inferior brain surface.

The trends toward minimally invasive cranial surgery have also led to increased interdisciplinary collaboration. Interdisciplinary teams may consist of neurosurgeons, otolaryngologists, maxillofacial surgeons, and/or radiologists, depending on the appropriate approach. Skull base surgeries can be divided into anterior and lateral skull base procedures. The anterior skull base is often approached endonasally with the assistance of otolaryngologists. In contrast, the lateral skull base is often approached in collaboration with neurotology fellowship-trained otolaryngologists. Anatomically speaking, anterior skull base structures amenable to surgical resection include: pituitary gland, sella turcica, suprasellar and pre-pontine cisterns, clivus, petrous apex, anterior craniocervical junction, olfactory groove, cribriform plate, orbit and cavernous sinuses, frontal, sphenoid and ethmoid sinuses, and pterygopalatine and infratemporal fossae. In contrast, the lateral skull base includes but is not limited to the cerebellopontine angle, tentorium, facial and trigeminal cranial nerves, tegmen, and jugular foramen.

In 2016, the CDC released a consensus guideline for opioid prescription in the setting of chronic pain outside of active cancer, palliative, and end-of-life care [2]. However, no such generalized guidelines exist in the setting of acute perioperative pain management, particularly in the non-chronic or opioid-naïve patient. Several barriers to obtaining such a consensus exist, and these have been discussed in previous chapters. Although several specialty-specific barriers exist, there are several challenges that pertain to all surgeons from all specialties alike. These include the numerous alternative non-opioid options available which render it

difficult to establish a robust multimodal non-opioid plan. Also, the need to establish exact quantities and durations for prescriptions is extremely difficult given the myriad of contributing factors to making such decisions. Moreover, the nature of postoperative pain and the need for early pain control in perioperative setting render it difficult to prescribe opioids in the same way they are prescribed in the chronic pain setting, as one cannot simply titrate to lowest effective dose and further monitor. In addition, the level of pain varies with the nature of procedure and invasiveness, and the training history and institutional history of each surgeon contribute tremendously to ordering preferences. Therefore, in order to address these barriers, it is appropriate to organize guidelines for perioperative pain management at a more granular level. For example, it is easier to determine a multimodal pain plan with exact dosing if guidelines can be established based on specific procedures for specific patients, including the delineation between the opioid-naïve and chronic pain patients.

Cranial Surgery

Intracranial procedures have been the topic of controversy for acute postoperative pain management for many years [3]. The long-standing conventional thinking has been that patients undergoing craniotomies experience less pain in the postoperative setting than those undergoing other types of surgeries. However, in the early 1990s, this traditional outlook, which was largely based on anecdotal experiences, was widely challenged. With the exception of a single, now refuted, retrospective report that reinforced the old belief [4], a flurry of evidence has since emerged to support the contrary [3, 5]. The incidence of acute post-craniotomy pain ranges from 30% to 90%, values that are far too large to be considered minimal. The variability in incidence in part reflects the numerous perioperative factors that contribute to postoperative pain, but it also highlights the lack of robust prospective epidemiological studies [3, 5]. The perioperative risk factors for post-craniotomy pain are extensive and unfortunately often conflicting. Chowdhury et al. provide a comprehensive review of

perioperative factors including age, gender, surgical site, surgical technique, psychologic factors, and tumor characteristics [3]. Findings worth highlighting include less pain with increasing age, craniotomies are less painful than craniectomies, completing a cranioplasty after a posterior fossa craniotomy reduces postoperative pain, extent of temporalis and posterior cervical muscles resection correlates with increased pain, and a translabyrinthine approach to acoustic neuroma leads to less persistent pain as compared to a retrosigmoid or suboccipital approach [3]. Acute post-craniotomy pain was not found to differ in emergent versus non-emergent cases for days 1–3 after surgery [6]. With regard to timing, 69% and 48% of patients reported moderate to severe pain (greater or equal to 4 on a 0–10 scale) on the first and second postoperative days, respectively. Even further studies show the plurality of patient's pain report within the first 48-hour window after craniotomy [5, 7], which is pulsating and pounding in character [3]. Despite substantial data to refute old thinking and to support the high incidence of severe acute post-craniotomy, there is growing evidence that acute post-craniotomy pain is often neglected and inadequately treated [3, 5, 8, 9]. Although the exact reasons for this have yet to be elucidated, managing post-craniotomy pain poses unique challenges that may be contributing to the lack of consensus in establishing a standardized treatment plan. This in turn has fostered the potential for inadequate pain management. In neurosurgery, most notably, there is a fear of adverse effects of opioid analgesics as high doses may lead to respiratory depression and subsequent hypercapnia, which in turn may lead to intracranial hypertension. This not only can increase the risk for post-craniotomy complications such as intracranial hemorrhage but also can compromise the neurological exam rendering it difficult to monitor these patients during the postoperative hospitalization [3, 5]. On the other hand, inadequate analgesia in itself can cause sympathetic activation which has been shown to increase intracranial pressures. This in turn can increase the risk of post-craniotomy complications, hospitalization period, and mortality [3, 5]. This delicate balance of pain control at the expense of central depression is an added challenge to approaching post-craniotomy analgesia for the neurosurgeon and neuroanes-

thesiologist alike. Therefore, given the decreased central effects of non-opioid analgesics, it is not surprising that there has been a substantial effort to support their utility. Of note, determining appropriate post-craniotomy analgesia stems beyond avoidance of intracranial hypertension and its consequential postoperative complications. There is evidence that the intensity of acute pain and prolonged inflammation in the post-neurological surgery setting is correlated with an increased likelihood of developing chronic pain [9]. Although the management of chronic post-craniotomy pain is beyond the scope of this text, the significance of this pain entity should not be undermined. One study estimates that up to 56% of patients who undergo supratentorial approaches to the cranial cavity report pain 2 months after surgery. Chronic post-craniotomy pain is certainly prevalent and burdensome on the patient and the healthcare system. There is some evidence that managing acute high-intensity post-craniotomy pain may in turn reduce the risk of developing chronic post-craniotomy pain [10].

Scalp Blockade

Assuming that the need to control acute post-craniotomy pain is recognized and accepted as standard practice, the pharmaceutical options that are available are diverse. In addition to the myriad of opioid and non-opioid analgesic options that are available across all disciplines, other options unique to open craniotomies include scalp local anesthetic infiltration and scalp nerve blocks. In scalp infiltration, the surgical incision sites are infiltrated with local anesthetic typically ropivacaine 10 minutes prior to incision. On the other hand, scalp blocks can be achieved via targeted delivery of long-acting local anesthetic such as ropivacaine to the supraorbital, supratrochlear, auriculotemporal, occipital, and postauricular branches of the greater auricular nerve [10, 11]. It is proposed that the use of local analgesic modalities in conjunction with systemic analgesia leads to optimized postoperative pain control and decreased opioid requirements for patients undergoing cranial surgery [10–12]. Although the use of local cranial analgesics in improving intraoperative hemodynamic and anesthetic stability is

well established, the extent of its benefit with regard to acute postoperative pain is still under investigation, and results are often conflicting. Moreover, the specific approach to scalp blockade is also variable both in site and timing of administration [10]. Published randomized control trials for scalp blockade are limited; however, a meta-analysis out of the United Kingdom supports the utility of regional scalp blocks in patients undergoing craniotomy, demonstrating reduction of pain scores up to 8 hours postoperatively. This study also demonstrates that pain reduction can be extended to up to 12 hours when the local block is administered post-incision closure in the immediate postoperative setting [13]. Nevertheless, the role of scalp blocks continues to be investigated. In 2020, a randomized control trial with 89 patients reported that postoperative administration of bilateral scalp blocks using bupivacaine with epinephrine failed to reduce mean postoperative pain scores and overall opioid consumption within 24 hours after surgery [14]. Given that dura mater is not innervated by peripheral nerves and that infratentorial tissues lack consistent and distinct peripheral innervation, it is reasonable to assume that scalp blockade in itself provides insufficient analgesia, especially within the context of infratentorial dissection [10].

Systemic Therapies

Traditionally, acute post-craniotomy pain was managed with low-dose opioids in order to avoid the aforementioned consequences of higher doses with respect to the neurological exam. Consequently, there is a push to utilize multimodal analgesic approach to craniotomies to supplement the use of low-dose opioids [15]. In the modern pharmaceutical era, systemic options for postoperative analgesia are extensive, and the cranial vault is no exception. Perhaps the most recent and comprehensive systematic review evaluating the prevention of acute postoperative pain in craniotomies was a Cochrane Review conducted by Galvin et al. in 2019 which investigated 42 completed randomized controlled trials encompassing 3548 participants [16]. The authors report high-quality evidence that nonsteroidal anti-inflammatory drugs

(NSAIDs) reduce pain for up to 24 hours postoperatively (Table 13.1). Other non-opioid options including scalp blocks or local infiltration, dexmedetomidine, pregabalin, or gabapentin had less certain analgesic benefits with very-low-to-moderate-quality evidence. They report a role for scalp blocks and dexmedetomidine in reducing overall analgesic requirements, albeit with low-quality evidence. Moreover, acetaminophen did not deliver pain reduction within 12 and 24 hours postoperatively with moderate-quality and high-quality evidence, respectively [16]. Lastly, previous literature has encouraged the use of numerous non-opioid analgesics due to inherent secondary properties deemed beneficial within the neurosurgical context. For example, gabapentinoids are purported to offer improved nausea control, while intraoperative dexmedetomidine can reduce post-craniotomy hypertension [15]. However, Galvin et al. demonstrate that such claims are supported by low-quality evidence, at best [16]. The most common risks of each analgesic are listed in Table 13.1; however, the most common adverse reaction seen in the study by Galvin et al. was nausea and vomiting overall. A common concern for use of NSAIDs in post-craniotomy patients is bleeding risk. Currently, there is little literature supporting this risk, but the theoretical risk has caused much apprehension. A case-control study revealed an increased risk of post-craniotomy hematoma in patients who received perioperative flurbiprofen [17]. Another retrospective study showed no association between post-craniotomy hemorrhage and ketorolac in pediatric patients in the perioperative period. More studies are needed to come to a clear conclusion on this manner, but as such, the efficacy of NSAIDs should be weighed against the risk of postoperative hemorrhage.

At this point in time, despite the downsides to opioid analgesia in post-craniotomy management, its use remains widespread due to its efficacy in pain reduction. Moreover, there is a scarcity of randomized controlled trials attempting to elucidate choice of opioid agent and route of administration. Despite general postoperative guidelines that advocate opioid patient-controlled analgesia (PCA) over boluses and a recent clinical trial elucidating its safety in the post-craniotomy setting, there remains hesitance in

Table 13.1 Perioperative analgesic choices post craniotomy

Type of analgesia	Level of evidence	Efficacy	Benefits	Risks/complications	Benefit/risk assessment	Cost
Acetaminophen	Moderate-high level	No analgesic efficacy	Mild-moderate analgesic with good safety profile	Hepatotoxicity, nephrotoxicity, hypersensitivity reactions	Balance of benefit and harm	Low
Gabapentin/pregabalin	Low level	Mild-moderate	Reduce risk of nausea and vomiting after surgery	CNS depression, respiratory depression	More benefit than harm	Moderate
Local anesthetic	Low-moderate level	Mild-moderate	Quick-onset action, incisional pain reduced, good safety profile	Cardiovascular toxicity, hypertension	More benefit than harm	Low to moderate
Low-dose opioids/PCA	High	High	Highly effective pain management for moderate-severe pain	CNS depression, respiratory depression, constipation, nausea and vomiting, dependence	Balance of benefit and harm	Moderate
NSAIDs	High	High	Mild-moderate analgesic with good safety profile	Risk of hemorrhage, gastric ulcers, nephrotoxicity, hypersensitivity reactions	Balance of benefit and harm	Low to moderate
Nerve blocks	Low-moderate level	Mild-moderate	Quick-onset action, incisional pain reduced, may reduce need for systemic medications	Local anesthetic systemic toxicity, nerve injury	More benefit than harm	High

PCA patient-controlled analgesia

its use [15, 18]. Nevertheless, trends toward multimodal therapy have triggered numerous clinical trials evaluating opioid-free approaches which may prove particularly useful in neurological surgery.

Anterior and Lateral Skull Base Surgery

Today, large infiltrative tumors that would have been removed using an open approach in the past can now be done using a minimally invasive endoscopic approach. Most recently, there has been a drive for transorbital approaches to the infratemporal fossa and parapharyngeal space [19]. This is an alternative to highly morbid transcranial approaches, therefore inevitably reducing the perioperative analgesic requirements in cranial surgery. Due to the complexity of skull base cases along with this rapid innovation and movement toward minimally invasive surgery (MIS), the skull base field in particular has adopted a widely interdisciplinary approach, often involving both otolaryngology and neurosurgery and sometimes ophthalmology and plastic surgery as well. This interdisciplinary approach via "skull base teams" can however pose additional challenges with regard to establishing a consensus for perioperative analgesia management as there are always differing specialty and provider preferences. In practice, this variation may be the result of numerus demographics including surgeon experience, era in which the surgeon was trained and level of training in perioperative analgesia, and opioid versus non-opioid options. For example, it has been shown that within the field of otolaryngology, males in their midcareer (11–20 years) were more likely to write greater than 50 prescription, with the region with the highest number of prescriptions being from the Midwest [20]. This not only highlights a lack of consensus within a single field but also leads one to speculate that this could be the case in other fields as well.

Perioperative pain following skull base procedures has been found to occur in up to 65–85% of patients [21], although the overall severity of this pain in this patient population has not been discussed. Much of the literature regarding perioperative analge-

sia in skull base tumors is regarding anterior skull base resections specifically transsphenoidal procedures of the pituitary. One of the important aspects of successful transsphenoidal surgery includes adequate pain management. Insufficient analgesia can lead to agitation, hypertension, and vomiting, which in turn can increase the risk of postoperative hemorrhage and return to the operating room. Typically, NSAIDs are used to control postoperative pain in transsphenoidal procedures with some papers emphasizing patient-controlled analgesia (Table 13.2) [21]. With a shift toward MIS in skull base surgery, there is a smaller surgical field with less invasion of surrounding tissue that consequently reduces postoperative pain, in addition to a shorter length of hospital stay, a reduction in the time to return to work, and decreased overall cost [22]. Other safer non-opioid analgesic alternatives that are often considered include acetaminophen, gabapentin, local anesthetics, and alpha-agonists. The value of opioid alternatives has been explored in otolaryngology, but there have been no comprehensive reviews characterizing the overall quality of evidence for their use in anterior skull base surgery. A large series by Flynn and Nemergut showed that postoperative analgesic requirement is actually very low in patients undergoing transsphenoidal surgery. It is thought that this is due to the release of endogenous opioids from the pituitary gland from manipulation during surgery, therefore leading to little to no requirement of exogenous opioids postoperatively [23]. This was supported in a review by Dunn and Nemergut which cited a retrospective review of 900 patients that found that the median postoperative opioid requirement for patients was less than 4 mg of morphine [24]. It is speculated that more aggressive perioperative analgesia could possible reduce long-term pain, but this has not been proven.

Systematic reviews have been performed regarding perioperative anesthesia for patients undergoing septoplasty, rhinoplasty, and endoscopic sinus surgery, but no such systematic review exists yet for anterior skull base surgery [25, 26]. These studies cite the utility of immediate and aggressive postoperative analgesia in potentially decreasing the need for opioids. It is purported that early managment of pain reduces inflammatory cytokines, postoperative anxiety and other pain-related complications. Patient and

Table 13.2 Perioperative analgesic choices in anterior and lateral skull base surgeries

Type of analgesia	Level of evidence	Benefits	Risks/complications	Benefit/risk assessment	Cost
Acetaminophen	Low	Mild-moderate analgesic with good safety profile	Hepatotoxicity, nephrotoxicity, hypersensitivity reactions	More benefit than harm	Low
Gabapentin/ pregabalin	Low	Reduce risk of nausea and vomiting after surgery	CNS depression, respiratory depression	More benefit than harm	Moderate
Local anesthetic	Low	Quick-onset action, incisional pain reduced, good safety profile	Cardiovascular toxicity, hypertension	More benefit than harm	Low to moderate
Low-dose opioids/PCA	High	Highly effective pain management for moderate-severe pain	CNS depression, respiratory depression, constipation, nausea and vomiting, dependence	Balance of benefit and harm	Moderate
NSAIDs	High	Highly efficacious, mild-moderate analgesic with good safety profile	Risk of hemorrhage, gastric ulcers, nephrotoxicity, hypersensitivity reactions	Balance of benefit and harm	Low to moderate
Nerve blocks	Low	Quick-onset action, incisional pain reduced, may reduce need for systemic medications	Local anesthetic systemic toxicity, nerve injury	More benefit than harm	High

family anxiety can even be further decreased by developing a perioperative pain management plan to enhance patient-physician communication, provide informed consent, and increase overall patient satisfaction. In the systematic review regarding perioperative analgesia in endoscopic sinus surgery, the utility of gabapentin for perioperative analgesia was discussed and noted to have an overall significant beneficial impact on both pain scores and need for other analgesics, particularly within the first 24 hours after surgery.

Although certain portions of perioperative management of the lateral skull base were summarized in the cranial section of this chapter since these procedures usually require a craniotomy (retrosigmoid and middle cranial fossa approaches), there are certain otologic procedures that require mention since they may not require a craniotomy. A mastoidectomy can be used to approach the lateral skull base such as through a translabyrinthine approach. Perioperative pain management in such cases can be managed with non-opioid alternatives as well as low-dose opioids as shown in a review of randomized controlled trials for tympanomastoidectomies (Table 13.2) [27]. Low-dose opioids in combination with acetaminophen and NSAIDs have been shown to be equally efficacious in reducing postoperative pain. Acetaminophen alone was not as effective as NSAIDs or acetaminophen with codeine in one RCT. There is conflicting evidence for greater auricular nerve blockade in management of post-mastoidectomy pain with one RCT revealing no advantage and another revealing half of patients receiving complete analgesia [28, 29]. There are no randomized controlled trials for evaluating local infiltration alone in lateral skull base pain outcomes; however, this is a low-cost, low-risk modality that has widespread use. The most common risks for all perioperative analgesic choices for the anterior and lateral skull base are listed in Table 13.2. Again, it should be noted that because of the theoretical risk of increased bleeding with NSAIDs, surgeons are cautious when using NSAIDs in the perioperative period for anterior (due to risk of epistaxis and hematoma formation) and lateral (risk of hematoma formation) skull base procedures. There is no high-quality evidence revealing an increased risk of bleeding and hematoma formation with NSAID use in these skull base pro-

cedures. Thus, the high pain reduction must be weighed against the theoretical risk of bleeding in the perioperative use of NSAIDs until further high-quality studies are conducted.

Despite the highlighted complexities and intricacies of managing perioperative pain in cranial and skull base surgeries, the task is often left at the hand of surgical trainees. Surgical residents make up a significant portion of physicians prescribing narcotics; however, residency training in opioid prescription between programs is extremely variable. A study done by Yale School of Medicine Department of Surgery in 2018 surveyed categorical and preliminary general surgery residents of all postgraduate years on opioid-prescribing habits, influences, and training experience. This study found that 90% of residents have not had formal training in best practices of pain management or opioid prescription [30]. Another survey study by Davis and Carr in 2016 found that only five states require all or nearly all physicians to obtain continuing medical education on pain management and controlled substance prescription. Both of these studies support the need for increased physician education on postoperative pain management in order to help reduce opioid-related morbidity and mortality [31]. Moreover, despite the clear specialty-by-specialty variation that exists in approaching perioperative pain management, a survey study has yet to be conducted within the otolaryngology and neurosurgery resident population. Further elucidating the current status on resident training in these fields could prove invaluable in driving improved perioperative pain outcomes.

Conclusion

Intracranial and skull base surgeries constitute some of the earliest surgical procedures in the historic record. Inherent to these anatomic regions lies the need for an invasive approach to achieve extirpation of disease and therefore increase the potential for severe postoperative pain. Numerous factors render perioperative analgesia in cranial and skull base surgeries complex. These include the historic controversies in incidence and severity of postoperative pain, the direct impact of uncontrolled

pain on the postoperative site and consequently on implicated complications, the effect of opioid overprescription on postoperative monitoring, the breadth of procedures inter- and intra-specialties, the trend toward MIS approaches without concomitant de-escalation of analgesic needs, and the trend toward encouraging complicated multimodal management without provision of adequate education to surgical residents or fellows. Although our understanding of these factors has grown tremendously, there remains a need for high-quality procedure-specific randomized controlled trials and systematic evidence-based reviews on perioperative analgesia in cranial and skull base surgeries addressing both opioid and non-opioid multimodal approaches.

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14 Perioperative Analgesia for Orthopedic Surgery

Jessica Hanley and Anthony LoGiudice

Introduction

Orthopedic surgical procedures are often some of the most painful procedures performed in medicine. In 2001, treatment of patients' pain became a significant focus in healthcare, and thereafter, pain was considered the "fifth vital sign" [1–3]. This created a new priority of aggressively treating pain symptoms with narcotics, which unfortunately resulted in increasing rates of narcotic dependence and addiction. The heavy reliance on narcotic pain medications developed into widespread use. This lead to a dramatic increase in opioid related complications, such as addiction, diversion, and fatal overdose. Thus, the modern-day "opioid epidemic" is a national issue that stresses the need for appropriate and responsible pain treatment. There is a delicate balance between managing a patient's pain and creating an overreliance on narcotic pain medication. In an effort to reduce the use of narcotic medications for perioperative pain control, there has been an increased focus on alternative methods of pain control for all surgical procedures. The Centers for Disease Control (CDC) has already man-

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dated regulations on the number of narcotics given by day or oral morphine equivalent (OME) [4, 5]. However, it is also the surgeon's responsibility to understand the many options available to aid in reduction of postoperative discomfort.

Orthopedics is a broad, comprehensive surgical specialty, and procedures are quite diverse in how invasive and/or painful they can be. Classically, we categorize orthopedic surgeries into major and minor procedures, depending on the extent of soft tissue dissection or osseous manipulation, need for inpatient stay, overall morbidity to the patient, complexity of postoperative rehabilitation, and the level of pain expected after surgery.

Major orthopedic surgeries are usually performed under general anesthesia or monitored anesthesia with or without regional anesthesia. Examples include total joint arthroplasty/replacement (hip, knee, ankle, elbow, and shoulder), most periarticular fracture care, long bone or pelvic trauma, spinal surgery, tumor and limb salvage procedures, and major ligament repairs or reconstructions (rotator cuff, labrum, anterior cruciate ligament, etc.) including those performed arthroscopically. Any of these surgeries may involve aggressive manipulation of the bones and/or ligaments/soft tissues with associated violation of joint space and deep fascial compartments. They tend to cause significant pain postoperatively, and patients usually need to spend at least one night in the hospital after surgery.

Alternatively, minor orthopedic procedures can be performed under general anesthesia and monitored anesthesia care with local or by a technique referred to as "wide awake local anesthesia no tourniquet", more commonly known as WALANT. These cases tend to be outpatient surgeries and generally do not result in the same level of postoperative discomfort as major surgeries. Examples of minor orthopedic procedures include closed fracture reductions, nerve decompressions, laceration repairs, wound debridement, biopsies, or tendon releases.

Regardless if a surgeon is performing a major or minor procedure, it is extremely important to have a discussion with the patient about pain control strategies and expectations throughout the entire perioperative period [6]. There are many options for multimodal pain control preoperatively, intraoperatively, and postoperatively depending on the location and the nature of

surgery. This chapter is designed to outline the numerous options a surgeon has to choose from when considering perioperative pain control in the orthopedic patient.

Preoperative

During more invasive or extensive surgeries, the patient may be "pre-medicated" with IV or PO medications upon arrival to the pre-op suite. These most commonly include IV or oral acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), or oral neuromodulating agents such as gabapentin or pregabalin [7–9]. There are many studies supporting the use of preemptive multimodal analgesia [10].

However, the most frequently utilized adjunct to major orthopedic surgery is a regional nerve block with the use of short-, intermediate-, and/or long-acting local anesthetics. These are usually administered by the anesthesiologist prior to surgery under the assistance of neurostimulation or ultrasound guidance. The use of peripheral nerve blocks has generally led to better postoperative pain control with reduced narcotic requirement [11–16]. Depending on the location of the procedure, many different options or combination of blocks exists. Blocks can be performed as a "single shot" or employed as a continuous nerve catheter. A single-shot block is a one-time dose of local analgesic medication that is injected around the nerves that usually lasts for 12 hours or more. Alternatively, a continuous nerve catheter is a medication pump that is temporarily implanted, allowing a slow and steady infusion of anesthetic during and after the procedure.

Upper Extremity Nerve Blocks

Brachial plexus blocks are the mainstay of regional anesthesia for many major upper extremity procedures, especially about the shoulder. The most commonly performed blocks in the upper limb are interscalene, supraclavicular, infraclavicular, and suprascapular/axillary nerve blocks [11, 17, 18].

Interscalene

Interscalene blocks are administered between the anterior and posterior scalene muscles, just posterior to the sternocleidomastoid. This provides blockade of most of the brachial plexus (C5–C8 dermatomes) and however often inadequately covers the inferior trunk, including C8. This is called ulnar sparing and can lead to difficulty with procedures requiring coverage to the C8 distribution along the axilla, medial arm, elbow, and forearm [11, 17]. Therefore, interscalene blocks are generally preferred for procedures of the clavicle, shoulder, or proximal humerus. If an interscalene block is chosen for a more distal procedure, it is often necessary to supplement with an additional ulnar nerve block.

Complications of an interscalene block are primarily related to unintended extravasation of the local medication to surrounding nerves, as is the case with many regional blocks. Often, this leads to temporary paralysis of motor nerves necessary for diaphragmatic function (phrenic nerve) or vocal cord function (recurrent laryngeal nerve). The phrenic nerve (C3–5) is temporarily affected in 70–100% of interscalene blocks [18, 19]. Vocal cord dysfunction may present with hoarseness and difficult phonation, whereas phrenic nerve paralysis will present with varying degrees of shortness of breath as well as hemidiaphragm elevation on chest radiograph. Interscalene nerve blocks are generally avoided in patients with baseline severe respiratory disease as it can lead to further respiratory decline.

Supraclavicular

Supraclavicular nerve blocks are performed with injection of local anesthetic just superior to the clavicle around the level of the first rib. This allows for more coverage of distal nerve distributions but sacrifices more proximal and superior shoulder anesthetic coverage. For this reason, supraclavicular blocks are commonly used for procedures involving the distal humerus, elbow, forearm, wrist, and hand.

Complications of supraclavicular blocks also include paralysis of the phrenic nerve, albeit much less commonly than an interscalene block. Studies show that phrenic nerve paralysis occurs in 17–50% of supraclavicular nerve block procedures [20]. Given the anatomic

proximity, however, supraclavicular injections do carry risks of pneumothorax as well as injury to the subclavian artery [17].

Infraclavicular

Infraclavicular blocks are administered below the clavicle at the level of the brachial plexus cords. The shoulder is not well covered with an infraclavicular block, so it is not recommended for clavicle, shoulder, or most humerus procedures. This block provides the best analgesia for the distal two-thirds of the arm, elbow, forearm, wrist, and hand [11, 17]. Complications of the infraclavicular block are low especially with regard to pneumothorax, where the risk is less than 1% [21].

Suprascapular and Axillary

Suprascapular nerve blocks are rarely used in isolation but rather are commonly combined with an axillary block. This combination is excellent for shoulder procedures, particularly in patients with respiratory disease, COPD, and sleep apnea or those at high risk for pulmonary complications. The suprascapular and axillary nerve block combination has similar analgesic profile in the shoulder but fewer respiratory complications than a more proximal block [22, 23]. Typical shoulder procedures ideal for this block combination include arthroscopic vs open rotator cuff repair, biceps release and/or tenodesis, labral repairs, and acromioclavicular resections/distal clavicle resections. Complication rates are quite low and include inadvertent intraneural infiltration or prolonged motor deficits postoperatively [24].

Lower Extremity Nerve Blocks

Blocks of the lower extremity have a variety of applications, with the majority being employed distal to the lumbosacral plexus. In addition, neuraxial blocks also have utility in many patient populations. Commonly used regional blocks in orthopedics include the lumbar plexus block, femoral nerve block, sciatic nerve block, saphenous nerve block, and popliteal block. Neuraxial blocks include spinal or epidural anesthesia. These blocks are

incorporated in the perioperative care of patients undergoing elective joint replacement, soft tissue repair and/or reconstruction, and certain fracture care.

Lumbar Plexus/Psoas Block

Also referred to as a psoas block, the lumbar plexus block is directed into the psoas muscle compartment usually via a paravertebral approach just lateral to the L4 spinous process. It is particularly useful for anterior hip, thigh, and anterior knee procedures and may be paired along with sciatic nerve blocks to augment total analgesic effect in the lower extremity [25, 26]. Like in upper extremity blocks, side effects and complications are commonly a result of inadvertent diffusion of analgesic medication. Epidural dispersion is observed in 3–27% of cases, and a complete spinal block can result from direct intrathecal injection [27–30]. Other complications are often related with intravascular injection with possibility of an associated retroperitoneal hematoma, as well as fall risk if patients attempt ambulation without assistance prior to resolution of the block or residual motor deficits remain due to nerve damage [31].

Femoral Nerve Block

Femoral nerve blocks are widely used for elective surgeries of the knee, both open and arthroscopic procedures [32]. Femoral nerve blocks are administered within the femoral (Scarpa's) triangle, just lateral to the femoral artery. There is some debate in the literature with regard to how significant the improvements in pain control are with femoral nerve blocks performed in isolation. There are several studies that demonstrate significant improvement in pain scores and lower narcotic use; however, some research reveals only a modest effect postoperatively [33–36]. Femoral nerve blocks can be performed in combination with sciatic blocks, which has been shown to be beneficial for pain control in complex knee surgeries [37, 38].

While complications are uncommon, femoral blocks carry a risk profile that can result in significant challenges for patients. The close proximity of the femoral artery exposes injections to misdirection intravascularly at a rate of 5.7% [39]. Intraneural

injection can result in toxicity or increased risk of falls related to prolonged or even permanent quadriceps weakness [39, 40].

Sciatic Block

As discussed above, sciatic nerve blocks can often be combined with femoral nerve or psoas blocks for procedures of the thigh or knee. However, when used alone, sciatic nerve blocks can provide adequate coverage for surgery involving only the lower leg, ankle, or foot [26, 36]. Similar to femoral nerve blocks, complications are rare but quite serious. These include direct nerve injury, intravascular injection, or vascular puncture/injury (6.6%). Prolonged nerve blockade without expected timely resolution can lead to ulceration of the heels and motor deficits such as foot drop [31, 39].

Saphenous Nerve Block

This block is often combined with a popliteal or sciatic block for more acral procedures of the leg. Saphenous nerve block can be performed at the mid-thigh in the adductor canal or just below the knee depending upon the desired area of anesthesia [15, 26, 32, 41]. Innervating only sensory nerves, this block is particularly effective for medial leg soft tissue procedures, including arthroscopic partial meniscectomies. In these patients, saphenous nerve blocks were reported to improve pain at rest, pain with activity, and weight-bearing pain [42].

Popliteal Block

As stated above, this block is often combined with a saphenous nerve block for procedures of the knee, foot, and ankle [15, 26, 43]. Injection is performed at the level of the popliteal fossa [44]. Noted complications include intraneural or intravascular injections and associated damage, local abscess, hematoma formation, and persistent foot drop and risk for latent plantar pressure necrosis [15, 45].

Epidural/Spinal Anesthesia

Neuraxial anesthesia, which refers to spinal and epidural anesthetics, has been widely implemented in elective lower extremity

total joint arthroplasties, particularly of the hip and knee. Given the magnitude of total hip and total knee arthroplasties being performed annually, large cohorts of patients have been available to study the outcomes of neuraxial anesthesia as compared with general anesthesia. While implementation is variable by surgeon and anesthesiologists, neuraxial anesthesia has largely been considered equivalent to general anesthesia in both efficacy and safety [46].

Although the literature has demonstrated appropriate safety and/or at least equivalence to general anesthesia, not all studies have been able to delineate which patients may particularly benefit. A large cohort of over 18,000 patients undergoing primary and revision total joint arthroplasty was studied between 2005 and 2016, with subgroups identified as "frail," "vulnerable," and "non-frail," as based on a preoperative frailty index [47–51]. No difference in risk between general or neuraxial anesthesia was found in the "non-frail" or "frail" patients; however, there was significantly decreased mortality and wound complications in the "vulnerable" patient population. Other studies have shown similar conclusions, with at least equivalent and often improved outcomes among TKA and THA patients [46, 47].

Complications of neuraxial anesthesia include infection, dural leak, postdural headache, epidural and spinal hematoma, nerve damage, or neuropraxia [52]. These can render significant morbidity to the patient during a postoperative period characterized by difficult mobility and function. Furthermore, patients on anticoagulation, those who have suffered prior spine trauma or have underlying neurologic deficits or disorders (e.g., multiple sclerosis), have undergone spinal fusion, or have advanced degenerative disease of the spine, may be contraindicated from attempts at neuraxial anesthesia [53].

Intraoperative

As patients are almost always intubated or sedated during orthopedic procedures, pain control relies heavily on intravenous medications provided by our anesthesia colleagues. Narcotics such as

Dilaudid or fentanyl are often employed to provide adequate pain control during major orthopedic procedures. However, there are many adjuncts, such as IV acetaminophen and ketorolac, that are used to supplement or reduce the need for high doses of narcotics.

Ketorolac is a nonsteroidal anti-inflammatory drug (NSAID) analgesic that is available in oral, intravenous, and intramuscular forms. It is effective in providing excellent pain control and decreasing morphine requirements for both adult and pediatric patients undergoing major and minor orthopedic procedures. It is a good alternative or adjunct medication for use in patients without contraindications such as underlying renal disease or increased risk of bleeding [54–57].

There are some concerns in the orthopedic community about the use of ketorolac and other NSAIDs during or after surgery, as there are reports of higher rates of nonunion in certain procedures, such as lumbar spinal fusion [58–60]. There is no strong consensus on whether or not NSAIDs and ketorolac should be avoided in situations where bony healing is of utmost importance. This is generally left to the discretion of the surgeon and often is a decision made on the patient's risk of nonunion, depending on their unique biology, smoking status, and other comorbidities. As mentioned previously, IV acetaminophen is also employed as an adjunct medication to reduce narcotic use for patients without significant liver disease or other contraindications [61].

Single nerve blocks, field blocks, or periarticular injections can also be administered intraoperatively to augment pain control and decrease postoperative narcotic requirements if a block was not given before surgery. For example, a median nerve block can be administered by the surgeon after a distal radius fracture fixation for postoperative pain control. There is evidence that surgeon-administered local blocks given intraoperatively are as effective as preoperative anesthesiologist-administered nerve blocks [62]. Field blocks, with or without epinephrine, are especially prevalent in orthopedic procedures where the surgical field is smaller, such as hand cases or single-level spine surgery.

Periarticular injections or "joint cocktails" are also an increasingly popular and effective way to manage postoperative pain. The location, technique, and "recipe" for these injections are

highly variable. The base ingredient often consists of a local anesthetic which is then mixed with opioids, neuromodulators, and anti-inflammatory medications, including steroids. A multimodal drug mixture has been shown to be superior in reduction of narcotic requirements and pain control when compared with an injection of a single medication in the same region [9, 63]. There is evidence to support the use of periarticular joint injections in many settings, like joint arthroplasty or hip fracture fixation, to allow patients earlier joint mobility and rehabilitation, in addition to reducing the need for pain medications [64, 65].

Postoperative

The use of narcotic pain medications in the postoperative setting is ubiquitous after nearly any orthopedic procedure. Patients and providers consider this the primary method of pain control after surgery until a patient can transition to non-opioid medications such as acetaminophen or NSAIDs. As has been championed during prior phases of an orthopedic case, postoperative multimodal analgesia has demonstrated superior outcomes when paired against single medication choices [65]. Postoperative pain protocols today can offer a wide integration of narcotics with NSAIDs, acetaminophen, topical anesthetics, muscle relaxants, and post-procedural regional infusions.

Most surgeons have adopted the prescription of narcotic painkillers as a significant facet of medical care over the past decades, with rising concerns that this has been mostly used to enhance patient satisfaction scores. Many studies have investigated not only the relationship of narcotics and their comorbidities but also the general prescribing practices in the postoperative period. There is evidence that many providers may be "defensively" prescribing an abundance of pills to avoid postoperative emergency visits or calls as well as readmissions for pain control [66–68]. A recent study demonstrated that patients are being prescribed about three times the necessary amount of opioids [69].

With this in mind, the diversion of these leftover narcotic pills has grown, and their use for recreation, self-treatment, or sales has

been an evolving focus. Goyal et al. demonstrated the efficacy of preoperative instructions on decreasing the consumption of narcotic pain medications in the postoperative period while maintaining patient outcome scores. The authors studied a cohort of 305 patients undergoing upper extremity surgery and identified risk factors for increased opioid consumption. This data was then used to develop an "opioid calculator" to determine the necessary number of narcotic pills to implement for a second cohort of 221 patients undergoing a similar distribution of surgeries. This calculated regimen was also combined with a standardized pre- and postoperative surgical instruction set that included instructions for disposal of extra pills. As a result, 63% fewer opioids were prescribed, and 58% fewer opioids were consumed leading to 62% less opioid waste/diversion. These results underscore the growing need to approach postoperative pain management with careful judgment, patient education, and an armamentarium of non-opioid adjuvants [70].

Extensive research focusing on objective and subjective outcome scores has influenced every level of physician care, particularly during the postoperative phase of care. Depending on the magnitude of surgery, patients may expect pain requiring this multimodal approach with narcotic integration to continue for several days to weeks postoperatively. It is very important for patients to be well informed by their surgical team regarding the anticipated pain course and management once they are home on their own. Usually, a course of narcotic weaning is incorporated per the surgeon's preference, and the use of therapies and modalities such as ice, heat, elevation, compression, and early range of motion (when appropriate) can be added for optimization of comfort and swelling.

Conclusion

Orthopedics is a broad surgical subspecialty covering everything from extensive spinal fusions and limb reconstructions to ankle fractures and trigger finger releases. There is enormous variability in the level of pain that is experienced after orthopedic surgery, as

each procedure is vastly different and every patient is unique in their reaction to and tolerance for pain. It is essential that healthcare providers at every level understand the nearly limitless combinations of analgesics available to alleviate discomfort after orthopedic surgery while minimizing reliance on narcotic pain medications with informed patient education and guidance.

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15

Evidence-Based Perioperative Analgesia for Urologic Surgery

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Evaluation of Pain

Objectifying pain has been a goal of multiple researchers, clinicians, and even hospital administrators. Pain perception between different individuals has been a challenge for many years. Questions that arise include how we should treat patients and what pain management options are available.

Various parameters have been used to evaluate for pain among urologists, but the most commonly used parameter in

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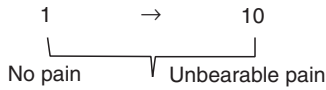

Fig. 15.1 Visual analogue scale: measurement tool to evaluate pain

urology has been the visual analogue scale (VAS), a measurement instrument that assesses pain [1]. This pain scale is gradually increased from 0 to 10 with facial expressions of pain ranging from "no pain" to "worst/agonizing/unbearable pain" on a 10 cm scale (Fig. 15.1).

Other simple methods include variations of numeric scales. In addition, a simple question of "Is your pain management adequate?" can be used. Postoperatively, these scales need to be used on a daily basis, at least twice or three times per day for inpatients (once per shift), in order to determine if the patients' symptoms are being treated adequately. It is essential for surgeons to ask these questions to patients during rounds. As mentioned above, not all pain scales can objectify pain. "Worst pain" is subjective and may vary from one person to another. However, a patient's response must still be acknowledged and documented for the purpose of selecting the most appropriate treatment.

Innervation of the Urogenital System

In order to understand the impact of pain and how it is managed, it is important to understand the innervation of the urogenital system. There are two commonly studied theories that describe how pain is transmitted. Pattern theory considers that receptors of any stimulus will give rise to a different experience depending on spatial and temporal patterns [2].

Specificity theory, on the other hand, considers that pain response is dependent on specific receptors that transmit signals to pain centers leading to a specific response [3]. In the ureter, there are two groups of afferent neurons that have been described. The first group responds to ureteral distension at low thresholds and peristalsis of the ureter. The second group has a high threshold and causes specific responses to more severe distention. The

second group is thought to respond to pain stimuli caused by obstruction [4].

Afferent innervation of the urinary bladder is composed of very small myelinated and unmyelinated sympathetic hypogastric and parasympathetic pelvic nerves. Distension of the bladder excites afferent myelinated neurons leading to the feeling of pressure correlated with increased volume. Inflammation of the bladder mucosa as in infective or interstitial cystitis induces viscerosensory mechanisms that lead to irritation and pain [5, 6].

The male genital area is rich in free nerve endings derived from A and C fibers. There are many myelinated and unmyelinated afferent fibers in the testis/epididymis area. Sensory somatic innervation of the testes is usually from the ilioinguinal nerve and genital branch of the genitofemoral nerve [7]. Sacral nerve roots from S2 to S4 via the pudendal nerve innervate the penis.

Perioperative Pain Treatment for Urogenital Surgeries

Preemptive Pain Management

Many institutes utilize preemptive pain treatment prior to urologic surgery in order to prevent central response to pain postoperatively and hence prevent the development of severe pain. Preemptive treatments are especially helpful in the setting of major surgeries in urology. The goal of this approach is to optimize comfort and alleviate more severe pain in patients following surgery.

Major surgeries might require a more extensive systemic approach to reduce pain incidence. For example, at our institution, we use a preoperative regimen of the following:

- Gabapentin 1200 mg PO
- Celecoxib 400 mg PO
- Tylenol 975 mg PO

These medications are administrated 2 hours prior to radical cystectomy while patients are in the preoperative area.

There is no consensus of the benefit of preemptive pain regimens in major surgeries in humans. Multiple papers show the benefit of these regimens, while others show a lack of efficacy. Preemptive pain management is not mandatory nor standard of care for treatment of pain prior to major surgery, and as such, the decision to administer a preemptive pain regimen is based on surgeon/institutional preference [8].

Prophylactic Pain Management

In addition to preemptive regimens, we also administer intraoperative prophylactic analgesia in patients undergoing major surgery. Based on studies done by Steffen et al. in Germany, prophylactic analgesia has demonstrated less postoperative dependence on opioids [9].

Local anesthesia has been shown to reduce postoperative pain significantly. Bupivacaine (0.25–0.5%) is the most commonly used agent for local anesthesia at incision sites.

In some situations, in patients that have a history of high sensitivity to pain, we elect to use epidural analgesia. Epidural analgesia has been used historically for urologic surgeries including prostatectomy and cystectomy. Combined spinal and epidural analgesia have shown significant reduction in postoperative pain usage leading to expansion of epidural prophylactic use during surgeries in various fields ranging from orthopedic surgery to abdominal surgery as well as vascular surgery [10].

Another important prophylactic technique in urologic pain management is the dorsal nerve block using lidocaine or bupivacaine. These medications are often used for surgeries of the male genitalia, and they work by blocking the S2–S4 innervation, thus reducing the incidence of postoperative pain in procedures such as circumcision [11, 12]. Pudendal nerve block is another technique similar to dorsal nerve block and is used mostly in obstetric and gynecologic procedures. In urology, this block can be useful in female pelvic reconstruction procedures to reduce the amount of postoperative pain [13].

Postoperative Pain Management

Despite pain management given before and during surgery, patients will still require some degree of pain control after surgery. As mentioned earlier, pain is perceived differently from one individual to another. Severe pain is a very common complaint after major surgeries. In endourological cases such as cystoscopy and ureteroscopy or scrotal procedures, there is typically less pain than in major cases such as prostatectomy and nephrectomy. Robotic or laparoscopic cases are understandably associated with less pain severity than in open cases with larger incisions. The severity and level of invasiveness direct how pain is managed. Nonsteroidal anti-inflammatory drugs (NSAIDs) or acetaminophen used in combination with opioid medication has shown a decrease in systemic opioid use and improvement of postoperative analgesia [14–17]. There is a high incidence of using opioids for less invasive procedures, as these medications lead to less patient complaints and greater satisfaction, not taking into consideration the high number of adverse effects that include those specific to urology such as urinary retention which may prolong length of stay. Based on a retrospective study performed in Michigan on 2392 surgical patients, the median number of opioid pills prescribed was 30 pills, but the average number used was nine pills [18, 19], which translates to a significant excess of prescribed pills.

In major urologic surgeries, the use of multiple pain regimens is common. This is termed "balanced" or "multimodal" analgesia, a concept that was outlined by the Danish physician Henrik Kehlet in the 1990s. This concept includes opioids and non-opioid regimens administered intravenously and orally. The trend is usually to start with opioid medication with the intention of weaning to non-opioids and to start with IV and wean to PO [20].

There are adjunctive methods to manage pain other than the use of medication including advancing diet as tolerated, early ambulation, and reducing the dependence on pain medications by using these only when a certain threshold is reached. These non-pharmaceutical interventions are part of multimodal pain therapy

that should be used in conjunction with pain medications as a systematic collaborative process.

Postoperatively, it is critical to exclude other causes of pain, such as surgical complications that may warrant additional intervention. Postoperative pain should not be ignored or dismissed as routine pain. After excluding an emergency, pain needs to be assessed with the aforementioned pain evaluation tools [21].

- *No pain*, may be followed by pain reassessment during each shift
- *Mild pain* (VAS score 1–3), common in shock wave lithotripsy and transurethral and transvaginal procedures
- *Moderate pain* (VAS score 4–6), common in laparoscopic, scrotal, penile, and inguinal procedures
- *Severe pain* (VAS score 7–10), common in open procedures with large perineal, transperitoneal, retroperitoneal, extraperitoneal, thoracoabdominal, suprapubic, and flank incisions

Systemic Analgesic Medications in Urology

Non-opiates

Acetaminophen

For many years, acetaminophen has been a safe and effective medication to control pain perioperatively [22]. It is widely used as a pain regimen for mild to moderate pain [23]. It is commonly used in the field of urologic surgery for mild pain in both PO and IV forms. In the United States, acetaminophen had only been available as an oral medication until 2010 when the US Food and Drug Administration approved intravenous use of acetaminophen, thus making it available for patients that are unable to take oral medications [22]. Since then, IV acetaminophen has been widely used in the field of urologic surgery, and multiple studies have compared it to other readily available IV medications.

Morgan et al. demonstrated that IV acetaminophen significantly decreased pain perception in management of renal colic [24]. In another study performed by Serinken et al. in 2012, IV

acetaminophen was compared with IV morphine in the treatment of renal colic, and it was found that both medications were equally effective [25]. A study performed by Bektas et al. evaluated intravenous administration of acetaminophen and reported effectiveness and reduction in the need for opiate analgesics, including morphine [26]. A randomized clinical trial of 244 patients comparing IV acetaminophen to IV placebo showed effective alleviation and tolerance of pain in postoperative management of laparoscopic abdominal surgery [27]. At our institution, acetaminophen is used for mild pain (VAS 1–3) or in combination with other analgesic agents as necessary.

NSAIDs

Nonsteroidal anti-inflammatory drugs (NSAIDs) including ketorolac, diclofenac, and COX-2 inhibitors are widely used in postsurgical pain management [28]. NSAIDs act by inhibiting the enzyme cyclooxygenase. These medications are used to reduce inflammation related to obstruction, as they relax the ureteral smooth muscle which reduces the incidence of spasms [29]. Earlier studies have shown equal effectiveness in treating pain related to urologic procedures as the early 1990s meta-analysis done by Labrecque et al. with over 60 articles reviewed showing equal effectiveness of parenteral NSAIDs to opioids in treating renal colic [30]. Based on a prospective study by Chow et al. in 2001, ketorolac provides subjective reduction in pain and reduction in opioid dependence after laparoscopic urologic procedures [31]. In addition, continuous infusion of ketorolac was found to be a safe nonnarcotic therapeutic option for pain control after percutaneous nephrolithotomy and laparoscopic donor nephrectomy according to a study performed at Mayo Clinic, Phoenix [32].

NSAIDs have a short duration of effectiveness, lasting up to 75–150 minutes, the equivalent of 10 mg of morphine [33, 34]. NSAIDs are associated with multiple side effects most commonly gastrointestinal toxicity, peptic ulcer disease, rarely renal impairment, and respiratory distress, and hence, these should be avoided in patients with GI or pulmonary symptoms [35]. COX-2 inhibitors are another option for pain management but have not been widely used in urologic surgery. At our institution, celecoxib

400 mg PO is used prior to radical cystectomy as a preemptive pain regimen.

Intravenous Lidocaine

There is limited data regarding the use of intravenous lidocaine in urologic procedures; however, IV lidocaine has shown promising results in multiple patients undergoing laparoscopic and open non-urologic procedures. McCarthy et al. performed a systemic review of over 764 patients undergoing non-urologic laparoscopic and open abdominal surgery with half of them receiving IV lidocaine. The results showed significant improvement in pain control postoperatively with less dependence on opiates. In addition, earlier return of bowel function and shorter hospital stay were demonstrated [36]. Another systemic review by De Oliveira et al. showed similar results with faster recovery and reduced dependence on opiates [37]. These two studies concluded that IV lidocaine is an effective, safe, and less expensive option for the management of pain in laparoscopic and open abdominal procedures. In urologic surgery, a 2019 study from Assiut University hospital in Egypt reported improved postoperative analgesia and earlier return of bowel function following radical cystectomy with ileal conduit in 111 patients [38]. This is a very promising pain regimen that may warrant further investigation in order to improve the quality of health after urologic surgery.

Pregabalin and Gabapentin

Neuropathic pain has been reported after urologic surgery and is one the most difficult complaint to manage after certain procedures [39]. Studies have shown that some patients report improvement of refractory pain after gabapentin; however. this is not typically a first-line regimen for pain control after urologic surgeries [40, 41]. Lee et al. reported that a single dose of pregabalin can be given as a single dose of 300 mg in patients that undergo endoscopic urologic surgery to reduce opioid-induced hyperalgesia [42]. Further investigation for gabapentin and pregabalin is needed to better assess pain control with these medications. At our institution, we prescribe gabapentin 1200 mg PO 2 hours prior to radical cystectomy in order to reduce the incidence of postoperative neuropathic pain.

Opiates

There are natural and synthetic substances that bind to opiate receptors. Opiates differ in terms of strength from weak to strong opiates.

Weak Opiates

Codeine

Codeine is a very weak opiate that is used widely for postoperative pain management especially when combined with acetaminophen in providing an effective and less expensive option for patients with less opiate side effects [43]. However, the Canadian Agency for Drugs and Technologies in Health published a report in 2019 indicating lack of literature for the treatment of pain after urologic and surgical procedures with codeine with or without acetaminophen [44].

Tramadol

Tramadol is a synthetic opiate with half-life of 5–6 hours. Tramadol can be used alone in high dose or in low dose in combination with acetaminophen for postoperative management. Studies have shown comparable results between the two regimens [45]. Also, tramadol is thought to have components of opiates and non-opiates, making it a weak opiate which helps with reducing the severity of the side effect profile of opiates and simultaneously having a stronger analgesic effect than acetaminophen and NSAIDs [46]. For this reason, tramadol is a preferred choice for postoperative analgesia by many urologists for patients with moderate pain [47].

Meperidine

Meperidine is another synthetic opiate that has been utilized since the 1930s as a potent analgesic that is safer than morphine, less addictive, and less expensive compared to other analgesics. In addition, it is more potent than codeine and less potent than morphine, making a great option for moderate pain management [48]. Climenko et al. published an article in 1943 in the Journal of Urology revealing that the spastic effects of the collecting system

that lead to pain are caused by the parasympathetic system. They further clarified that meperidine's atropine-like characteristics have a spasmolytic effect, leading to resolution of urologic pain in urology [49]. Meperidine has fallen out of favor in the United States due to its neurotoxic side effects but is still widely used in the United Kingdom and other countries [50].

Strong Opiates

Morphine

Morphine is among the more commonly used opiates postoperatively. In the field of urology, there has been an ongoing tendency to move away from morphine use due to its adverse effects of causing postoperative urinary retention, delayed return of bowel function, and resultant longer hospital stays [51]. Strong opiates such as morphine decrease the filling sensation of bladder by inhibiting the parasympathetic innervation of the bladder and increasing the sphincter tone by stimulating the sympathetic system leading to increased incidence of postoperative urinary retention, one of the more common urologic consults in inpatient setting [52]. In a retrospective study published by in Nature by Evans et al., the authors reported that a single dose of intrathecal long-acting morphine sulfate preoperatively combined with postoperative intravenous ketorolac improved neurologic analgesia, increased patient satisfaction, and decreased opiate dependence after radical prostatectomy [53].

Other Strong Opiates

Hydrocodone and Oxycodone are becoming reference pain medications in the treatment of pain after urologic procedures [54]. There are multiple studies that demonstrate the efficacy of these strong opiates in the urologic postoperative setting. Schroeder et al. reported that breakthrough opioids for pain have resulted in significant satisfaction in pain management in children undergoing urologic surgery [55]. Jinguo et al. reported that a single preoperative dose of intravenous oxycodone prior to transurethral resection of the prostate improved analgesia and delayed time of requesting the first dose of pain medication postoperatively with reduction in overall tramadol requests. In

addition, this regimen had minimal side effects on lower urinary tract symptoms [56]. However, some urologic procedures do not require similar opioid needs. Flynn et al. report that there is a rare need for opioids at 1 week following ureteroscopic procedures and that half of the prescribed opioid amount would remain unused [57]. Hence, there is a wide variation of post-urologic pain prescribing based on the procedure performed and the level of invasiveness. There is no consensus however on what specific medication to prescribe for each individual procedure. Ziegelmann et al. arrived at a similar conclusion and stressed the need for standardized urologic opioid prescribing guidelines based on a study of 11,829 patients that underwent 21 different types of urologic procedures [58].

There is a stepwise schematic approach for patients undergoing surgery that require perioperative pain management. According to the World Health Organization (WHO), selection of pain medication can be simplified to an "analgesic ladder" [59] as seen in Fig. 15.2.

The European Association of Urology published guidelines for pain management in urology by Bader et al. in April 2010. See Tables 15.1 and 15.2 for doses and frequencies.

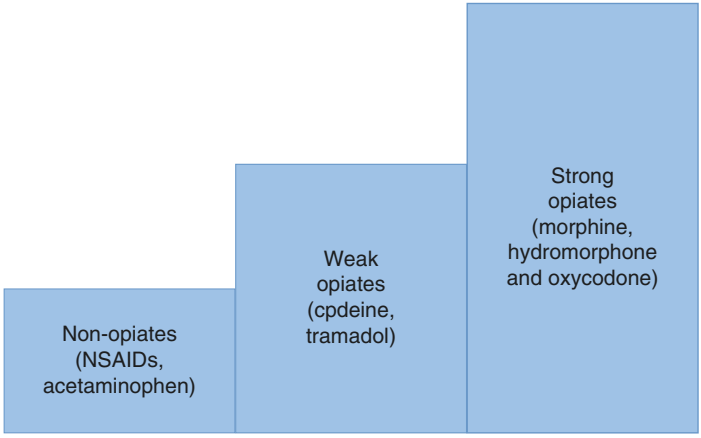

Fig. 15.2 Stepwise schematic approach to analgesic ladder as illustrated by the World Health Organization for treatment of postoperative pain

Mild to moderate pain regimen can be treated as follows:

- Acetaminophen.
- NSAIDs (ibuprofen, ketorolac, and others).
- Weak opiates can be used in combination.

Moderate to severe pain regimen can be treated as follows in opiate-naïve patients:

- Morphine
- Tramadol
- Hydromorphone
- Oxycodone

In patients that are dependent on opiate medications, when pain persists or is severe, the standard and breakthrough doses can be increased by 25%, and the frequency of administration can be reduced.

Table 15.1 Analgesia options for transurethral procedures showing drugs used with dosages, routes available, and frequency with common side effects

	Dosage	Route and frequency	Common adverse events
Acetaminophen [22]	650–975 mg (PO) 1000 mg (IV)	Oral or IV Every 6 hours	Hepatotoxicity
Ketorolac [28]	10 mg (PO) 15–30 mg (IV)	Oral or IV Every 6 hours	GI bleeding Renal damage
Ibuprofen [28]	200–800 mg (PO)	Oral Every 6–8 hours	GI bleeding
Tramadol [45]	50–100 mg (PO)	Oral Every 6 hours	Constipation Respiratory depression
Meperidine [48]	50–100 mg (PO) 25–100 mg (IV)	Oral, IM, or IV Every 4–6 hours	Constipation Respiratory depression

Table 15.2 Analgesia options after laparoscopic, robotic, and open urologic surgeries showing drugs used with dosages, routes available, and frequency with common side effects

Drug	Dosage	Route and frequency	Common adverse events
Acetaminophen [22]	650 mg (PO) 1000 mg (IV)	Oral or IV Every 6 hours	Hepatotoxicity
Ketorolac [28]	10 mg (PO) 15–30 mg (IV)	Oral or IV Every 6 hours	GI bleeding Renal damage
Morphine [51]	1–10 mg (IV)	IV 6–12 times daily	Constipation Respiratory depression Urinary retention
Tramadol [45]	50–100 mg (PO)	Oral Every 6 hours	Constipation Respiratory depression
Oxycodone [54]	5–10 mg (PO)	Oral Every 4–6 hours	Constipation Respiratory depression Urinary retention
Hydromorphone [54]	1–12 mg (PO) 0.2–4 mg/hr. (IV)	Oral and IV Every 4–6 hours Hourly	Constipation Respiratory depression Urinary retention

Failing these regimens may require obtaining a pain management consult. Clinicians also need to be aware of side effects of the prescribed medications and may add bowel regimens or breathing treatments to prevent adverse side effects.

Patient-Controlled Analgesia (PCA)

In ideal situations, patients may be allowed to control their pain after urologic procedures. This can be done with either epidural or intravenous catheters. In IV PCA, patients self-administer pain medications using an infusion pump with a reservoir filled with opiate medications. Gust et al. studied IV PCA with piritramide (fentanyl equivalent) pain control after prostatectomy and nephrectomy in 100 patients. They reported satisfactory pain management in these patients while cautioning about the need for

observation in these patients to prevent the risk of respiratory depression with medication overuse [60]. Patient-controlled epidural analgesia (PCEA) is another option where a catheter is placed in the epidural space. Liu et al. studied the postoperative effect in 1030 patients (126 of whom had urologic surgery) and reported effective and safe route of pain management [61]. There are multiple studies regarding comparison between PCA and PCEA. One study by Winer et al. showed no difference between PCA and PCEA in management of radical cystectomy in terms of length of hospital stay, return of bowel function, and other complications [62]. Another study by Rahbany et al. showed that PCEA resulted in an excellent analgesic effect with faster recovery than IV PCA in 30 patients that underwent major urologic pelvic surgery [63].

Pain Management for Specific Urologic Procedures

Transurethral Procedures

Transurethral procedures are the most common procedures performed in the urologic surgery arena. There is a large spectrum of patients undergoing transurethral procedures. Certain factors that can drive decision-making in terms of which analgesic agent to use preoperatively include the size of the instrument used, the use of stent, the use of an indwelling catheter, the size of the urethral opening, history or prior procedures, and the level of pain reported afterward. Intraoperative spinal anesthesia has shown to reduce the incidence of postoperative pain [64]. In addition, sedation with midazolam may be useful and safe during rigid and flexible cystoscopy and may be effective in relieving postoperative pain [65].

Kara et al. reported that NSAIDs are preferred over acetaminophen after transurethral surgeries at 6 hours postoperatively [66]. In addition to NSAIDs and acetaminophen, other groups of drugs can be given to reduce pain in the setting of transurethral surgeries. Patients with lower pain tolerance may benefit from 150 μg intrathecal morphine in terms of providing suitable pain control [67].

Schede et al. advised the injection of 2% lidocaine jelly for its pain-relieving effect in men undergoing transurethral surgery [68]. At our institution, 2% lidocaine jelly in syringes are injected transurethrally prior to and after urethral instrumentation. We noticed that patients report less pain after the procedure after intraurethral local administration. The size of the catheter placed directly impacts the level and intensity of pain reported. Most patients who report pain, especially males, report a burning sensation, likely from the movement of the catheter at the level of the urethral meatus. At the end of certain procedures such as transurethral resection of the prostate or bladder tumors, some surgeons tend to leave indwelling catheters on traction where the inflated catheter balloon compresses the prostate at the level of the bladder neck. This process helps with reduction of bleeding following these procedures. Patients commonly report discomfort in this setting, likely from catheter irritation of the bladder mucosa.

Any transurethral insertion of an endoscope can irritate the bladder mucosa leading to bladder spasms, which are acutely painful to some patients. Antispasmodic medication can be given to relieve the bladder spasm. In some instances, phenazopyridine is prescribed due to its analgesic effect on the bladder mucosa. It's thought to inhibit mechanosensitive Aδ fibers that have thin myelin sheaths [69]; however, there is not enough data to support this theory. At our institution, we have noted significant improvement of symptoms with administration of 100 mg or 200 mg of phenazopyridine as needed. Some minor side effects include nausea and headaches. Very rare major side effects include kidney injury and liver injury. Phenazopyridine tends to color the urine orange, and as such, it is important to inform patients about this very common and harmless side effect that does not require any medical intervention.

Other antispasmodics include anticholinergic medications, the most common of which is oxybutynin (5–10 mg), which is a muscarinic antagonist. Oxybutynin can cause dry mouth and anticholinergic effects like sedation, confusion, and delirium in elderly patients who comprise the majority of urologic transurethral patients.

Robotic, Laparoscopic, and Percutaneous Surgery

Percutaneous renal procedures, including nephrostomy access, are generally performed without general anesthesia with patients being awake. Patients typically require intraoperative local anesthesia with agents such as 0.5% bupivacaine (10–20 ml) and occasionally may also need sedation with midazolam or other sedatives to reduce pain and discomfort during the procedure [70]. NSAIDs, acetaminophen, and rarely opioids can be used postoperatively.

Robotic and laparoscopic procedures utilize intraperitoneal insufflation with CO_2. Patients often report shoulder pain after the surgery secondary to irritation of the diaphragm from the pneumoperitoneum which transmits referred pain through the phrenic nerve to the shoulder area. In addition, port site incisions are common locations of postoperative pain. Local anesthesia with 0.5% bupivacaine reduces port site pain [71].

Multiple studies have shown that a multimodal pain regimen is most effective in treating pain following laparoscopic and robotic urologic surgeries. The aforementioned analgesic ladder can be used to manage pain. Short-term courses of strong IV opioid therapy significantly improve postoperative pain and increase patient comfort and satisfaction. However, it is important to wean patients from IV to PO medication due to the significant side effects associated with IV opioids. These adverse effects could lead to worsening of a patient's postoperative course and increase the length of hospital stay in addition to increasing the incidence of opioid addiction that eventually leads to severe long-term side effects [72–74].

Open Surgery

Open surgeries require intraoperative local anesthesia to the incision site(s) to provide effective analgesic method to reduce the incidence of postoperative pain.

Depending on the type of procedure, perioperative pain management can be administered accordingly. Minor scrotal and penile surgeries generally require acetaminophen and NSAIDs with a dorsal nerve block as mentioned earlier in this chapter.

Testicular torsion requires surgical exploration for the purpose of detorsion and return of blood flow into the testicle with orchiopexy [75]. Chronic orchalgia that could result due to unknown etiology or post vasectomy can be treated with microsurgical denervation of the spermatic cord [76]. If patients fail pain medication, epididymectomy can be performed for pain localized to the epididymis [77]. Major surgeries including nephrectomy, prostatectomy, and cystectomy via an open surgical approach will require more extensive pain management, initially with IV strong opioids with a gradual wean off to PO NSAIDs and acetaminophen as needed.

Enhanced Recovery After Surgery (ERAS) Protocol

ERAS is a multimodal protocol that is designed to shorten recovery and reduce postoperative complications. Variations of this protocol have been used across surgical disciplines and have been successfully adopted in urology, particularly for radical cystectomy. This protocol continues to undergo dynamic changes to improve postoperative outcomes including pain [78]. Table 15.3 summarizes this protocol.

Renal Colic (Stone Surgeries)

Renal colic occurs due to obstruction of urinary flow most commonly in the setting of obstructive stone disease. Blockage of urinary outflow secondary to a stone lodged in the ureter, or due to a ureteral stricture, leads to obstruction and distension of the ureter and renal pelvis. The distension of the renal tissue and spasm of the ureter result in abdominal or flank pain. This pain can be exacerbated by ureteral peristalsis in waves leading to "colicky" pain. Urinary obstructive pain may also be constant in nature.

The phases of colic include the following:

– *Acute phase* is typically within 2 hours after onset of obstruction; this phase can last up to 18 hours. Despite

Table 15.3 Enhanced recovery after surgery protocol following radical cystectomy procedures with medical counseling and recommendations before, during, and after the surgery as illustrated by Cerantula et al.

Preoperative	Pre-op counseling with medical staff
	Carbohydrates and fluid loading
	Thoracic epidural placement
	Antimicrobial and LMWH prophylaxis
	Regular diet 6–8 hours prior to surgery
	Thoracic epidural analgesia
Intraoperative	Short-acting anesthetic agents
	Thoracic epidural analgesia
Postoperative	No nasogastric tube
	Early ambulation
	Early nutrition
	Gut motility stimulation
	Antiemetic when needed
	Non-opioid analgesia

being acute, it usually progresses gradually with increasing intensity until its peak in 2 hours.

- *Constant phase* is the persistence of pain until treatment or spontaneous resolution of obstruction. This is the most common phase of patient presentation for medical attention.
- *Relief phase* is the phase that is characterized by quick resolution of the pain after treatment. Usually lasts about 1–2 hours.

Neurologically, pain receptors are located in the submucosa of the renal pelvis. Distension of the renal pelvis leads to the majority of pain perception. Pain is then transmitted to pain fibers in the kidneys that are preganglionic sympathetic which reach the spinal cord at the T11–L2 levels which are then transmitted to the brain by the spinothalamic tract. Pain is also transmitted from the lower ureter to the ilioinguinal and genitofemoral nerves leading to referral of pain into the groin region. For this reason, pain is noted in the scrotal region in males and labia majora in females.

Nerve blocks have been used historically to relieve pain by injecting lidocaine in the area of renal pelvis (around 11th–12th

ribs) [79]. Resolution of the obstruction should be the aim of any treatment as obstruction can also lead to sepsis and mortality.

Depending on the cause of obstruction, the long-term treatment goal is to attain the relief phase by removing the obstruction. The short-term goal is to relieve the pain while obstruction is resolving, and this is mostly done with relaxing smooth muscles in the urinary tract.

Based on the American Urological Association guidelines, small stones (<1 cm) can be managed with medical expulsion by encouraging PO hydration to increase hydraulic pressure in order to force a stone from the ureter to the bladder, which can then easily pass easily through the urethra. In addition to encouraging hydration, pain control should be provided to reduce pain stimulation until a stone passes or requires surgical intervention.

NSAIDs, specifically ketorolac (15–30 mg), are used to reduce inflammation related to obstruction and also relax the ureteral smooth muscles, thus reducing the incidence of spasms [29]. Opioids are given for severe pain control to suppress CNS stimulation by binding to opioid receptors. NSAIDs have shown to be as effective as opioids in the treatment of renal colic with a lower side effect profile as per multiple studies [80].

Calcium channel blockers (CCB) have been studied to relax smooth muscle in the urinary system by suppressing the binding of calcium to calcium receptors, hence leading to prevention of the contractions, spasms, and peristalsis of the ureter. CCBs have issues of blood pressure changes and also have slow onset of action. For this reason, they are not recommended [81, 82].

Selective alpha-adrenergic antagonist (tamsulosin) is the most commonly used medication for stone pain management in the recent years. Tamsulosin leads to relaxation of smooth muscle contractions leading to reduction of spasms of the ureter and the renal pelvis. Treatment with tamsulosin for up to 4 weeks can expedite stone passage when the stone size is >5 to <10 mm with low cost and very few side effects [83].

Other medications under investigation include tadalafil (phosphodiesterase type 5 inhibitor), glucocorticoids, and silodosin (selective alpha-1A receptor antagonist). At this time, they are not recommended for medical expulsive therapy until further

investigation [84]. If medical expulsive therapy fails, kidney stones are >1 cm, or there are additional symptoms in addition to pain; urologic intervention is necessary to relieve the pressure. Relieving the obstruction can be achieved via percutaneous nephrostomy or ureteral stent placement. Patients generally report immediate relief of pressure pain after these procedures, and the obstructing stone can be addressed subsequently.

After stent placement, there is a spectrum of symptoms that patients experience. Some report discomfort while others report extreme pain. The etiology of this pain is secondary to irritation of the urinary tract mucosa by the stent or from retrograde vesicoureteral reflux of urine into the kidney at the time of voiding. Pain may be intolerable in some cases leading to the necessity of pain medication.

The aforementioned medications can be used to treat this irritation, especially tamsulosin, which in studies has shown relief of irritation symptoms through relaxation of the smooth muscle within the ureter. In addition to the above pain regimens used in stone pain management, there are other pain regimens that have been used for stent colic [85, 86]. Phenazopyridine, anticholinergic medications (i.e., oxybutynin, tolterodine), and benzodiazepines are commonly used for urinary irritative symptoms [87].

Extracorporeal Shock Wave Lithotripsy (ESWL)

Almost half of patients undergoing ESWL do not require significant analgesia [88, 89]. There are no guidelines for perioperative pain management for ESWL; however, surgeons have been known to prefer a variety of medications for preemptive management to better control pain and increase a patient's satisfaction after the procedure. Administration of NSAIDs and/or midazolam 30–60 minutes prior to surgery has been shown to reduce pain. Midazolam 2–5 mg can be administered prior to surgery followed by an NSAID, buprenorphine, or tramadol that will reduce the need of using stronger opioids and increase pain-free incidence up to 70% [90, 91].

Some patients report severe pain after this procedure that is refractory to non-opioid medication. Opioids such as fentanyl can

be used prior to procedure. There have been multiple studies reporting the effectiveness of fentanyl as not only a proper analgesic for shock wave lithotripsy but also showing significant improvement in outcomes of stone treatment. The downside of opioid usage arises from their inherent side effects as well as active monitoring required when utilizing this class of medication [92, 93].

Cancer Pain

Urologic cancer pain management is one of the most challenging areas in urologic surgery. Pain can be noted in up to 25% of new cancer diagnoses and up to 75% in patients with advanced disease [94].

Urologic cancer pain control is generally multidisciplinary in order to effectively relieve symptoms. It is not unusual for such patients to receive treatment from a urologist, medical oncologist, radiation oncologist, orthopedist, neurosurgeon, pain medicine specialist, endocrinologist, and nephrologist, among other specialists, for optimal management.

Urologic cancer pain management starts with evaluation of pain in this group of patients. As mentioned previously, evaluation and management need to be individualized and start with local treatment before switching to systemic treatment. The main goals of management of pain in cancer patients include prolonging survival and optimizing comfort.

The most definitive treatment of pain in urologic cancer patients is surgery to remove the malignant tumor. However, in some situations, patients may not be surgical candidates, or the tumor may have metastasized to a location that is not amenable to surgical intervention. Urologic cancers have high tendency to metastasize to the bone, leading to nociceptive pain that is localized most commonly in the vertebral column, and neuropathic pain from nerve compression leading to motor and sensory deficits in addition to neuropathic pain [95, 96]. Bone metastasis requires hormonal therapy, radiation therapy, chemotherapy, or combination therapy in addition to pain management. Bisphosphonates and denosumab, which help with calcium

metabolism, can be offered to bone metastasis patients to help with directing calcium to the bone, reducing risk of fractures, and providing relief for bone pain [97].

Neuropathic pain from bone metastasis can be managed by consulting with pain management experts. Multiple agents have been used with varying degrees of success:

- Tricyclic antidepressants (amitriptyline) [39]
- SSRIs (paroxetine and fluoxetine) [39]
- Anticonvulsants (gabapentin and pregabalin) [40, 42]
- Opiates [44, 54]
- Medications (lidocaine and capsaicin) [10, 71, 73]
- Steroids [84]

Lymphadenopathy is also another cause of pain in cancer patients. This type of pain is typically mechanical from a compressive effect on the muscles and nerves. The best treatment for lymphadenopathy-induced pain is appropriate chemotherapy that results in reducing the size of the involved lymph nodes leading to relief of pressure pain. Lymphocele formation after urologic surgeries can also lead to pain where surgical intervention is required to drain the lymphocele [98–101]. Mass effect is also involved in cancer pain with obstruction of the urinary system being a very common etiology of pain. Location of the tumor is the determining factor of the severity of pain. Some tumors are obstructive leading to urinary tract spasmodic pain.

Tubular organs have a higher tendency of obstruction given the elongated and narrow shape of these organs. The most common location of such obstruction is the ureter, whether extrinsically and intrinsically, leading to hydronephrosis and hydroureter-associated pain [102, 103]. If the ureter is involved, pain management is similar to that of stone management with percutaneous nephrostomy, which has superior results over retrograde ureteral stent placement in the setting of compressive pain. The reason for this superiority is that the extrinsic mass effect may override the effectiveness of an internal stent [104].

Another location of mass effect involvement is the urethra secondary to urothelial carcinoma or penile cancer with bladder out-

let obstruction. Pain starts with suprapubic pain due to the inability to empty bladder similar to severe cases of enlarged prostate. Pain management should involve draining the bladder and prevention of distension. Suprapubic tube placement should be considered in these patients. If suprapubic tube placement is not feasible, diverting the urine with a percutaneous nephrostomy can be employed. In some cases where the bladder is not involved, as in penile cancer, perineal (intrastromal) urethrostomy can be performed [105].

Inflatable Penile Prosthesis (IPP)

Inflatable penile prosthesis is the gold standard for treatment of erectile dysfunction that is refractory to medical therapy [106]. Preoperatively, pain control with spinal anesthesia and local anesthesia is well established in the literature. Postoperatively, pain management is not very well outlined, and multiple studies have pointed toward the need to establish new guidelines for pain management associated with this procedure [107]. NSAIDs and opiates are the most commonly used medications in IPP pain management postoperatively [108].

Conclusion

The treatment of pain is one of the most important tasks in medicine. Pain is the most common complaint for patients in the inpatient setting. Perioperative pain management in urologic surgery is similar to that in many other surgical fields. Urologic procedures require different types of therapies specific to the procedure performed. Evaluation and documentation of pain are necessary in order to determine which type of therapy is optimal to the situation. A multimodal evidence-based approach should be employed for mitigation of pain. It is of great importance to listen to the needs of the patient and to treat their pain subjectively, as patients' perceptions of pain are highly variable and so are the appropriate treatments.

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Obstetrics and Gynecology

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Tyler Muffly and Javier Gonzalez

Introduction

At the beginning of the new millennium, the US Congress declared the "Decade of Pain Control and Research" [1]. The United States developed government-endorsed national guidelines for pain management and expanded research into the basic science of pain. Previous gynecologic surgery postoperative pain management relied strongly on the use of opioid analgesics, which have delayed onset and significant side effects. The goals of modern multimodal perioperative pain management are to relieve suffering, achieve early mobilization after hysterectomy, reduce length of hospital stay, and achieve patient satisfaction [2].

Hysterectomy is the most common major surgery in women in the United States with more than 500,000 cases performed annually [3]. Hysterectomy has become a definitive treatment option for

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pelvic organ prolapse and abnormal uterine bleeding, and the demand for gynecologic surgery is increasing. Although hysterectomy provides durable long-term clinical results, early postoperative pain is a concern following gynecologic surgery, and it is an unfavorable outcome causing distress to patients, which often necessitates opioid medication. To facilitate early convalescence, adequate pain control is critical in the postoperative patient.

Pain after gynecologic surgery has two components: somatic and visceral, both initiated by nociceptor stimulation. Mechanical, chemical, and thermal stimuli all potentiate nociceptor activation that is transmitted via the spinothalamic tract to the brain stem and somatosensory cortex. Prostaglandins are potent chemical stimulators of nociceptors, and their inhibition is the basis for the effectiveness of nonsteroidal anti-inflammatory drugs. Opioid receptors play an integral role in pain transmission at different levels in the central nervous system as target sites for neurotransmitters and endogenous opiates such as enkephalins and endorphins.

Single analgesics alone are not able to provide adequate pain relief for most moderate or severe pain due to hysterectomy, and thus, perioperative pain management comprises numerous pharmacologic and nonpharmacologic treatment modalities which may include regional and local anesthesia or dissociative anesthesia. Nonpharmacologic methods include cognitive behavioral interventions and topical thermal applications of warm and cold compresses, among other therapies. Acute postoperative pain management regimens are based on the patient, type of gynecologic surgery performed, and current and anticipated postoperative pain. This chapter provides an evidence-based overview of preoperative, intraoperative, and postoperative pain management with a focus on opioid-sparing modalities in gynecologic surgery [4].

Preoperative Education and Perioperative Pain Management Planning

Effective perioperative pain management begins before hysterectomy with a thorough assessment of the expectations of both the patient and the patient's family and the expected level and duration of postoperative pain during the informed consent process. The

patient and family need to have information regarding the specific surgical procedure, expected severity of pain, and available pharmacologic and nonpharmacologic treatments available to them in a clear and simple manner. This discussion ideally takes into account the patient's level of education and is undertaken in their native language. Setting clear expectations of pain and management of pain in the preoperative period has been demonstrated to have a more rapid decline of pain postoperatively, decreased preoperative anxiety, and also increased postoperative pain control satisfaction [5].

Preoperative counseling serves as the beginning nonpharmacologic modality to managing preoperative pain. Enhanced recovery after surgery (ERAS) protocols for hysterectomy and gynecologic surgery have emerged to provide evidence-based guidelines on several preoperative pharmacologic modalities that target inflammatory pathways and modulation of the pain response in efforts to reduce total opioid use in the surgical patient. Enhanced recovery pathways are protocols that are focused on pre-, intra-, and postoperative strategies to decrease the length of hospital stays and hasten recovery. Data have emerged in many specialties outside of gynecologic surgery demonstrating decreased morbidity and cost while maintaining quality of patient care. Kalogera et al. have studied and outlined an ERAS protocol for gynecologic surgery that focuses on preoperative education, diet, analgesia and avoidance of bowel preparation, intraoperative fluid management, nausea prophylaxis, postoperative analgesia, and elimination of drain placement with resumption of regular diet in the postoperative period. These strategies also aim to minimize the use of opioid pain medication. With respect to postoperative pain, here, we share similar evidence-based strategies to optimize postoperative pain in the gynecologic surgical patient.

Systemic Pharmacologic Therapies

Nonsteroidal Anti-inflammatory Medications

Perioperative/periprocedural nonsteroidal anti-inflammatory drugs (NSAID) have a theoretical concern owing to their effect on platelet function; however, evidence suggests that the use of NSAIDs generally does not increase the risk for periprocedural

bleeding [6, 7]. Although more research needs to be done to determine the exact role of preoperative NSAID administration in assisted reproductive surgeries, it is reasonable to administer NSAIDs either preoperatively or intraoperatively for most hysterectomy patients given the favorable safety profile.

Cyclooxygenase-2 inhibitors have been identified in the nonsteroidal class of drugs to help decrease postoperative opioid demand. The COX-2 inhibitors target the synthesis of inflammatory products of the prostaglandin pathway and decrease peripheral pain sensitization and tissue inflammation and when administered in the preoperative period were associated with a significant reduction in morphine consumption at 24 hours postoperatively [7].

Acetaminophen

Acetaminophen likely functions via central COX enzyme inhibition and central serotonergic activation, although the mechanism of analgesia is incompletely understood [6, 8]. The addition of acetaminophen to opioid-based postoperative pain management results in a reduction in opioid consumption of 20–40% over the first 24 hours after various major and minor gynecologic surgical procedures [9]. Additionally, intravenous formulations of acetaminophen have been demonstrated in meta-analysis to be an effective analgesic option across a multitude of surgical procedures including laparoscopic procedures at a dose of 1 g [10].

Gabapentin

The mechanism of action of gabapentinoids is complex and occurs along several pathways. The gabapentinoids when given preoperatively reduce hyperalgesia and allodynia responses from surgical stimuli [11]. The suspected pathway for pain modulation is via calcium channel-dependent inhibition of synaptic neurotransmitter release, which results in peripheral blocking of pain due to tissue injury [12]. A meta-analysis among women undergoing abdominal hysterectomy demonstrated decreased opioid consumption with gabapentinoid use. Jokela et al. also found a better analgesia during the early recovery after day-case gynecologic laparoscopic surgery after premedication with pregabalin 150 mg by mouth in combination with ibuprofen 800 mg by mouth, but

there was no reduction in the postoperative analgesic requirement pain scores for the first 24 hours after surgery with preoperative gabapentin [13]. Preoperative gabapentin has also been shown to decrease post-laparoscopy shoulder pain in women undergoing laparoscopic gynecologic surgery [11].

Intraoperative Pain Control

Intraoperative pain considerations are an integral aspect of the pain management plan for the female patient. There are numerous opportunities to positively affect the postoperative course: from anesthetic medication options, to regional blocks, to surgical techniques. The ultimate goal is to provide adequate analgesia for treatment and minimize physical discomfort and negative psychological impact while ensuring the safety and welfare of the patient.

Perioperative pain with hysterectomy results from inflammation caused by tissue trauma (e.g., surgical incision, dissection, thermal burns) and less so with direct nerve injury (e.g., nerve transection, stretching, or compression). Tissue trauma may be high in hysterectomy as the technique relies on clamping pedicles of tissue instead of isolating specific blood vessels. In addition to tissue damage, other pain reported postoperatively includes visceral and shoulder pain. Visceral pain is predominant during the first 24 hours postoperatively, is short-lived, is unaffected by mobilization, and is increased by coughing. Visceral and incisional pain are most intense on the day of operation and then decreased following surgery. In contrast, shoulder pain gradually increased, peaking at 24 hours postoperatively [14]. The following discussions will focus on intraoperative considerations that affect postoperative pain.

Route of Hysterectomy Influences Pain

The first choice any gynecologist makes is the route of hysterectomy. The American College of Obstetricians and Gynecologists recommends vaginal hysterectomy as the "gold standard" for benign indications and has the least pain compared to other routes of hysterectomy. Despite the recommendations of the American

College of Obstetricians and Gynecologists, the laparoscopic approach to hysterectomy has increased, while vaginal hysterectomy numbers have decreased [15].

Vaginal Hysterectomy with a Vessel-Sealing Device to Avoid Pain

Tissue-sealing devices (LigaSure, Medtronic, Minneapolis, MN) have been described as decreasing operative time as well as improving patient postoperative pain without compromising the surgical procedure during a vaginal hysterectomy. While these surgical tools are increasingly adopted into surgical practice, their use is not widespread, and the standard traditional suturing method may be more widely used due to limited institutional resources and reflects standard teaching for resident physicians and trainees [16]. In respect to postoperative pain, surgeon comfort and patient safety are prioritized.

Laparoscopic Hysterectomy and Use of Local Anesthesia

Local anesthetic with classic or long-acting agents is a simple technique that may be performed during a laparoscopic procedure without additional expertise or personnel. However, there is a relatively short duration of effectiveness and uncertainty regarding the best agent and the ideal volume of injection. Additionally, in long-acting formulations, peak plasma levels normally occur approximately 24 hours after injection, leaving the early postoperative period relatively uncovered by the anesthetic agent. Liposomal bupivacaine is a long-acting local anesthetic used for wound infiltration of the viscera by blocking visceral nociception from the area of tissue damage and the peritoneum. The systemic absorption of local anesthetics through the peritoneal surface may also play a role in the analgesic effect by attenuating nociception [17, 18].

When compared to open hysterectomy, laparoscopic hysterectomy is less painful, needs shorter recovery time, and requires a shorter hospital stay. Previous studies have shown that preemptive

analgesia by local infiltration of anesthetic attenuates signals entering the spinal cord, which has comparatively better efficacy in controlling pain after surgical stimulus [19].

Laparoscopic Hysterectomy Techniques to Avoid Shoulder Tip Pain

Laparoscopic hysterectomy requires insufflation of the peritoneum with carbon dioxide and steep Trendelenburg positioning for pelvic exposure. Shoulder tip pain is caused by rapid distension of the peritoneum (associated with the tearing of blood vessels, traumatic traction of the nerves, and release of inflammatory mediators) and excitation of the phrenic nerve. Ninety percent of all laparoscopic hysterectomy patients complain of postoperative shoulder pain [17, 20].

Insufflation pressure has been studied with respect to postoperative pain. Pooled results of two randomized control trials measuring postoperative pain in 192 patients following laparoscopy were diminished during the immediate postoperative period (less than or equal to 6 hours) and at 24 hours using low intraperitoneal pressure of 8 mmHg compared to greater than or equal to 12 mmHg with no significant difference noted at 24 hours. However statistically significant, the clinical significance of the noted pain difference is low as there was no difference in length of hospital stay noted between the two groups and no information on analgesic use was reported in either trial [14, 21]. The use of lower intraperitoneal pressures during gynecologic laparoscopy cannot be recommended from a postoperative pain standpoint.

Specific techniques for releasing the pneumoperitoneum (extended assisted ventilation or actively aspirating intra-abdominal gas) reduce the severity of shoulder pain at 24 hours. Interestingly, gasless laparoscopy versus carbon dioxide insufflation may be associated with increased severity of shoulder pain within 72 hours postoperatively when compared with standard treatment [14]. Warmed and humidified carbon dioxide showed no difference with pain scores at 24–48 hours [22]. We also do not recommend placing an intraperitoneal drain for the purpose of releasing pneumoperitoneum.

Laparoscopic Hysterectomy Uterine Morcellation Techniques to Avoid Pain

To remove large uterine specimens, occasionally, manual morcellation techniques are required. Minilaparotomy versus a colpotomy for any vaginal approach has been compared at the time of laparoscopic hysterectomy. Similar pain scores were reported between minilaparotomy and contained vaginal extraction [23]. Limitations of the study were a short-term follow-up of 8 weeks. Long-term follow-up is needed to assess further postoperative outcomes (e.g., abdominal wall hernia formation). Another study by the same group demonstrated that there is no difference in incisional symptoms such as pain or infection following umbilical minilaparotomy versus a suprapubic minilaparotomy for tissue extraction [24]. While these studies had multiple limitations, either method can be considered for removal of large uterine specimens based on surgeon comfort and patient safety considerations.

Laparoscopic Hysterectomy Fascial Closure to Avoid Pain

Factors related to laparoscopic incisional pain include size of trocars, location on the abdomen, and fascial closure. Fascial closure devices (e.g., Carter-Thomason device [Cooper Surgical, Trumbull, CT]) are found to be faster than traditional closure using suture and S-retractors to visualize the rectus fascia. When closing laparoscopic ports, Lyapis et al. demonstrated that on postoperative day no. 1, use of fascial closure devices resulted in higher pain scores versus closing with a direct visualization of the fascia using retractors. Of note, the study was performed in patients undergoing robotic-assisted laparoscopic hysterectomy with an upper quadrant 12 mm port placed. Fascial closure device was significantly associated with higher postoperative pain at 24 hours (3.01 vs. 1.50, $P = 0.028$) but not 2 weeks (1.74 vs. 0.99, $P = 0.102$) post surgery. There was no significant difference in operative time. These data suggest that use of a fascial closure device does not decrease operative time and may be associated

with increased pain in the immediate postoperative period. Confounding variables such as baseline chronic pain and medications (narcotics, NSAIDs, antidepressants, neuropathics) were not controlled and may influence these results.

Pain Relief with Laparoscopic Intraperitoneal Lidocaine Infusion

The method of delivering local anesthetic directly to the intraperitoneal cavity was first described in 1951 by Griffin et al. Intraperitoneal administration of a local anesthetic has been shown to reduce postoperative shoulder pain and analgesic consumption following laparoscopic surgery as described in gynecologic and general surgery literature. Despite study heterogeneity, instillation of local anesthetic into the abdominal cavity during laparoscopy appears to reduce early postoperative abdominal pain while being reasonably safe [25, 26].

Vaginal Packing at the Conclusion of Hysterectomy

At the conclusion of the case, surgeons often consider packing the vagina with sterile gauze to reduce blood loss and hematoma. One particularly excellent randomized control trial has shown the packing is not effective at preventing hematoma and is a risk of discharging the patient home with the vaginal packing in place and at the expense of patient discomfort [27].

Postoperative Pain Control

Postoperative pain and nausea are the most common complications of hysterectomy. Both, particularly pain, prolong recovery and discharge times and contribute to unanticipated admission after ambulatory surgery. Pain and fatigue are most intense on the day of operation and the following day [28]. Despite multimodal analgesia regimens, administration of high doses of opioids is

often necessary. This can further lead to several adverse effects such as drowsiness and respiratory impairment as well as worsening postoperative nausea and vomiting. Vomiting after hysterectomy causes inflammation or local irritation around the vaginal cuff and/or peritoneum, further exacerbating pain.

The goal of postsurgical pain management is to maximize postoperative function while limiting the use of opioid medications to facilitate convalescence. Opioid-only analgesic regimens for hysterectomy are commonly associated with opioid-related adverse effects. These include nausea and vomiting, respiratory depression, somnolence, pruritus, sleep disturbances, urinary retention, constipation, and tolerance that may interfere with return to activities of daily life postoperatively [29]. The dependence solely on opioid medication and the subsequent long-term adverse effects of inadequate pain control have been well described. These consequences include nociception-induced central sensitization and opioid-induced secondary hyperalgesia. Both of these mechanisms may be involved in the pathogenesis of persistent surgical pain [30]. Furthermore, use of opioids can lead to opioid dependence and addiction.

Multimodal opioid-sparing approaches to postoperative pain are preferred and will be further discussed here. It should be noted that reduction in postoperative pain and opioid demand begins in the preoperative setting with enhanced recovery protocols as previously mentioned and is further optimized postoperatively. Regardless of the route of hysterectomy, these multimodal principles can be broadly applied for postoperative pain control and can likewise be applied to other non-hysterectomy gynecologic procedures.

Nonsteroidal Anti-inflammatory Drugs

The use of NSAIDs and their mechanism of action is discussed in the preoperative section of the chapter. Their use in the postoperative period has been demonstrated in systematic review to reduce morphine equivalents after surgery. Use of ketorolac is effective when compared to opioids in the postoperative period for pain

control and has not been found to have statistically significant increases in blood loss [7, 31, 32]. Scheduled use of acetaminophen, NSAIDs, and selective COX-2 inhibitors is strongly recommended unless contraindicated. A summary of pharmacologic preoperative, intraoperative, and postoperative pain control modalities can be viewed in Table 16.1.

Local Analgesia

Use of local anesthetics in gynecologic surgery, namely liposomal bupivacaine, at the operative site in the immediate postoperative period was previously discussed and has been found to reduce total overall morphine equivalents and should routinely be considered [19]. Peripheral nerve blocks such as the transversus abdominis plane (TAP) block have been evaluated for postoperative pain management, and data suggests that this particular modality works in the short term (within 24 hours) to reduce pain scores and morphine requirements and however does not provide a sustained pain control benefit at 48 hours, and routine use is not strongly recommended but can be considered [33–35]. Epidural anesthesia use has been found to provide superior pain relief as compared to systemic opioids; however, use must be weighed against the side effects of placement including bladder dysfunction, hypotension, pruritis, and nausea/vomiting [36]. A summary of regional anesthesia modalities can be viewed in Table 16.2.

Alternative Modalities

Acupuncture has been studied as an adjunctive therapy for postoperative pain. Meta-analysis suggests that acupuncture is effective at reducing postoperative opioid consumption; however, studies demonstrated significant heterogeneity in the samples, and results should be interpreted with caution [37].

Other common nonpharmacologic therapies include cold and heat therapy, both of which have been studied with inconclusive evidence to neither support nor discourage use although robust

Table 16.1 Pharmacologic methods for managing pre-, intra-, and postoperative pain

	Dose	Route	Frequency	Mechanism	Notes
Preoperative					
Acetaminophen	1000 mg	PO	Once, preoperatively	COX enzyme inhibition	Not to exceed 4 g from all sources, adjust dosing in hepatic impairment
Gabapentin	600 mg	PO	Once, preoperatively	Calcium channel inhibition of neurotransmitter release	
Celecoxib	400 mg	PO	Once, preoperatively	COX-2 enzyme inhibition	
Intraoperative					
Liposomal bupivacaine	266 mg (20 mL) maximum	Infiltration	Once, intraoperatively	Depolarization inhibition, sodium ion blockade	Injection to surgical incision site(s) postoperatively
Intraperitoneal local anesthetic	Weight based, specific to anesthetic	Instillation	Once, intraoperatively	Depolarization inhibition, sodium ion blockade	Instillation into abdominal cavity, toxicity depends on which local anesthetic is used and is weight based
Postoperative					
Acetaminophen	1000 mg	PO	Every 6 hours, scheduled	COX enzyme inhibition	Not to exceed 4 g from all sources, adjust dosing in hepatic impairment

Ketorolac	15–30 mg	IV/IM	Every 6 hours, scheduled	COX enzyme inhibition	Not to be used concurrently with ibuprofen
Ibuprofen	800 mg	PO	Every 6 hours, scheduled	COX enzyme inhibition	Not to be used concurrently with ketorolac
Oxycodone	5–10 mg	PO	Every 4 hours, as needed	Opioid agonist	

Table 16.2 Regional anesthetic modality summary

Regional anesthesia	Duration	Benefits	Limitations
Transversus abdominis plane block	24–48 hours	Ease of administration	Short duration
Epidural anesthesia	Immediate until removal	Superior pain relief	Side effect profile – bladder dysfunction, hemodynamics, pruritis, nausea/vomiting

studies are not available in the gynecologic surgery population. The use of modalities such as transcutaneous electrical nerve stimulation (TENS) has been found to reduce postoperative analgesic use although specific regimens for use vary in the literature [29, 38].

Cognitive Behavioral Modalities

As with other alternative modalities, cognitive behavioral therapies and methods have been noted to have some positive effects on postoperative pain, however, with wide practice variation and heterogeneity. For the purposes of this chapter, these methods should be considered, but there is no one agreed upon approach in the postoperative period [29].

Conclusion

Pain control in gynecologic surgery demands a broad, multidisciplinary approach with collaboration between the patient, surgeon, anesthetist, nursing and ancillary staff. A multimodal approach beginning in the preoperative period is essential in providing adequate care to the surgical patient. Many preoperative, intraoperative, and postoperative interventions and management strategies are available and continue to evolve for reducing and managing postoperative pain.

As economic pressures to perform major gynecologic surgical procedures on an ambulatory basis increase, any strategy for pain management that can decrease the period of hospitalization and disability clearly will have significant implications for the overall cost of treatment and loss of income often sustained by patients during hospitalization.

Guidelines for the management of perioperative gynecologic pain should promote evidence-based, effective, and safer postoperative pain management in women, addressing areas that include preoperative education, perioperative pain management planning, use of multimodal pharmacologic and nonpharmacologic modalities, and transition to outpatient care.

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Perioperative Analgesia and Pain Management in Pediatric Patients

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Introduction

Managing perioperative pain in pediatric patients is often challenging for both medical providers and caregivers. Recent literature suggests that inadequate perioperative pain control in children persists in many clinical settings and has proven to be an underacknowledged surgical complication associated with increased overall morbidity and mortality [1–3]. Regardless of the type of intervention, surgery is a stressful event for children. Relieving preoperative anxiety and postoperative pain in children is necessary to reduce negative responses to medical care, as well as maladaptive postsurgical behavior and long-term effects [4]. The American Academy of Pediatrics recommends a combination of pharmacologic and non-pharmacologic strategies to address pediatric patient pain and distress [5]. With data incorporated from randomized controlled trials, case series, and large audits, recommendations for management continue to evolve over time. The scope of perioperative care is now extending beyond the immediate perioperative period to also include perioperative anxiety, pain following discharge, and potential preventive strategies for persistent postsurgical pain [6]. Implementing evidence-based recommendations and quality improvement strategies for perioperative pain management is essential to maintaining patient safety and optimizing surgical outcomes.

Some patient factors pose greater challenges than others for managing perioperative pain. Children who are either very young or nonverbal are limited in their capacity to communicate their pain experience [7]. In addition, children with developmental disabilities experiencing pain or distress may not reflect behaviors commonly observed in typically developing children [8]. Alternate strategies must be taken to approach these patients, especially with regard to pain assessment. Other patients with significant medical comorbidities or genetic abnormalities may also encounter significant limitations on what types of treatments and interventions are safe to administer. Alternatively, some patients who have previously experienced inadequate pain control develop greater sensitivity to subsequent painful stimuli and

experience decreased efficacy of future analgesics, thereby increasing the risk of developing chronic pain [9–11]. If traditional pain regimens are ineffective or potentially harmful, pharmacologic and non-pharmacologic adjustments often must be made. Panella et al. suggest that optimal care is provided when the medical team understands and respects the child's developmental level, includes family members and caregivers in decision making, and works to create a positive medical experience [12]. Recognition of and adaptability to the needs of patients can significantly affect the surgical experience for patients and their families.

With a greater number of outpatient pediatric surgeries, a shift has emerged toward cost-containment efforts that discourage time-intensive behavioral interventions in hospitals [2]. In this case, non-pharmacologic interventions are more difficult to coordinate without specific systems or protocols in place. While the focus of pain management has traditionally centered on acute postoperative care, several recent studies among pediatric patients have emphasized the impact of preoperative anxiety, coping methods, and prior pain experience affecting outcomes [8, 13, 14]. Even in the context of a perfectly executed operation, patients may still encounter considerable morbidity depending on the extent and implementation of their pain management plan. Effective perioperative analgesia seeks to provide adequate treatment while minimizing the use of opioids and preventing the long-term consequences of pain [1].

Codeine

Opioid medications continue to be an important component of treatment and at the forefront of active research across multiple medical specialties, and strong emphasis has been placed on a reduction in their use during perioperative care [15]. Codeine and other narcotic medications have been associated with numerous adverse events in children, including fatalities. With immature physiology and a wide array of metabolic responses to

pharmacotherapy, many children do not have a standard response to treatment. For example, patients with duplication of the gene encoding cytochrome PD4502D6 (CYP2D6) have ultra-rapid metabolism of codeine, which may lead to life-threatening respiratory depression from morphine intoxication, a reported cause of multiple fatalities [16]. Therefore, in 2012 the World Health Organization (WHO) issued guidelines straying away from their widespread use [17]. As a result, there has been a growing trend to reduce or eliminate the use of opioids to prevent adverse events [1]. While the reduction of opioid overprescription has shown promise in combating the current opioid epidemic in the United States, minimizing the risk of opioid-related adverse events should not be achieved at the expense of adequate analgesia [18].

A great deal of postoperative pain is managed by either applying protocols or trial and error, which can often lead to significant undertreatment or overtreatment [1]. Given the wide interindividual variability in morphine concentration-response, which is influenced by pharmacokinetic, pharmacodynamic, and pharmacogenomic factors, titration against individual response remains essential in clinical care [18]. However, the combined use of simple non-opioid analgesics, such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), with a multimodal approach may limit the need for opioids, thus decreasing the risk of toxicity and dose-related side effects [1]. Identifying evidence-based practices for safe postoperative prescribing, effective patient and parent education, and proper disposal avenues for unused medications are necessary to improve surgical recovery and prevent opioid-associated morbidity and mortality [19]. Although surgeons are limited in how much time and effort they can commit to ensure optimal pain management before surgery and after discharge, recognizing the impact of perioperative pain on a patient's physical, emotional, and psychological well-being is crucial for reducing overall morbidity and improving surgical outcomes. The primary goals of pain management in pediatric patients include managing perioperative expectations, controlling anxiety, preventing, and reducing acute pain while maintaining functional capacity to facilitate a safe healing trajectory.

Pediatric Pain Assessment

Pain assessment tool	Age range	Type of pain
Faces scales (Wong-Baker, FPS-R) [20, 21]	4+ years	Acute, procedural, postoperative
Parent's postoperative pain measure [22]	0–18 years	Postoperative
FLACC pain assessment tool [23]	0–18 years	Acute, procedural, postoperative
Visual analog scale [24]	8+ years	Acute, procedural, postoperative, chronic

Comprehensive pain assessment plays a significant role not only in the acute postoperative phase but also in the management of the preoperative period. This task can be highly nuanced and may be more challenging to elicit in some patients than others depending on a child's developmental stage and capacity. As referenced previously, most children under the age of three or suffering from developmental disabilities may not have adequate sensory perception or communication skills to express pain and discomfort reliably, and certain medications have variable sedative and analgesic effects in children. In these cases, targeted clinical observations and physiologic markers may be more indicative guides to pain assessment than traditional means [25].

Several strategies and validated tools have been developed in order to aid with pediatric pain assessment [26]. While pain is largely subjective, multiple tools may be used to monitor and quantify a patient's pain experience. For example, some widely utilized strategies include self-reporting (e.g., faces scales), behavioral cues (e.g., Parents' Postoperative Pain Measure and FLACC Pain Assessment Tool), and even physiologic biomarkers [23, 27–29]. Other common techniques include self-reporting methods, projective methods, and structured interviews. Behavioral assessment has been shown to be most useful in the preverbal phase. As children often have difficulty separating pain from mood, facial analog scales are an imprecise measure of pain when used alone [30]. Reliability improves significantly when used in combination with other self-reporting methods such as projective methods and

questionnaires. However, the latter methods generally require the patient to be cognitively developed enough to communicate reliably with caregivers [26]. Despite these measures, a child's postoperative pain often remains inadequately recognized by both physicians and parents alike [2, 31–33].

Preoperative Strategies

Indications for surgery in children are wide-ranging, both in scope and acuity, and pain management strategies should be guided by specific needs of the patient rather than a one-size-fits-all model. Studies have shown that teaching the patient and family about the surgical procedure and establishing expectations before and after surgery is best done during the preoperative period [14]. As various psychological, physiological, and cultural factors influence a patient's pain experience, engaging each of these aspects will likely result in a greater standard of perioperative care.

Untreated anxiety and pain have significant implications for children's short- and long-term recovery and future interactions in the medical environment [2]. Regardless of the type of operation, surgery is often a tremendous stressor among children and their families [12, 13]. Coping with an invasive procedure, dealing with the uncertainty of the surgical outcome, and managing the stress of hospitalization each contribute substantial preoperative anxiety which has shown to have a significant impact on patient outcomes [13]. Several studies have found that children who are highly anxious before surgery are more likely to experience higher postoperative pain, delayed hospital discharge, and a higher incidence of emergence delirium as well as sleep disturbances and other maladaptive behavioral changes that may last up to a few weeks following surgery [2, 6, 14]. High parental anxiety also may perpetuate high anxiety in the child, so it is also important to address the fears and concerns of the child's family members and involve them in the child's care [12]. Therefore, although preoperative anxiety is frequently minimized or disregarded, evidence strongly supports the value of addressing it proactively.

The rising demands for efficiency and productivity in the surgical space have created some unintended consequences within

the conventional infrastructure of perioperative care. As a result, the use of traditional behavioral preparation programs for surgery, which were once very popular and readily available in hospitals, has decreased significantly in the United States [2]. According to Fortier et al., the idea that day of surgery counseling measures can replace traditional preparation programs conducted several days prior to the procedure is simply not valid. However, child life specialists have come to the forefront of preoperative and postoperative on-site care. Methods of engagement of child life specialists along with various behavioral strategies and preoperative pharmacotherapy comprise the primary management strategies for children prior to surgery.

Involvement of Child Life

Having first been introduced in 1955, child life programs have now become the standard in large pediatric settings to address the psychosocial concerns that accompany hospitalization and other healthcare experiences for children. Child life specialists work with children in healthcare settings striving to alleviate anxiety and help children and families cope with a variety of health care experiences [14]. As pain has both physiological and psychological components, these services can be particularly helpful when utilized in the perioperative period. Most major medical centers, children's hospitals, and some outpatient centers have child life departments that provide formal surgical preparation programs, generally led by child life specialists [12]. Compared with other methods of preparation such as films or books, the preparation conducted by a child life specialist has been found to significantly reduce children's anxiety related to surgery [14]. They can effectively explain and prepare children and families for medical events, such as anesthesia and surgical procedures, in developmentally appropriate ways. Although more research is needed, there is evidence that child life services help to contain costs by reducing the length of stay and decreasing the need for sedation and analgesics [34].

Using therapeutic play, expressive modalities, and psychological preparation as primary tools, in collaboration with the entire healthcare team and family, child life interventions facilitate

coping and adjustment at times and under circumstances that might otherwise prove overwhelming for the child [34]. Diversionary activities, such as children's movies, toys, arts, and crafts, are commonly used in the perioperative period for these purposes. Some inpatient services coordinated by child life departments may also include playrooms, art studios, hospital school programs, pet therapy, organized games, and other special events. In addition to forming a strong therapeutic relationship, child life intervention strategies also generally serve to promote optimal development, educate children and families about health conditions, plan and rehearse useful pain management and coping strategies, and help children work through feelings about past or impending experiences [12, 34].

Before surgery, child life specialists often escort patients to the operating room for induction. Regarding child life intervention in ambulatory surgery, Brewer et al. found statistical evidence supporting that all children, not just those with a perceived need, can benefit from preparation with child life specialists, reducing anxiety associated with medical and surgical encounters [14]. When preoperative preparation by a certified child life specialist cannot be provided, perioperative nurses are in the best position to assist children and family members in coping with the surgical environment and its routines. In appropriate settings, perioperative nurses can seamlessly integrate many elements from formal child life programs into their work. By taking into consideration the child's developmental level and the associated parental concerns, nurses can make alterations in their care to provide adequate preparation while performing preoperative assessments and tasks [12]. Overall, in recognizing the broader needs of pediatric healing and coping, child life specialists seek to encourage recovery by treating the whole child.

Behavioral Strategies

While many behavioral and coping techniques may be implemented with the help of child life specialists, some other behavioral strategies have been cited in the literature as being useful in

the preoperative setting. A 2018 Cochrane review focused on the utility of cognitive behavioral therapy (CBT) in the management of pain associated with venipuncture, IV insertion, and vaccine management [35]. While pharmacologic interventions are sometimes necessary, utilizing non-pharmacologic pain control for placement of perioperative needle sticks or routine procedures is preferred. Although the quality of evidence in this review was rated low to very low, the use of CBT, breathing interventions, hypnosis, and distraction demonstrated efficacy in reducing pain associated with several preoperative procedures. In a recent study, Vagnoli et al. describe the role of relaxation-guided imagery in reducing preoperative anxiety due to previous surgery experiences and postoperative pain [4]. While this technique requires specific psychological training to administer, it has offered positive results in challenging patients. Given that the overwhelming majority of children's surgery is outpatient, Fortier et al. have proposed a conceptual framework for a tailored, web-based behavioral preparation program that is accessible repeatedly at times convenient to the child and family, and includes coping skills training and modeling, and provides unique output based upon child and parent characteristics known to impact perioperative pain and anxiety [2]. This model can be used throughout the perioperative period. As the structure of the medical system advances over time, it is important for innovations to fill the gaps in offering comprehensive patient care. When approaching pain control with behavioral therapy, it is most effective as an integrative, multidisciplinary approach in combination with pharmacologic treatment [36].

Preoperative Pharmacotherapy

Depending on the scope and indication for the surgical intervention, preoperative pharmacotherapy can be useful in pediatric patient care. The most commonly used medications prior to induction may include antiemetics, anticholinergics, sedatives, and simple analgesics. Moreover, patients experiencing significant nausea or vomiting may benefit from preoperative ondansetron

and/or a scopolamine patch, which is generally reserved for older children over 13 years of age [37]. Acetaminophen and midazolam are also commonly used in the preoperative period for their analgesic and sedative properties. While surgeons may offer these at their discretion, anesthesiologists may be likely to designate preoperative pharmacotherapy in accordance to their protocols and experience. The majority of perioperative pharmacotherapy for analgesia is initiated upon induction of anesthesia and continues into the immediate postoperative period. When administering medications to pediatric patients, the WHO recommends oral and intravenous (IV) delivery methods over intramuscular injections in order to limit any additional burden of pain [17]. Ultimately, while these guidelines are highly recommended, they are not prescriptive, and adjustments should be made to tailor therapy to the specific needs of the individual child.

Drug (preoperative)	Indication	Dosage
Ondansetron [38]	Nausea or vomiting	Patient <40 kg: 0.1 mg/kg/dose (IV) Patient >40 kg: 4 mg/dose (IV)
Scopolamine [39]	Nausea or vomiting	6 mcg/kg/dose, max 0.3 mg/dose (IV, IM, SubQ)
Midazolam [40]	Analgesia or sedation	0.1–0.15 mg/kg 30–60 minutes before surgery; range: 0.05–0.15 mg/kg; doses up to 0.5 mg/kg have been used in more anxious patients; max 10 mg/dose (IM)
Clonidine [41]	Analgesia (non-narcotic)	4 mcg/kg (oral)

Intraoperative Strategies

Narcotic Pharmacotherapy

In response to the boxed warning released on codeine use in children, there has been a wealth of ongoing research working to nearly eliminate the use of opioids in perioperative management [7]. However, opioids still play a major role in perioperative analgesia and can be used safely at appropriate dosages. Morphine

and fentanyl are both commonly and effectively used intraoperatively. One study of patients undergoing bilateral myringotomy compared efficacy of routes of administration between intranasal fentanyl (2 mcg/kg), IV morphine (0.1 mg/kg), and IM morphine (0.1 mg/kg) [42]. It was found that there was no difference between the drugs or routes in either postoperative pain or emergence delirium in these patients [42].

Non-narcotic Pharmacotherapy

Research continues to find novel, opioid-free methods to manage surgical pain. This section presents a highly abbreviated list of some of these reported strategies. Non-narcotic medications may be given systemically, such as IV acetaminophen or ketorolac, to decrease the need for postoperative opioid use [43]. Peripheral and regional anesthesia has also been used to reduce the need for oral medications [43, 44]. For example, the use of a combined femoral and sciatic nerve block with ropivacaine during ACL repair has been shown to significantly reduce intraoperative opioid usage and improve pain scores in the post-anesthesia care unit (PACU) [44]. With increasing availability of ultrasound technology, regional anesthesia has become highly effective in controlling pain during operation [45, 46]. Continuous infusion of lidocaine intraoperatively has been shown to reduce opioid consumption, reduce pain scores, and allow faster recovery of bowel function following abdominal operations [34]. Intraoperative injections of onabotulinumtoxin-A into the detrusor muscle during bladder reconstructive surgery reduces both opioid and anticholinergic requirements postoperatively [47]. Intraoperative dexmedetomidine, at dosages of at least 0.5 micrograms/kg, has been shown to reduce postoperative pain and the need for postoperative narcotic pain medications when compared with intraoperative placebo or opioid [41, 48]. A single dose of dexamethasone has also demonstrated a reduction in pain scores among children undergoing tonsillectomy [41]. Both ketamine and clonidine decrease pain in the early postoperative period following minor surgeries [41]. Recent studies have also outlined the use of intercostal nerve cryoablation in the minimally invasive repair of pectus excavatum by the Nuss

procedure [49]. Cryoablation offered comparative pain control while decreasing both hospital length of stay and opiate requirement in comparison with traditional thoracic epidural analgesia [49]. In addition to the aforementioned methods of opioid-sparing analgesia, there are numerous others actively being studied and developed. These novel methods of pain management allow a continued reduction in use of narcotics intraoperatively, resulting in equivalent analgesia with decreased risk for the patient.

Drug (intraoperative)	Indication	Dosage
Morphine [50]	Analgesia	0.05–0.01 mg/kg/dose with max 4 mg administered 5 minutes prior to procedure (IV)
Fentanyl [51]	Analgesia or general anesthesia	Age 2–12 years: 2–3 mcg/kg/dose (IV) Age 13–18 years: Initial 2–20 mcg/kg/dose with maintenance 1–2 mcg/kg/hour (IV)
Acetaminophen [41, 52]	Analgesia (non-narcotic)	Age < 2 years: 7.5–15 mg/kg/dose every 6 hours (IV) Age > 2 years: 15 mg/kg/dose every 6 hours (IV) 40–60 mg/kg (rectal)
Ropivacaine [53]	Nerve block	Dosage dependent on anatomical region and length of procedure
Dexmedetomidine [41, 48]	Analgesia (non-narcotic)	Minimum 0.5 mcg/kg (IV)
Dexamethasone [41]	Analgesia (non-narcotic)	Single dose of 0.4–1.0 mg/kg (IV)
Ketamine [54]	Analgesia (non-narcotic)	0.5 mg/kg (IV)

Postoperative Analgesia

Assessment in Children <3 Years Old

The vast majority of children under age 3 years old are often unable to verbally communicate their pain reliably. This limitation

can hinder postoperative management of analgesia as nurses and parents may struggle to accurately assess the child's pain threshold [55]. There have been several proposed tools to assess pain in children who are unable or unwilling to verbalize the severity of their pain. Notably, the FLACC (face, legs, activity, cry, consolability) pain scale has been largely validated for children up to the age of 16 years old and allows objective rating of pain based on behavioral observation [7]. Each of the listed categories is rated with a score of 0, 1, or 2 based on a range of behaviors resulting in a pain score between 0 and 10 [7]. Studies have shown that utilization of the FLACC scale is most effective when consistently "scaled" by the same caregiver [7]. One notable finding in regard to the FLACC scale was the potential for overestimation of scores in the context of postoperative emergence delirium [7]. This should be taken into consideration in the immediate postoperative period.

The analgesia nociception index (ANI) is another tool that was developed to objectively measure acute postoperative pain based on heart rate variability and may be useful to ascertain pain intensity in children who are young or cognitively impaired [56]. It has been less extensively validated, but has the strength of utilizing objective measurements over subjective scaling.

To compensate for the lack of verbal communication, the care team involved in the postoperative period should be trained in validated, age-appropriate assessment tools [55]. In addition, the parents or caregivers responsible for medication dosing following discharge should be provided adequate training in the use of these assessment tools.

Assessment in Children >3 Years Old

Often, older children are able to effectively communicate their pain. In cases when it is difficult for them to verbalize, the mechanisms listed above are generally acceptable in older children as well. Specifically for older children, the Faces Pain Scale-Revised (FPS-R) utilizes a series of six faces ranging from "no pain" to "most pain." This scale has excellent reliability in defining pain in children age 4 years old and up [20, 21, 57].

Behavioral Modifications

Behavioral modifications can be effective at reducing postoperative pain. These nonpharmacologic methods, such as appropriate elevation or ice therapy following orthopedic operations, are easily overlooked or underrepresented to patients following operations [43]. Children have reported a need for improved communication between their nurses and caretakers regarding management of their pain after discharge [55]. They report that parental presence during the postoperative time period is the best way for parents to help them cope with pain [55]. In addition, other methods such as distraction and positioning have been recommended by children as important forms of nonpharmacological pain management [55]. While these exercises can be useful in managing the psychological impact of pain, they are rarely able to provide analgesia on their own and children still report a need for pharmacological therapy [55].

Pharmacologic Strategies

Following surgery, it is highly recommended to switch to enteral analgesia as soon as the patient can tolerate a diet [43]. Multimodal analgesia including acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) is highly recommended and is often able to serve as the sole source of analgesia in pediatric patients, regardless of route given [41, 43]. It is important to note that different routes of administration will impact dosage required to provide analgesia. For example, rectal acetaminophen requires a minimum dosage of 40 mg/kg, while IV acetaminophen requires only 15–30 mg/kg [41]. Many children describe nausea and vomiting as unpleasant or painful and may be hesitant to report their pain to nurses because they feel the pain medications induce nausea [55]. Because of this, it is highly recommended to include an antiemetic regimen in the postoperative care plan to reduce the fear of analgesic medications and allow for better control of children's pain [55].

One study in colorectal surgery found that implementation of a pediatric-specific enhanced recovery protocol (ERP) significantly

reduced length of stay, time to normal diet, dose of narcotics, and volume of intraoperative fluids [58]. The ERP was a comprehensive plan describing preoperative management as well as a postoperative pain regimen including scheduled antiemetics, ketorolac, gabapentin, and acetaminophen alongside morphine and hydromorphone for breakthrough pain [58].

Opioids

Though not first-line analgesia, opioids are appropriately prescribed as needed at safe dosages such as morphine (0.2–0.5 mg/kg, every 4–6 hours), oxycodone (0.05–0.15 mg/kg, every 4–6 hours), and hydrocodone (0.1–0.2 mg/kg, every 6–8 hours) for breakthrough pain [58]. The most recent guidelines recommend that if opioids are given postoperatively, they should be used at low doses with watchful titration and continuous pulse oximetry [46]. It is important to note that opioid over-prescription is not uncommon and often leads to problems regarding use or disposal of the unused pills. One study surveying high school seniors found that 80% had recreationally used their leftover pain medication from legitimate prescriptions [43], indicating the need to revise the standard quantity of pills prescribed postoperatively and better educate families about appropriate disposal of unused medications [43].

Drug (postoperative)	Indication	Dosage
Acetaminophen [41, 52]	Analgesia (non-narcotic)	Age < 2 years: 7.5–15 mg/kg/dose every 6 hours (IV) Age > 2 years: 15 mg/kg/dose every 6 hours (IV) 40–60 mg/kg (rectal)
Ondansetron [38]	Nausea or vomiting	Patient <40 kg: 0.1 mg/kg/dose (IV) Patient >40 kg: 4 mg/dose (IV)
Morphine [58]	Analgesia	0.2–0.5 mg/kg every 4–6 hours
Hydrocodone [58]	Analgesia	0.1–0.2 mg/kg every 6–8 hours
Oxycodone [58]	Analgesia	0.05–0.15 mg/kg every 4–6 hours

Anesthesia

As briefly mentioned above, regional nerve blocks can be employed in numerous operations to help reduce pain associated with surgery. Nerve blocks are advantageous in that they provide effective local analgesia without the systemic side effects seen with oral or intravenous therapies [59, 60]. Due to the nonsystemic delivery, nerve blocks have lower incidence of postoperative bleeding, nausea, and vomiting [59]. Nerve blocks commonly employ a combination of bupivacaine with epinephrine [60]. Though very rare, they are not without adverse effects and may cause hematoma or a variety of paralytic effects depending on the location of injection [60].

Conclusion

Management of perioperative pain in the pediatric population is optimally performed in the setting of a multidisciplinary team including the physician, nurse staff, child life specialist, a variety of therapists, and the patient's home caregiver. To effectively minimize the psychological and physical morbidity surrounding surgery, appropriate preoperative communication with the patient and family is important to set expectations and provide education on the operation as well as the perioperative management plan. Communication between the healthcare team, patient, and family is of highest importance in the perioperative window and should be conducted intentionally in regard to the needs of each patient.

It can be challenging to manage postoperative pain in children as the patient may be unable to communicate effectively and often the medication must be given by a caregiver. In addition, if patients have traveled for an operation, postoperative follow-up can be challenging as the patient may not return to the operating physician. It is important to exercise great care in these situations to provide optimal analgesia for patients while also stewarding medications appropriately. Preoperative counseling and expectation management can help alleviate the postoperative anxiety for both patients and caregivers.

In addition to traditional opioid management, there is ample literature to support the use of acetaminophen, NSAIDs, dexamethasone, ketamine, clonidine, and dexmedetomidine to reduce perioperative pain and opiate usage [41]. There are numerous studies in the adult population regarding novel approaches to pain control that have yet to be validated in the pediatric population. This represents an area of great need for future research efforts.

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Conflicts of Interest None.

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18

Approaches to Perioperative Pain Management in the Plastic Surgical Patient

Jacob I. Tower and Boris Paskhover

Introduction

The United States and other nations are in the midst of an opioid epidemic that has resulted in a surge of addiction, overdoses, and preventable deaths for approximately two decades [1, 2]. The cause of the epidemic is multifactorial, but partly rooted in pressure on physicians and other prescribers to control patients' pain, which is measured as an indicator of quality of care and tied to reimbursement [3]. Other factors including pharmaceutical marketing, patient demand, and the perceived "safety" of opioid analgesia have contributed to the prescription epidemic [4]. Inadequate pain control results in worse surgical outcomes and confers an increased risk of chronic post-surgical pain. It is more imperative

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than ever that surgeons learn to balance the demands of pain management, patient satisfaction, and desired surgical outcome while also being good stewards of opioid medications that are known to be addictive and which can lead to serious health problems and death. In this chapter, we will consider methods of perioperative pain control with the aim of providing multimodal analgesia for plastic surgical patients under a range of operative situations.

Plastic surgery is unique in that the specialty encompasses procedures that are performed all over the body and range from simple (e.g., scar revision) to extremely complex (e.g., microvascular free tissue transfer). Many of the principles of perioperative pain management transcend this particular field and may be applied broadly when managing surgical patients; however, in this chapter we will consider how new and emerging perioperative pain control techniques are influencing the management of plastic surgical patients. The diversity of pain control modalities discussed will reflect the diversity of plastic surgery, and will inform an evidence-based practice.

This chapter will emphasize non-opiate perioperative pain control modalities. Evidence is growing that non-opiate pain medications and perioperative techniques can be used to minimize postoperative analgesia requirements in plastic surgical patients. Multimodal analgesia is the use of two or more medications with different mechanisms of action to control postoperative pain (Fig. 18.1). Such agents often include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentenoids, and regional anesthesia [5]. These medications have been used in tandem with evidence of reducing postoperative opiate consumption in surgical patients. Multimodal anesthesia and enhanced recovery after surgery (ERAS) pathways represent paradigm shifts in caring for plastic surgical patients, many of whom are undergoing elective procedures.

Opioids

Opioid analgesics encompass a broad category of drugs including both alkaloids and semisynthetic derivatives extracted from poppy seeds (morphine, oxycodone, hydromorphone, etc.), synthetic

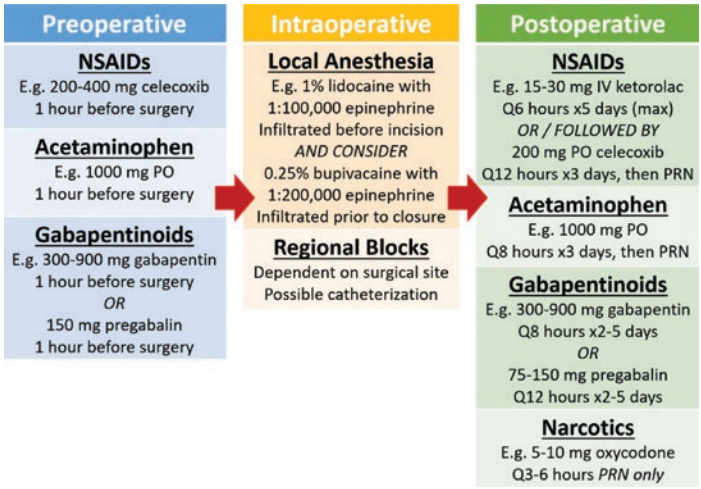

Fig. 18.1 Example multimodal analgesia regimen. *PO* oral, *IV* intravenous, *PRN* as needed, *Q* every

phenylpiperidines (meperidine, fentanyl), and synthetic pseudopiperidines (methadone) [6]. These drugs act on μ, δ, and κ receptors which are distributed widely throughout the central and peripheral nervous systems and each have their own endogenous ligands. Opioids also act broadly on other organ systems, accounting for many of the adverse, non-analgesic properties such as respiratory depression, cough suppression, constipation, nausea, and bradycardia (Table 18.1).

Despite the adverse effects of opioid analgesics, these medications often form the foundation of perioperative pain control. In the United States, up to 75% of patients are prescribed opioids at hospital discharge after minor surgery, and the risk of misuse increases by 44% per week of repeat prescription after discharge [7, 8]. In a recent survey of members of the American Society of Plastic Surgeons, the most commonly prescribed narcotics were hydrocodone with acetaminophen (42.5%) and oxycodone with acetaminophen (38.1%), followed distantly by oxycodone (7.0%), and codeine with acetaminophen (5.5%) [9]. Tramadol was prescribed for only 2.2% of procedures. The results of this survey closely mirror those of a survey administered to the American

Table 18.1 Common analgesic modalities and their properties

Modality	Examples	Advantages	Disadvantages	Other	Usual adult dosages
Acetaminophen	–	*Opioid sparing IV and PO formulations available*	*Hepatotoxic*	*Often included in narcotic agents—Take into account if prescribing mixed formulations*	*650–1000 mg PO/IV once preoperatively 650 mg PO Q4-6H postoperatively Maximum 4000 mg/day*
NSAIDs	–	*Opioid sparing*	*Platelet dysfunction, increased risk of GI adverse events*	*Prolonged use is more likely to cause adverse events*	–
COX-1/-2 inhibitor	Ketorolac	IV and PO formulation available	Nephrotoxic, maximum 5 days use combined IV/PO, non-selective COX inhibition	Avoid use in patients with CKD, lower dosages in geriatrics	15–30 mg IV Q6H; maximum 120 mg/day 10 mg PO Q4-6H (following IV therapy) Maximum 5 day use
COX-1/-2 inhibitor	Ibuprofen	IV and PO formulation available, over-the-counter	Nonselective COX inhibition	Avoid prolonged use due to COX-1 inhibition	400 mg PO Q4-6H postoperatively

Selective COX-2 inhibitor	Celecoxib	Selective COX-2 inhibition resulting in less GI side effects and platelet dysfunction	Expensive, prescription only	Possible higher risk of cardiac adverse events (controversial); consider avoiding in patients at risk of heart attack	200–400 mg PO once preoperatively 200 mg PO Q8H postoperatively
Gabapentinoids	–	*Opioid sparing*	*PO formulations only; somnolence, dizziness, peripheral edema*	*Renal excretion, use with caution in patients with CKD*	*Approximate 6: 1 conversion ratio of gabapentin: Pregabalin*
CCB	Gabapentin	Available as generic	Less potent, less predictable pharmacokinetics	–	300–600 mg PO once preoperatively 300–900 mg PO Q8H postoperatively
CCB	Pregabalin	Available as generic, more potent, predictable pharmacokinetics	Less data in plastic surgery	–	150 mg PO once preoperatively 75–150 mg PO Q12H postoperatively

(continued)

Table 18.1 (continued)

Modality	Examples	Advantages	Disadvantages	Other	Usual adult dosages
Local anesthetics	–	*Fast onset, targeted action, opioid sparing*	*Invasive administration, potential CNS and CV toxicity*	*Only given intraoperatively via local infiltration, regional nerve block, or via catherization/ pump*	*Variable depending on surgical site*
NaCB (amide)	Lidocaine	High maximum safe dosage	Short duration of action	Buffering with sodium bicarbonate may cause improper dosing	Maximum 4 mg/kg without epi (not to exceed 300 mg total) Maximum 7 mg/kg with epi (not to exceed 500 mg total)
NaCB (amide)	Bupivacaine	Long duration of action	Prolonged latency of onset	Buffering with sodium bicarbonate may cause improper dosing	Maximum 2 mg/kg without epi (not to exceed 175 mg total) Maximum 3 mg/kg with epi (not to exceed 225 mg total)
NaCB (amide)	Liposomal bupivacaine	Slow release lasting up to 72 hours	Expensive	Liposomal delivery system; more commonly used in regional blocks	266 mg bolus dose

Narcotics	–	*Fast onset, highly potent*	*Addictive potential, physical dependence, tolerance, withdrawal, constipation, respiratory depression, nausea, potential paradoxical hyperalgesia*	*Potency measured in morphine milligram equivalents (MME) Higher dosages (>50 MME/day) are associated with higher risk of overdose and death*	*Use caution and prescribed at the lowest effective dose; consider prescribing naloxone if prescribing > 50 MME/day; postoperative use only*
μ opioid agonist	Morphine	IV, PO liquid, and extended release formulations available	–	MME conversion factor: 1.0	2–5 mg IV Q3-4H (breakthrough only)
μ opioid agonist	Oxycodone	Liquid, extended release and acetaminophen-containing formulations available	–	MME conversion factor: 1.5	5–10 mg PO Q4-6H (immediate release)

(continued)

Table 18.1 (continued)

Modality	Examples	Advantages	Disadvantages	Other	Usual adult dosages
μ opioid agonist	Hydrocodone	Liquid, extended release and acetaminophen-containing formulations available	–	MME conversion factor: 1.0	5–10 mg PO Q4-6H (immediate release)
μ opioid agonist	Codeine	Liquid and acetaminophen-containing formulations available	Greater potential for toxicity in CYP2D6 ultra metabolizers; less effective in CYP2D6 poor metabolizers	MME conversion factor: 0.15 Contraindicated in children <12	15–60 mg PO Q4H
Weak μ opioid agonist/SNRI agonist	Tramadol	Lower risk of addiction Less constipation Minimal respiratory depression	Less potent analgesic Lowers seizure threshold Increased risk of serotonin syndrome in those taking serotonin reuptake inhibitors	MME conversion factor: 0.1 Contraindicated in children <12	50–100 mg PO Q4-6H

MME morphine milligram equivalents, *PO* oral, *IV* intravenous, *CKD* chronic kidney disease, *COX* cyclooxygenase, *CCB* calcium channel blocker, *NaCB* sodium channel blocker, *NSAIDs* non-steroidal anti-inflammatory drugs, *GI* gastrointestinal, *CNS* central nervous system, *CV* cardiovascular

Academy of Otolaryngology—Head and Neck Surgery, among which a large proportion are fellowship trained facial plastic surgeons [10]. These statistics are relevant because various opiate pain medications seem to have varying degrees of addictive potential. Regarding the two most commonly prescribed opioid analgesics, oxycodone and hydrocodone, there is substantial evidence that oral oxycodone has an elevated abuse liability profile when compared to hydrocodone [11].

Though tramadol represents only a small slice of opioid prescriptions among plastic surgeons, it deserves special attention. Among the opioids most commonly prescribed by plastic surgeons postoperatively, tramadol is a unique opioid medication that works by very weak μ-opioid receptor activation as well as inhibition of serotonin and norepinephrine reuptake (SNRI). Tramadol hydrochloride is less potent as an analgesic than other opioids or NSAIDs, but has a relatively lower risk of addiction, less constipation, and minimal respiratory depression [12]. While these properties make tramadol appealing as an analgesic, the medication is associated with a higher incidence of seizures and therefore should be used with caution in patients with a history of seizure. Also, being a SNRI, tramadol should be used cautiously in patients taking serotonin reuptake inhibitors because there is an increased possibility of serotonin syndrome.

A recent systematic review shows that postoperative prescription opioids often go unused, with 67–92% of patients reporting unused medications [13]. Moreover, these unused medications are often stored in unlocked containers and go undisposed which has created a large reservoir of opioids that can be used for nonmedical purposes. A recent study of plastic surgical procedures shows that surgeons may be prescribing almost double the amount of opioids consumed by patients after surgery [14].

Although there will always be a role of prescribing opiate pain medications perioperatively, it is important to understand the negative consequences of administering and prescribing these pharmaceuticals. In addition to the constipation, nausea, cough, and respiratory suppression that may result from these drugs and impair recovery from surgery, opioid analgesics may result in tolerance, dependence, addiction, and hyperalgesia. Paradoxical

opioid-induced hyperalgesia (OIH) is an increased sensitivity to pain which may be caused by acute or prolonged exposure to opioids. For example, infusion of remifentanil for 30 minutes is sufficient to cause OIH, and higher doses of intraoperative remifentanil have been associated with higher postoperative morphine consumption and increases in postoperative pain scores [7]. In such patients with OIH, pain may worsen with further opioid dosing; however, there is no specific test for this state, and if left untreated it can increase the risk of developing persistent postsurgical pain [7]. If OIH is suspected perioperatively, opioid dosing can be tapered, the agent can be rotated, and the addition of multimodal non-opioid analgesics may be employed. Administering NMDA receptor antagonists (i.e., ketamine) and employing regional anesthetics when possible has also been suggested [15]. There is evidence that for patients with chronic pain on chronic high-dose opioids, an intraoperative ketamine infusion may reduce opioid consumption and pain intensity postoperatively [16]. The adverse effects of tolerance, dependence, addiction, and hyperalgesia highlight the need for multimodal approaches to perioperative analgesia in the plastic surgical patient, and the use of medications with opioid-sparing effects to minimize these risks.

Nonsteroidal Anti-inflammatory Drugs and Acetaminophen

Although widely available and commonly used, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) may be overlooked as a foundation of postoperative analgesia. There is overwhelming evidence that the concurrent use of these agents with opioids postoperatively produces superior analgesia and an opioid-sparing effect that is associated with decreased postoperative nausea, vomiting, and sedation. NSAIDs, acetaminophen, and aspirin act through the inhibition of cyclooxygenase (COX-1 and COX-2) and prevent the conversion of arachidonic acid to prostaglandins which decreases pain and inflammation (Fig. 18.2). It is the differential distribution of the COX-1 and COX-2 isozymes in the tissues of the body that allows for the differences in

clinical action between non-selective COX-1/-2 inhibitors such as NSAIDs, aspirin, and acetaminophen and selective COX-2 inhibitors such as celecoxib. COX-1 is *constitutively active* in most tissues with important homeostatic functions in the gastric mucosa, renal tract, cardiovascular, and hematologic systems. Inhibiting constitutive prostaglandin and thromboxane synthesis mediated by COX-1 in these tissues causes reduced gastric mucus synthesis, increased gastric acid secretion, and platelet dysfunction. On the other hand, COX-2 is *inducible* and upregulated in inflamed tissues. Inhibiting prostaglandin synthesis in injured tissues with selective COX-2 inhibition reduces the localized hyperalgesia and pyretic effects without affecting constitutive COX-1 activity elsewhere in the body. In the United States, NSAIDs and acetaminophen are available as IV preparations and over-the-counter oral formulations, whereas selective COX-2 inhibitors (coxibs) are available by prescription only.

NSAIDs have an analgesic ceiling and are associated with platelet dysfunction, GI tract irritation and bleeding, and renal dysfunction. Due to the associated platelet dysfunction, there is a longstanding belief that the perioperative use of NSAIDs may

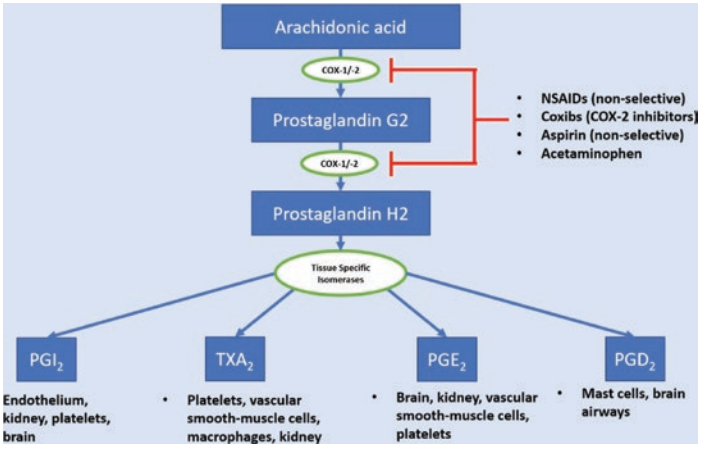

Fig. 18.2 COX inhibitors prevent the production of prostaglandins in tissues throughout the body

confer an increased risk of bleeding during or after surgery. NSAIDs inhibit the conversion of arachidonic acid to thromboxane A2, and therefore inhibit platelet aggregation which causes a theoretical risk of operative bleeding and postoperative hematoma, despite lack of evidence. By convention, surgeons typically withhold ibuprofen and other NSAIDs for 1 week before and after surgery. However, the evidence in the plastic surgical literature challenges this viewpoint [12]. A systematic review that analyzed randomized controlled trials of ibuprofen in plastic surgery revealed that ibuprofen was not associated with an increased risk of bleeding in the perioperative setting [17]. These randomized controlled trials collectively included over 400 patients undergoing a broad spectrum of procedures. Another systematic review and meta-analysis of NSAIDs (ibuprofen, ketorolac, and celecoxib) in plastic surgery also found no evidence of increased risk of perioperative bleeding or hematoma [18]. Additional studies of ibuprofen used for palatoplasty and tonsillectomy have also revealed no additional risk of bleeding compared to controls [19, 20]. A safety analysis of intravenous ibuprofen in 1752 patients revealed no association with increased risk of bleeding compared to placebo [21]. An even broader meta-analysis of 27 randomized clinical trials comprising 2314 surgical patients in a variety of settings found no difference in postoperative bleeding between patients taking ketorolac and controls [22]. Based on this evidence, it seems that NSAIDs are generally safe for use in the perioperative period with regard to bleeding in plastic surgical patients without other risk factors, and possess qualities of improved pain control and decreased opioid use that make them particularly appealing adjuncts.

Celecoxib is a selective COX-2 inhibitor that deserves special notice. The prolonged bleeding times and GI side effects associated with NSAIDs are generally attributed to inhibition of constitutively expressed COX-1, and therefore the selectivity of celecoxib provides it with some advantages [18]. For example, surgeons who feel that a patient may be high risk for hematoma or are concerned about individual patients with history of gastrointestinal disease, bleeding, or ulceration may choose celecoxib for its pharmacologic advantages. Several studies that have investigated postoperative celecoxib after plastic surgical procedures

found no increased rate of hematoma when compared to control groups [23, 24]. On the other hand, there is no evidence of superiority of celecoxib over nonselective NSAIDs when it comes to risk of postoperative hematoma in plastic surgery. Moreover, similar to other nonselective NSAIDs, celecoxib has been shown to reduce opioid use postoperatively, decrease postoperative pain, and enhance recovery after plastic surgical procedures such as breast augmentation, abdominoplasty, and rhytidectomy by reducing nausea and sedation and allowing patients to return to normal activities sooner compared to control groups [23, 25].

Coxibs (selective COX-2 inhibitors) have an interesting clinical history that also bears mentioning. When coxibs were first developed as additions to the NSAID family and approved by the FDA in 1999, there was great optimism about the medications due to their improved side effect profiles [26]. However, in 2004 concerns for cardiovascular toxicity caused rofecoxib to be withdrawn from the market and additional data suggested an increase rate of cardiovascular events in patients taking celecoxib for long durations (e.g., for arthritis) [27]. A cardiovascular safety trial for celecoxib was mandated by the FDA over these concerns, resulting in the PRECISION randomized controlled trial which for now has largely put these concerns to rest by showing that celecoxib is noninferior to ibuprofen or naproxen with regard to cardiovascular safety [28]. Moreover, the trial affirmed the lower risk for serious GI events compared to the nonselective NSAIDs. In light of this, for plastic surgery patients who are taking coxibs for only brief durations perioperatively, the potential concern of any cardiovascular risk would seem unfounded; however, for patients with a history of GI bleeds or ulcerations, there continues be a theoretical benefit when compared to other NSAIDs. In general, based on a preponderance of evidence, NSAIDs generally have the perioperative benefits of an opioid-sparing effect and enhanced recovery.

Gabapentinoids

The gabapentinoids (pregabalin and gabapentin) have traditionally played important roles in the management of neuropathic pain and seizure disorders, but the evidence to suggest a

perioperative role for these medications is growing. The gabapentinoids are structural analogues of gamma-aminobutyric acid and are classed as voltage-sensitive calcium channel blockers. The mechanisms of action of gabapentinoids in pain pathways are poorly understood; however, the analgesic effects may be related to depression of dorsal horn sensitivity, inhibition of descending serotonergic facilitation, stimulation of descending inhibition, and anti-inflammatory actions [29].

Gabapentinoids have been studied in the perioperative setting as a component of multimodal analgesia. It has been suggested that gabapentin administration in the perioperative window may expedite time to postoperative pain resolution and opioid cessation. A randomized clinical trial in a mixed surgical cohort found that 1200 mg of gabapentin given preoperatively and 600 mg 3 times a day postoperatively had no effect on pain resolution, but did have a modest effect on promoting opioid cessation after surgery compared to controls [30]. A similar randomized clinical trial of head and neck mucosal surgery patients found that 300 mg of gabapentin twice daily before surgery and up to 72 hours after surgery did not result in reduced narcotic use, but did improve pain scores [31]. A study of patients undergoing breast reconstruction with free tissue transfer found that gabapentin use resulted in the greatest reduction in postoperative opioid use and self-reported pain more than any other perioperative modality [32]. In this study, patients were premedicated with 600 mg of gabapentin 1 hour prior to surgery, and 300 mg every 8 hours for 1 week after surgery. This regimen was associated with a 59.8 mg decrease in postoperative milligram morphine equivalent per day and 21% decrease in self-reported pain.

Overall, as a newer drug, pregabalin has less evidence than gabapentin in the realm of plastic surgery; however, some studies of pregabalin are of interest. In general, despite what it lacks in plastic surgical evidence, pregabalin may have certain theoretical advantages over gabapentin including more predictable pharmacokinetics, increased potency, and fewer side effects. Broadly, from RCTs across many surgical specialties, pregabalin given perioperatively as a single preoperative dose, or for up to 2 weeks postoperatively can effectively reduce postop opioid requirements and opioid adverse effects, with greater effects seen at greater doses.

With regard to plastic surgery, a randomized double-blind placebo-controlled trial of patients undergoing oculoplastic procedures found that giving 150 mg preoperatively reduced postoperative pain scores and the need for adjunctive pain medication (acetaminophen) over the following 48 hours [33]. On the other hand, a randomized placebo-controlled trial of pregabalin in cosmetic plastic surgery (predominantly liposuction, with some augmentation mammoplasty and abdominoplasty) was performed, and there were no differences in postoperative pain scores, opioid, or NSAID requirements between the intervention and control groups [34]. Of note the patients in the study took 75 mg of pregabalin twice preop and then twice daily for 4 days following outpatient surgery as part of a multimodal analgesia regimen (150 mg/day). It has been suggested that the benefits of pregabalin are probably more pronounced, and outweigh the risks, for painful procedures that are expected to require large doses of opioids and that for minor day-surgery procedures the risks may outweigh the benefits [16].

In summary, gabapentinoids are now commonly administered perioperatively as part of ERAS protocols. They are associated with adverse effects including sedation, dizziness, and peripheral edema, and in elderly patients they should be used with caution or the dose should be decreased. In addition, because the gabapentinoids are renally excreted the dose should be adjusted for patients with renal dysfunction [12]. These medications are commonly given once preoperatively for outpatient day-surgery to minimize risk of side effects, and for additional 2–5 days postoperatively for procedures when higher intensity pain and opioid requirements are anticipated. Higher preoperative gabapentinoid doses ($\geq$ 900 mg gabapentin and $\geq$150 mg pregabalin) appear more effective than lower doses at decreasing postoperative pain with a dose-response relationship curve [35].

Local Anesthetics

The fascinating history of local anesthetics begins with the coca leaves which are native to the South American tropics, and in particular the major species *Erythroxylum coca* with its high concentrations of cocaine alkaloids which originated in eastern Peru. "Erythroxyline"

was first isolated in 1855 by Friedrich Gaedcke, then separately by Albert Niemann in 1860 who coined then name "cocaine," and in 1884 Carl Koller in Vienna was the first to apply the substance as a local anesthetic during human surgery for a patient with glaucoma [36]. Cocaine became virtually an overnight sensation and within the same year, William Halsted and others had already found clinical use for the drug in a multitude of ways, including nerve blocks and intradermal administration [37]. There is no doubt that the advent of local anesthesia ushered in a new era of surgical innovation in 1884, and that innovation continues to this day.

Over the past century, a number of additional local anesthetics with improved toxicity profiles and a range of pharmacokinetics have become available. Procaine was first synthesized in 1904, followed by lidocaine in 1948, and mepivacaine and bupivacaine in 1957, among others in the twentieth century [36]. Administration of local anesthesia in plastic surgery is commonplace, but there is wide variation in the agents used based on differing onset and duration of analgesia (Table 18.2 [5, 38]).

All of the local anesthetics work by binding voltage-gated sodium channels and consequently preventing the propagation of action potentials along nerve fibers. The nerve fibers that are key to nociception are A-δ and C nerve fibers which convey sensations of sharp pain, pressure, temperature, and firm touch [38].

Table 18.2 Local anesthetics, their durations of action and maximum safe dosages

Local anesthetic	Duration of action (h)	Maximum safe dosage (mg/kg)
Lidocaine (plain)	1.5–2	4
Lidocaine (with epi)	2–2.5	7
Bupivacaine (plain)	3–6	1–2
Bupivacaine (with epi)	6–10	2–3
Mepivacaine	2.5–3	7
Ropivacaine	6–10	1–2.5
Cocaine	0.75–3	3–4
Liposomal bupivacaine	24–72	266-mg bolus dose

Whereas cocaine is classified as an ester, lidocaine, bupivacaine, mepivacaine, and ropivacaine are all amides. In general, cocaine has a short duration of action and high toxicity profile and is seldom used as a local anesthetic anymore except for topical application, such as septorhinoplasty. Cocaine is known for its highly toxic potential which can lead to hypertension, tachycardia, dysrhythmias, and risk of myocardial ischemia, infraction, or pulmonary edema [38]. Among the amides, lidocaine is the most widely used local anesthetic in the world, with a quick onset and duration of action of approximately 1.5–2 hours for plain lidocaine (2–2.5 with epinephrine). Mepivicaine is a close cousin with a duration of action of 2.5–3 hours, and bupivacaine has an even longer duration of action of 3–6 hours (6–10 hours with epinephrine). The disadvantage of bupivacaine is a prolonged latency of onset which may be delayed approximately 20 minutes. Therefore, facial plastic surgeons commonly use a combination of 0.5–1.0% lidocaine with 1:100,000 epinephrine, and 0.25–0.50% bupivacaine with 1:200,000 epinephrine for lengthier procedures such as rhytidectomy [38].

The administration of local anesthetic is limited by its toxicity. Whereas lidocaine can be administered intravenously, other longer-acting anesthetics like bupivacaine and ropivacaine are not because of toxicity concerns. As sodium channel blockers, the most dangerous toxicity of the local anesthetics is its cardiac toxicity and risk for profound hypotension, myocardial infarction, and death. The more lipid soluble a local anesthetic is, the riskier its toxicity profile will be. For example, lidocaine, which is less lipid soluble than bupivacaine, has a higher maximum safe dosage. In addition to cardiac toxicity, CNS toxicity can occur with symptoms of restlessness, disorientation, headache, tinnitus, dizziness, slurred speech, and twitching, and a severe reaction can result in tonic-clonic seizures and cardiovascular collapse.

Over the years a number of innovations have sought to potentiate and prolong the action of local anesthetic drugs. Simple methods such as the application of a tourniquet around a limb undergoing an operation to prolong analgesic action were reported soon after cocaine's anesthetic properties were first described, and since then more sophisticated techniques have emerged [36].

Many standard preparations of local anesthetics now come combined with epinephrine which substantially prolongs the duration of action and has the added benefit of vasoconstriction and improved hemostasis at the site of infiltration.

In addition to epinephrine, sodium bicarbonate is a relatively common additive to local anesthetic preparations. Adding sodium bicarbonate alkalinizes the local anesthetic agent to approximately physiologic pH which is considered to be less irritating to local tissues and less painful when injected [38]. Buffering local anesthetic solutions has the additional consequences of decreasing latency of onset, and it may also increase the potency and duration; therefore, this is a popular modification among some plastic surgeons. However, imprecise mixing may cause agents to precipitate and sodium bicarbonate should therefore be applied cautiously, if at all, because of this problem and risk of improper dosing.

Liposomal bupivacaine, a controlled-release anesthetic, is a relatively new local anesthetic that deserves special attention. Liposomal bupivacaine was approved by the FDA in 2011 for administration into a surgical site to produce postsurgical anesthesia [39]. The liposomal delivery system releases the bupivacaine at a slow rate with a prolonged plasma concentrations lasting up to 96 hours after administration [40]. It is becoming increasingly popular in multimodal analgesia regimens and for regional anesthesia because of its lengthy duration of action and apparent opioid-sparing effect in plastic surgical procedures.

Liposomal bupivacaine has not been studied as extensively for uses in the head and neck region, including facial plastic surgery. A retrospective case-control study of pediatric pharyngoplasty patients showed that those who were administered liposomal bupivacaine had shorter hospitalizations, improved postoperative oral intake, and required lower average opioids [41]. Likewise, data from children undergoing palatoplasty suggests that liposomal bupivacaine appears to be a safe and effective aspect of multimodal postoperative analgesia [42]. The only randomized trial of liposomal bupivacaine in the head and neck region for adults to date studied post-tonsillectomy patients and found that injection into the wound bed improved pain intensity scores for the first

24 hours after surgery, but no decrease in usage of pain medications [39]. The authors of the trial concluded that liposomal bupivacaine had minimal indication for use given the cost and limited benefit of the medication.

A Cochrane systematic review of studies that assessed liposomal bupivacaine nerve blocks found the quality of evidence to be very low and recommended further research into the role of liposomal bupivacaine as a nerve block to treat pain after surgery [43]. None of the trials included in the Cochrane review involved plastic surgery, and generally more data is needed to either support or refute the use of liposomal bupivacaine for peripheral nerve blocks to manage postoperative pain. A separate Cochrane systematic review of liposomal bupivacaine infiltrated into the surgical site to reduce postoperative pain found improved pain control compared to placebo, but not superiority to bupivacaine hydrochloride based off the current evidence [44]. Among the trials included in the review, a study by Smoot et al. of patients undergoing breast augmentation was the only one in the domain of plastic surgery [45]. There was no significant difference between liposomal bupivacaine and bupivacaine hydrochloride in mean cumulative pain score through 72 hours; however, total opioid consumption was significantly lower in the liposomal bupivacaine group through 24 and 48 hours. A systematic review by Vyas et al. found liposomal bupivacaine to be equivalent or more effective than traditional protocols in postoperative pain management [46]. In summary, liposomal bupivacaine has unique pharmacokinetic properties that make it a promising adjunct in multimodal postoperative analgesia, but more data is needed to understand its best uses in plastic surgery.

Regional Blocks

A number of regional analgesic techniques exist for use in plastic surgery. These techniques can be broadly categorized as neuraxial (epidural and spinal/intrathecal administration) and peripheral (e.g., brachial plexus, paravertebral, and transversus abdominis plane blocks). Typically, opioids or local anesthetics are administered

directly by injection, pump, or catheter into the site to induce a regional analgesic effect. In plastic surgery, peripheral techniques are more often used and blocks are performed either preoperatively by the anesthesiologist, or intraoperatively by the surgeon.

Among the most common peripheral nerve blocks used in plastic surgery are brachial plexus blocks for upper extremity surgery, paravertebral blocks for breast surgery, and transversus abdominis plane for autologous breast reconstruction and abdominal surgery (i.e., abdominoplasty). The four brachial plexus block techniques include interscalene, supraclavicular, infraclavicular, and axillary blocks, each with its own advantages and disadvantages which will not be discussed in detail here. Each method works by anesthetizing the brachial plexus at the trunks, cords, or nerves and produces varying extent of surgical anesthesia with the ideal block depending on the procedure [5]. Paravertebral blocks work by isolating and anesthetizing the T1 to T6 nerve roots as they exit the intervertebral foramen. These blocks can reduce postoperative pain score and opioid use in patients undergoing breast reconstruction, and are typically performed preoperatively. Transversus abdominis plane blocks work by anesthetizing the anterior abdominal wall by administering local anesthetic into the plane between the internal oblique and transversus abdominis muscles. This can be done intraoperatively under direct vision or preoperatively under ultrasound guidance and can result in significantly less postoperative pain and opiate consumption which will be discussed in further detail below (*Considerations in General Plastic Surgical Procedures*).

Considerations in Facial Plastic Surgical Procedures

Rhinoplasty

Opioid analgesics remain a mainstay of postoperative pain control for patients undergoing rhinoplasty. On average, patients will experience 2–3 days of relatively mild pain [47]. Most surgeons prescribe 20–30 opioid tablets for septoplasty and rhinoplasty,

with <10% prescribing 10 or fewer. This pattern is likely contributing to a large reservoir of unused opioids that can potentially be abused for nonmedical purposes. There is evidence that opioids may be frequently overprescribed in this setting as a number of studies have investigated the amount of narcotic consumed by patients versus how much has been prescribed. By convention, a provider may typically prescribe 20–30 tablets of 5 mg hydrocodone with 325 mg acetaminophen (or equivalent opioid doses); however, the majority of rhinoplasty patients without a history of chronic pain or recent opioid use will likely consume less than half of those tablets [10–15] regardless of whether the procedure was a primary vs. revision, and whether septoplasty, osteotomies, or turbinate reduction were included [47–49]. In practice, it also seems that decreasing the number of pills prescribed to less than 10 doses does not lead to an increase in postoperative telephone calls for pain, additional prescriptions, or pain complaints at the postoperative visit [50].

Improving patient satisfaction and reducing opioid analgesics in rhinoplasty and their unwanted adverse effects may also be achieved by multimodal anesthesia regimens including local anesthesia, NSAIDs, gabapentin, and α-agonists [51]. Several prospective, double-blinded RCTs have been performed to compare gabapentinoids to placebo with various administration regimens. In a review of these RCTs, six out of seven studies reported significantly lower VAS/NRS (visual analog scale/numeric rating scale) perioperative pain scores as compared to placebo [51]. In one such study, patients that were administered 300 mg pregabalin 1 hour before surgery consumed significantly less opiate medication postoperatively; patients who were also administered 8 mg dexamethasone consumed even less [52]. A similar double-blind randomized clinical trial of patients undergoing septorhinoplasty found that a single low dose of 75 mg pregabalin administered 1 hour before anesthesia significantly reduced the mean VAS pain score compared to controls, and the use of rescue fentanyl in PACU and postoperative nausea was also reduced [53].

Similar to gabapentinoids, employing NSAIDs as part of a multimodal perioperative analgesia plan in rhinoplasty has been

increasingly investigated and adopted due to encouraging results. In particular, the use of NSAIDs as "pre-emptive" analgesics prior to surgery suggests that postoperative opioid consumption and pain scores can be further reduced. In a prospective, randomized, double-blinded study of patients undergoing septorhinoplasty, patients who were administered 800 mg of IV ibuprofen 30 minutes preoperatively had significantly lower postoperative VAS scores over the first 24 hours after surgery, lower postoperative fentanyl consumption, and less postoperative nausea and vomiting [54]. These findings have been replicated in a separate study, which has also suggested that a single preemptive dose of 1000 mg acetaminophen has a similar though less effective results [55]. Similar findings of preemptive IV ibuprofen have been replicated in abdominal surgery and orthopedic surgery. Moreover, additional prospective, double-blinded RCTs of alternative NSAIDs such as rofecoxib have shown similar results when these medications are included as part of a multimodal analgesic plan [51, 56].

Local anesthetic agents are routinely employed in rhinoplasty for both pain control and due to the vasoconstrictive effects when combined with epinephrine. Numerous single- and double-blinded RCTs have demonstrated a preponderance of benefit over harm for these medications in the rhinoplasty setting [51]. Selecting which agent to use may depend on the surgeon's priorities. In terms of postoperative analgesia, a prospective single-blinded study has shown infiltration with levobupivacaine to achieve significantly more potent and longer lasting analgesia when compared to lidocaine with epinephrine [57]. Bilateral infraorbital nerve blocks can further prolong the effective analgesia time postoperatively (Fig. 18.3) [58]. The infratrochlear and external nasal nerves are also suitable targets. In the authors' experience, we find that infiltrating 1 cc of liposomal bupivacaine in septal flaps and 1 cc under nasal flap at the conclusion of the procedure to significantly reduce postoperative pain, often eliminating the need for opiate analgesia, and instead patients requiring only NSAIDs and acetaminophen for adjunctive pain control.

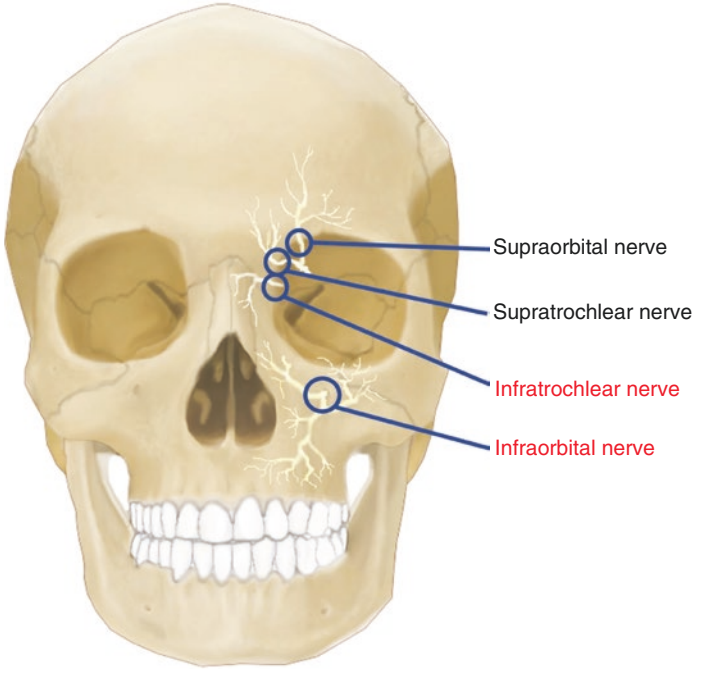

Fig. 18.3 Bilateral infratrochlear and infraorbital nerve blocks can be performed during rhinoplasty as part of a multimodal analgesia plan

Rhytidectomy

Effective analgesia is critical to successful rhytidectomy. By effectively administering local anesthesia, the amount of narcotic that is used intraoperatively can be decreased. The volume and type of local anesthetic infiltrated prior to incision varies widely among practices. A typical regimen may be 20 mL of 1% lidocaine with 1:100,000 epinephrine mixed with sodium bicarbonate per side [59]. It is the preference of some surgeons to infiltrate a 1:1 mix of 1% lidocaine with 1:100,000 epinephrine and 0.5% bupivacaine with 1:200,000 epinephrine for the theoretical advantage of lidocaine's faster onset and bupivacaine's longer duration [60].

The use of NSAIDs in the setting of rhytidectomy is controversial. Although previously discussed in this chapter with regard to intraoperative and postoperative bleeding risk, and an evidence base that suggests NSAIDs can be used safely, the rhytidectomy literature suggests that one should use caution due to hematoma risk [61]. Against longstanding dogma, evidence is emerging in support of perioperative use of NSAIDs. By giving 200 mg celecoxib to patients the night prior to surgery, morning of surgery, and standing every 12 hours for 5 days postoperatively, pain levels, opioid administration, and nausea can all be reduced for rhytidectomy patients [25]. Celecoxib is also used as a component of some surgeons' office-based rhytidectomy protocol performed under local anesthesia with oral sedation, administered as 400 mg the night before surgery [59]. IM ketorolac can also be given intraoperatively as a safe and effective means of reducing postoperative pain [62]. However, in general more prospective studies are needed to determine whether NSAIDs can be added to a multimodal analgesia regimen without increasing the risk of postoperative hematoma. Given the uncertainty and general lack of evidence, IV acetaminophen may be a preferable non-opioid analgesic that can be added to a multimodal regimen to further blunt postoperative pain [63].

Considerations in General Plastic Surgical Procedures

Reduction Mammaplasty

Reduction mammaplasty operations are performed commonly, with over 100,000 surgeries yearly in the United States. Like other plastic surgical procedures, reduction mammaplasty often involves prescription of opioid medications which often go unused [14].

Breast reduction has been traditionally performed under general anesthesia with the adjunct use of opioids; however, an opioid-free approach has been successfully employed which demonstrates advantages of a multimodal approach [24]. The

multimodal approach employed by Parsa et al. included administration of 1200 mg gabapentin and 400 mg celecoxib preoperatively, infiltration of 0.25% lidocaine with 1:400,000 epinephrine prior to incision and during surgery (7.0–7.6 mg/kg), infiltration with 3 mg/kg of 0.25% bupivacaine with 1:200,000 epinephrine before wound closure, and 1000 mg oral acetaminophen every 6 hours as needed postoperatively. Opioid-free reduction mammaplasty can be performed under IV sedation or with general anesthesia with numerous benefits such as less postoperative nausea and vomiting, decreased time to discharge, and reduction in unplanned postoperative hospital admissions; however, performing surgery under IV sedation alone confers risk of exceeding the maximum safe infiltration of 7 mg/kg lidocaine.

Augmentation Mammaplasty and Alloplastic Breast Reconstruction

Implants are the most common breast reconstruction procedure, accounting for approximately 60% of all reconstructions [64]. Pain management for breast reconstruction patients is critical, and inadequate control can contribute to delayed mobilization and prolonged hospitalization among other problems.

Traditionally narcotics are the mainstay of perioperative analgesia for these patients; however, evidence is emerging that enhanced recovery after surgery (ERAS) pathways with multimodal analgesia plans are likely superior. An example regimen would include 300 mg gabapentin, 400 mg celecoxib, 1000 mg acetaminophen, and 10 mg oxycodone controlled-release given preoperatively; local nerve blocks and infiltration with 0.25% bupivacaine with 1:200,000 epinephrine given intraoperatively; and, 200 mg celecoxib every 12 hours for 2 doses, 200 mg gabapentin every 8 hours for 2 doses, tramadol-acetaminophen every 3–4 hours as needed, and 200–400 mg ibuprofen every 6–8 hours as needed postoperatively [65]. A regimen such as this has been shown to result in less severe pain and increased patient satisfaction when compared to traditional narcotic-based treatment. In addition to analgesics, the ERAS pathway also includes a more

deliberate focus on preadmission counseling, decreased preoperative fasting, and goal-directed fluid resuscitation.

Liposomal bupivacaine has been utilized in the setting of implant-based breast reconstruction with encouraging results [66]. Field blocks of the breast pockets can be performed with intramuscular infiltration of the pectoralis major along the caudal border of the clavicle, along the ipsilateral parasternal line, and 1 cm posterior and parallel to the anterior or axillar line, extending under the pectoralis major muscle in the axilla. These injections target the supraclavicular nerves, first to sixth intercostal nerves, and lateral cutaneous branches of the second to seventh intercostal nerves, respectively. In addition, liposomal bupivacaine is infiltrated in the area of placement of deep sutures. In a prospective, randomized, single-blind trial, this technique significantly reduced opioid and benzodiazepine consumption, length of stay, and hospital charges when compared to traditional field blocks with 0.25% bupivacaine with epinephrine.

Autologous Tissue Breast Reconstruction

Autologous tissue reconstruction (pedicled or free tissue transfer) accounts for approximately 40% of all breast reconstructions [64]. After breast surgery, pain is a major problem that affects 20–50% of patients, and approximately 50% of women undergoing mastectomy and reconstruction experience postoperative pain syndromes [67]. Like many other major surgical procedures, systemic opioids have been the conventional cornerstone for autologous tissue breast reconstruction. However, peripheral nerve blocks and multimodal analgesic regimens have become increasingly popular.

Autologous breast reconstruction often utilizes abdominally based flaps including the transverse rectus abdominis (TRAM) flap and deep inferior epigastric perforator (DIEP) flap. As previously discussed (*Regional Blocks*), the transversus abdominis plane (TAP) block involves blocking the anterior abdominal wall sensory nerves before innervating the abdominal musculature. A double-blind, placebo-controlled, randomized trial of transversus abdominis plane peripheral nerve block has demonstrated

numerous benefits in abdominally based (TRAM and DIEP) autologous breast reconstruction [67]. By inserting bilateral transversus abdominis plane catheters and giving 0.25% bupivacaine every 8 hours for 2 postoperative days, the amount of morphine consumed by patients in the early postoperative period was significantly reduced. Similarly, in multiple studies bilateral ultrasound-guided transversus abdominis plane blocks have been demonstrated to reduce the pain scores and cumulative opiate requirements of DIEP and TRAM flap patients after surgery [68, 69]. By employing these and similar regional anesthesia techniques based on transversus abdominis plane blocks, it is possible to nearly completely eliminate the need for postoperative opioids while also facilitating early hospital discharge [70].

Multimodal analgesia can be effectively implemented in an enhanced recovery after surgery (ERAS) pathway for autologous breast reconstruction with many advantages. Autologous breast reconstruction patients treated in ERAS pathways have been shown to use significantly less postoperative opiate [71]. The multimodal analgesia plan involved in a typical ERAS pathway includes 1000 mg acetaminophen, 600 mg gabapentin, and 200–400 mg celecoxib administered 1 hour before surgery, bilateral TAP or rectus sheath blocks 1 hour before surgery or intraoperatively, and postoperatively 1000 mg acetaminophen every 8 hours, gabapentin 300–900 mg every 8 hours, 15–30 mg IV ketorolac every 6 hours or 200 mg PO celecoxib every 12 hours, and 5–10 mg oxycodone every 3 hours as needed [32, 71]. In addition to reducing postoperative opiate, these protocols can reduce length of stay and perioperative costs while increasing patient satisfaction. These advantages are the reasons that ERAS pathways with multimodal analgesia are increasingly becoming the standard of care of in autologous breast reconstruction.

Conclusion

There are numerous tools for the plastic surgeon to optimize perioperative pain management. Due to the vast diversity of plastic surgery, there will never be a one-size-fits-all approach to

perioperative analgesia. However, in nearly all settings a multimodal opioid-sparing approach is preferred in order to reduce the adverse effects of narcotic medications and improve patient satisfaction. For complex surgery that may require admission or multiday hospitalizations, ERAS pathways with multimodal analgesia have shown enormous benefit in reducing length of stay, postoperative opioid consumption, patient satisfaction, and reduced patient pain scores. A typical multimodal analgesia strategy involves utilizing NSAIDs, acetaminophen, and gabepentinoids preoperatively, thoughtful application of long-acting anesthetics intraoperatively, and postoperative use of scheduled acetaminophen, NSAIDs, and gabapentinoids with short-acting opioids only given as needed. Plastic surgeons should adopt techniques that have been proven safe and effective to help combat the opioid crisis and aiming for the eventual goal of nonnarcotic surgery.

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