Chapter 1
Pain Assessment and Treatment for the Trauma and Burn Patient

Shaina Drummond, Robert S. Ackerman, and Alwin Somasundaram

Pain Management of the Trauma Patient

Introduction

Management of the acute and chronic pain manifestations of a patient with trauma can be a challenge to all clinicians. Traumatic injuries can include the brain, spinal cord, chest wall, bones, and visceral organs, each with diagnostic and therapeutic distinctions. The mainstay of pharmacotherapy with opioids has been well studied but more recently presents with more limitations and cautions. Non-opioid medications, interventional pain procedures, and other non-pharmacologic therapies play a role in the multimodal and multidisciplinary approach to managing pain in this population. This chapter reviews many common traumatic pain pathologies, describes the current evidence for pharmacological interventions, and relates the indications and utility of various procedures and strategies. A detailed discussion of assessment and management of the patient with burn injury follows this section.

S. Drummond (✉)
Department of Anesthesiology and Pain Management, UT Southwestern Medical Center, Parkland Ambulatory Surgery Center, Dallas, TX, USA
e-mail: shaina.drummond@utsouthwestern.edu

R. S. Ackerman
Department of Anesthesiology and Pain Management, UT Southwestern Medical Center, Dallas, TX, USA
e-mail: robert.ackerman@utsouthwestern.edu

A. Somasundaram
UT Southwestern Medical Center, Dallas, TX, USA
e-mail: alwin.somasundaram@utsouthwestern.edu

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Traumatic Pain Pathologies

Chest trauma Chest wall trauma is common and contributes to several hundred thousand emergency room visits. The most common causes are from blunt injuries – motor vehicle crashes, falls, and crush. The morbidity and mortality of chest trauma varies widely, largely related to injury of intrathoracic structures, organ contusion, number of rib fractures, and age [1]. Acute pain control is paramount as it can afford the greatest ability to ambulate, cough, breathe deeply, and perform pulmonary exercises needed to recover from the injury fully. Long-term complications of chest wall trauma can include chronic pain, disability, and occupational challenges, including unemployment [1]. As further discussed later, local anesthetics and regional anesthetics may offer better analgesia than opioids for this type of injury while limiting the patient's risk for opioid dependence.

Bone pain Traumatic bone pain arises primarily from fractures of long bones, hips, and joints. Skeletal pain can be attributed to a simple bone fracture but is often reviewed in relation to each patient's comorbidities; non-traumatic causes of skeletal pain include hyperparathyroidism, sickle cell disease, metastatic cancer, and arthritis [2]. In the elderly, hip fractures are one of the most common injuries and present a clinical challenge to the primary practitioner and the rest of the treatment team [3]. Post-injury recovery strongly emphasizes full participation in physical therapy and early mobilization, both of which can be impaired by post-fracture skeletal pain. A multimodal analgesic strategy may be best employed in this patient group as the potential for oversedation with opioid medications may prolong recovery and increase the likelihood for a skilled nursing facility disposition postoperatively [3]. Patients with trauma to the extremities often require hospital-based trauma partly due to severe levels of post-injury pain. The transition from acute to chronic pain in this group has been well documented and could be detrimental to post-injury quality of life such as the ability to perform activities of daily living [4]. Functional magnetic resonance studies showing changes in the brain's response to nociception 6 months post-injury further emphasize the necessity of adequate pain control in both the acute and chronic phases of post-trauma care [4].

Vertebral compression fractures Vertebral compression fractures involve a decrease in height of part of the spinal vertebrae compared to baseline. Clinical management is often challenging as they do not often come to attention at the time of injury and are diagnosed late. Furthermore, co-existing osteoporosis can increase the risk of a future fracture [5]. A patient-centered approach to treatment of a vertebral compression fracture is important given the variety of fracture morphologies and characteristics of back pain [6].

Spinal cord injury Patients with spinal cord injuries often develop neuropathic and nociceptive pain. Nociceptive pain is often treated with opioids and non-steroidal anti-inflammatory drugs (NSAIDs) [7]. A meta-analysis of pharmacologic therapies for neuropathic pain demonstrated the best evidence and strongest recommendation for the use of tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, and gabapentinoids. Evidence for the use of lidocaine and capsaicin patches as

well as the opioid tramadol was weaker, with the weakest evidence related to the use of strong opioids [8]. In addition to medications, other therapeutic strategies for the treatment of neuropathic pain include patient education, treatment of comorbidities (such as depression), continued follow-up, and referral to subspecialists and psychologists when appropriate [8]. Treatment of spinal cord injury refractory pain may involve intrathecal medications using an implanted pump [7]. Non-pharmacological treatments such as acupuncture and hypnosis have been less studied in this population [9]. In addition to pain, patients with spinal cord injuries often exhibit increased stress and decreased well-being, coping abilities, self-efficacy, and illness acceptance, all of which hinder the emotional recovery from such a traumatic injury [4].

Traumatic brain injury Pain after a traumatic brain injury (TBI) is often complicated by the concurrent headaches, psychological stress, and anxiety after the injury. It is not always clear whether the pain is a consequence of the brain injury or related to comorbidities such as post-traumatic stress disorder [10]. Chronic pain is reported in over half of TBIs with headaches and neck, shoulder, and back pain being the common manifestations. Further confounding pain management of this demographic are post-injury disabilities and legal concerns [10].

Assessment of Pain in the Trauma Patient

An accurate and holistic assessment of pain in the patient with trauma can be quite challenging. In addition to the traumatic injury itself, concurrent emotional distress, anxiety, and fear can confound an accurate description. A patient could be unconscious, delirious, or acutely intoxicated and fail to report any descriptors of the pain such as severity, location, quality, and other key features [11]. The size of the wound and estimated blood loss do not always correlate with the true injury severity. For most cooperative, alert, and oriented adults, the numerical rating scale, visual analog scale, and verbal rating scale can provide a sufficient self-report from the patient [11]. Further qualifying with other pain characteristics enhances the pain assessment. In patients mechanically ventilated, other parameters such as painful gestures, hemodynamic changes, and overall autonomic function can best guide a pain assessment and assist with medication dosing and selection. Patients in acute delirium often require a more detailed diagnostic evaluation as to the underlying cause and potential treatments of such [12].

In addition to assessing characteristics of pain and other related factors, the initial interview and encounter should complete other significant communication goals. Establishing a positive relationship and discussing realistic expectations of pain management can augment treatment benefits, alleviate anxiety, and increase satisfaction [13]. Often, relating functional recovery goals can be more beneficial than targeting a certain pain score. Additionally, screening for opioid abuse and addiction can not only help guide medication selection but also reinforce a non-judgmental relationship between the patient and his or her care team [13].

Opioid Medications

For procedural sedation in a patient with acute trauma pain, one study found a combination of propofol and fentanyl to have both improved analgesia and improved sedation compared to propofol and ketamine [14]. While some studies describe a benefit to the combination of morphine and ketamine compared to morphine alone for out-of-hospital trauma pain management, a meta-analysis showed no superior medication in terms of pain relief – fentanyl compared to morphine, ketamine compared to morphine, ketamine and morphine compared to morphine alone, etc. [15, 16]. In a randomized trial of patients with long bone fractures, both morphine and ketamine decreased pain severity, but neither medication was superior to the other [17]. When high-dose morphine was compared to low-dose morphine for patients with acute trauma pain in the emergency department, there was a significant reduction in pain 1 hour after medication administration in the high-dose group, but no notable difference 30 minutes after administration [18].

While opioids have a clear role in the acute management of pain from trauma, the long-term effects of opioids can introduce cautions with its appropriate patient population and indications. The concern of opioid-induced respiratory depression exists, especially when patients also present acutely intoxicated. In one study, patients who received opioids had higher Injury Severity Scores and initial pain scores than those who did not receive opioids; however, they were less likely to be intubated within 4 hours of admission and had lower blood alcohol levels [19]. In addition, opioid administration versus no opioid administration was not associated with an increased risk of respiratory depression, though higher cumulative fentanyl dose was found to be a risk factor [19].

When patients have been on opioids for more than 3 months, over half of them continue to use them years later, this transition from acute to chronic pain being a major risk in use of this medication class for patients with trauma-related pain [20]. It is believed that opioids for chronic pain carry an increased risk for overdose, abuse, and major cardiac events [21]. Additionally, it has been recently shown that opioid use can contribute to adrenal insufficiency and hypogonadism, both endocrine consequences that limit quality of life [22, 23]. One study of opioid prescribing habits related a higher likelihood of opioid prescription as discharge in patients with a higher Injury Severity Score with male sex and anxiety being negative predictors of prescription. This correlates with an appropriate prescribing practice, not one solely based on regulations alone [24].

Non-opioid Medications

Given the aforementioned cautions with opioid therapy and the potential issues from the transformation of acute, traumatic pain to chronic, debilitating pain, there is a strong emphasis on multimodal analgesic techniques to minimize opioid use

while treating pain effectively. The addition of concurrent muscle relaxants, gabapentinoids, and clonidine can reduce the total opioids prescribed without compromising pain relief [25]. Several non-opioid medications have been both studied and hypothesized to have a clinical benefit in patients with trauma pain.

Gabapentin and pregabalin Gabapentinoids, which act via blockade of the alpha-2-delta voltage-gated calcium channels, include the medications gabapentin and pregabalin. They are believed to mechanistically decrease excitatory neurotransmitter release, activate noradrenergic pain inhibitory pathways, and influence the levels of pro-inflammatory cytokines [26]. This class of medication has best shown to provide relief for neuropathic pain, most pronounced for peripheral neuropathy secondary to diabetes mellitus and post-herpetic neuralgia and less so for spinal cord injury [27]. Its role in the patient with trauma is not well studied, though it is believed that gabapentinoids can potentially reduce the severity of acute and chronic pain post-thoracotomy [28].

Acetaminophen Acetaminophen is in a class of medications unique to itself, with multiple mechanisms of action, most notably cyclooxygenase inhibition and decreased prostaglandin synthesis. This class of drugs provides analgesic and antipyretic effects with minimal gastrointestinal and renal toxicity due to its low affinity for plasma proteins and acid-base neutrality [12]. One study of patients with limb trauma found no difference between morphine and acetaminophen in overall analgesic effects or need for rescue analgesia [29]. A study of hip fracture patients also demonstrated the analgesic benefits while also reporting decreased length of stay and incidence of opioid-related complications [30]. However, it is believed that acetaminophen alone cannot treat trauma pain sufficiently, but plays an important role as an adjunct to other analgesic modalities.

Non-steroidal anti-inflammatory drugs (NSAIDs) This class of medications, which includes ibuprofen, ketorolac, and naproxen, also inhibits the cyclooxygenase enzyme and decreases downstream prostaglandin synthesis, both in the central and peripheral nervous systems [12]. These medications provide most benefit for inflammation-based pain with indications such as musculoskeletal sprains, synovitis, and soft tissue injuries [31]. The low analgesic ceiling and dose-dependent side effects of the digestive, renal, and cardiovascular systems provide the greatest risk. Gastrointestinal side effects alone include dyspepsia, gastric ulcers, and abdominal pain [12, 31]. There has yet to be sufficient evidence demonstrating superior benefits in the patient with trauma pain.

Muscle relaxants The anti-spasmodic medication class that includes cyclobenzaprine and methocarbamol is believed to be beneficial in acute musculoskeletal pain, its primary mechanism related to sedation. An extension of its intended physiology, side effects include drowsiness and headaches [31]. Research into its use for trauma pain is limited.

Ketamine Ketamine, an antagonist of the N-methyl-D-aspartate (NMDA) receptor, has shown significant analgesic benefits in several patient populations and

demonstrates concurrent amnesia and dissociation. The principal benefits of this medication in patient with trauma are the ventilatory maintenance and cardiovascular stimulation, though agitation, hallucinations, and airway secretions limit its use [12]. As mentioned before, a comparison of ketamine, fentanyl, and morphine showed no medication superiority in trauma pain relief [15]. Both ketamine and morphine reduced pain severity significantly, but not compared to each other [17]. Pre-hospital administration of ketamine yielded better physiologic parameters in patients with higher Injury Severity Scores compared to opioid analgesics, while a similar study of pre-hospital analgesics did not show an analgesic benefit, but reported increased agitation in the ketamine group [32, 33]. When formulated as a patient-controlled analgesic (PCA) for patients with trauma in the intensive care unit, ketamine was shown to decrease total opioid consumption and supplemental oxygen use compared to hydromorphone, though it yielded more frequent hallucinations [34]. Two similar studies comparing ketamine as an infusion to placebo found no analgesic benefit nor a reduction in total opioids administered. However, when stratified for higher Injury Severity Scores, one study found a reduction in total opioids administered [35, 36]. A long-term study comparing persistent pain 6–12 months after trauma found no perceived superiority in either the ketamine or morphine groups [37]. While ketamine has clear physiologic benefits compared to other analgesics, evidence is mixed, and its benefits are less pronounced in the trauma pain literature.

Botulinum toxin (Botox) Commonly referred to as "botox," botulinum toxin interferes with the transmission of acetylcholine across the synaptic cleft. It has been shown to improve pain, mood, and activity levels in patients with post-traumatic neuralgia, though further benefits have been less pronounced in the literature [38].

Serotonin-norepinephrine reuptake inhibitors (SNRIs) Antidepressants including the amine reuptake inhibitor duloxetine are believed to yield most clinical benefit in neuropathic pain relief via action of the noradrenergic descending pathways. Its anti-pro-inflammatory cytokine effects and neuroplasticity have also recently been described [26]. Some studies have found decreased opioid consumption and longer times to rescue analgesics with SNRIs, though this has not been shown in the trauma literature [39].

Tricyclic antidepressants (TCAs) Similar in effect to SNRIs, tricyclic antidepressants such as amitriptyline are believed to have mechanistic action via increasing norepinephrine in the spinal cord with downstream effects on the locus coeruleus and descending inhibitory pain pathways [40]. Shown to improve pain, sleep, and depression in patients with trauma injuries and neuropathic pain, the extent of the evidence relating these benefits is limited [12].

Benzodiazepines The benzodiazepine class of medications, which acts at the GABA receptor, includes midazolam, diazepam, and lorazepam. The analgesic

component is believed to be related to anxiety exacerbating pain and the medication's anterograde amnesia improving a patient's perception of pain [12]. While it ideally would best help patients with high anxiety and severe pain, it was not found to augment or provide synergy with morphine for pre-hospital treatment of trauma pain [41]. It can be administered intranasally or rectally in patients with difficult intravenous access [42].

Clonidine Clonidine, an alpha-2 adrenoreceptor agonist, has been known to be synergistic with opioids and local anesthetics [43]. Its role for the management of trauma pain is largely unstudied, but its prolongation of local anesthetics and reduction of perioperative analgesics make it a viable agent to consider its use. However, a hemodynamically unstable trauma patient may have exacerbated hypotension with administration of clonidine [12].

Steroids Corticosteroids inhibit the phospholipase A2 enzyme, inhibiting downstream prostaglandin and other inflammatory mediator synthesis [31]. It is suspected to have the most benefit in extremity radicular pain, peripheral nerve injuries, spinal cord injury, and soft tissue damage [12]. Side effects include psychological changes, insomnia, and hyperglycemia [31]. Weak evidence exists for perineural steroids in short-term analgesia for peripheral neuropathy related to a traumatic or compression injury [44].

Topical creams Topical analgesics exist from several medication classes including local anesthetics, NSAIDs, TCAs, and gabapentinoids. Topical NSAIDs can alleviate a focal area of pain while minimizing systemic toxic effects [31]. Lidocaine patches are indicated for acute herpetic neuralgias [45]. The use of topical creams for trauma-related pain has not been well studied.

Medical marijuana Cannabinoids, such as THC and CBD, act as agonists at the cannabinoid receptor and are believed to have strong analgesic effects if the psychotropic reactions are minimized. The evidence supporting its use is often anecdotal with some relation to the medication's physiologic mechanisms. Examples of diseases and conditions with supposed benefits include fibromyalgia, multiple sclerosis, phantom limb pain, and autoimmune disease [46, 47]. Benefits specific to trauma pain have not been shown.

Infusions Medication infusions, such as ketamine and lidocaine, have been proposed for the treatment of both acute and chronic pain [48]. While the trauma pain demographic has very limited evidence, the fibromyalgia, complex regional pain syndrome (CRPS), and diabetic neuropathy populations have more related research.

Vitamin supplementation Vitamin supplementation as an analgesic modality has not been proven or applied in clinical practice, but a study of several week supplementation of vitamin C showed a decreased incidence of CRPS type 1 1 year after a wrist fracture [49].

Interventional Pain Procedures

Peripheral nerve blocks It is believed that regional anesthesia techniques can potentially reduce the severity of acute and chronic pain post-thoracotomy [28, 50]. The intercostal block has been shown to improve pain scores while minimizing total hospital days and mechanical ventilator days for patients with chest wall trauma [1]. Other studies have shown improved peak expiratory flow rates and oxygen saturation after administering the block in patients with rib fractures [51]. Beyond the improvement in mean pain scores, sustained maximal inspiratory lung volumes, length of stay, and mechanical ventilation rates were found to be improved in patients who received continuous intercostal nerve block with catheter placement [52]. The evidence for paravertebral and intrapleural anesthesia is more limited with no strong guidelines or clinical recommendations for their use over other therapeutic modalities [51]. One meta-analysis reports improvement in acute pain scores (postoperative day 0) and hospital stay, but no improvement in pain scores at 24 hours [46]. Of more interest is the potential use of a paravertebral block in patients receiving anticoagulant or antiplatelet therapy, known contraindications for neuraxial anesthesia per the American Society of Regional Anesthesia and Pain Medicine. While the paravertebral block is not officially endorsed or recommended for patients who present with this contraindication to neuraxial anesthesia, the primary concern is the potential for blood loss and less so for neural deficits [53]. The most recently utilized erector spinae plane block has been shown to target the ventral and dorsal rami of spinal nerves with coverage of the anterior, lateral, and posterior thorax, providing fair coverage to the sites of interest in post-thoracotomy pain syndrome. While far less studied than other regional modalities, the erector spinae plane and other technically easier myofascial plane blocks can benefit patients with acute and chronic pain syndromes after surgery [54, 55]. Fractures and crush injuries of the upper and lower extremities are often managed with regional anesthetic techniques. The interscalene, supraclavicular, infraclavicular, and axillary nerve blocks can be advantageous for shoulder, forearm, arm, and hand analgesia. The lumbar plexus, femoral, and sciatic nerve blocks can be used for lower extremity analgesia [12]. For example, femoral nerve blocks for patients with hip fractures can both decrease pain intensity and the need for rescue analgesics [56, 57].

Neuraxial anesthesia Epidural anesthesia is strongly recommended with a fair amount of evidence for its use in patients with rib fractures and chest trauma [51]. Retrospective reviews have shown decreased mortality in patients with blunt chest trauma who received thoracic epidural anesthesia compared to traditional intravenous opioids; patients in the epidural group also were older, fractured more ribs, and had more frequent comorbidities such as pneumothoraces, lung contusions, and flail segments [58]. The most important perceived benefits include subjective pain perception and pulmonary function testing postoperatively [8]. The side effects of opioids are further limited. Local anesthetics and opioids are most often administered via the epidural catheters providing both sodium channel blockade and opioid receptor agonism, respectively. A major

disadvantage is the segmental spread of anesthesia and potential hypotension from preceding sympathectomy [12].

Kyphoplasty and vertebroplasty Both the kyphoplasty and vertebroplasty procedures have shown small benefits in back pain after acute vertebral compression fracture compared to non-operative management [59]. They can decrease morbidity and increase survival. No one procedure is superior to the other, though kyphoplasty is often more expensive and takes longer to perform [6].

Non-pharmacological Interventions

Hypnosis While not well studied in the trauma pain population, the practice of hypnosis is believed to improve subjective pain intensity for both acute (periprocedural) and chronic conditions. A careful understanding of the patient's pain can better guide the hypnotist in drafting suggestions for dissociations from unpleasant and painful conditions [12, 60].

Biofeedback Biofeedback therapies are described as relating information to patients that would be unknown otherwise; these can relate to the cardiovascular, respiratory, or neuromuscular systems [61]. In a study of biofeedback in chronic back pain, coping strategies were improved, while depression, disability, and muscle tension all decreased [62]. The benefits of biofeedback in trauma pain are not known.

Transcutaneous electrical nerve stimulation (TENS) The use of TENS as an adjunct in treatment of trauma pain has been mildly described. In addition to its analgesic benefits, it was also shown to improve respiratory dynamics in patients with rib fractures [12]. Further uses in trauma have been hypothesized, but not well studied.

Acupuncture The pain mechanisms of acupuncture involve the ascending inhibitory and descending analgesic pathways, as well as cortical, subcortical, and brainstem processing. It is believed to be most beneficial in inflammatory, neuropathic, and cancer pain via its many actions in the central and peripheral nervous systems [63, 64]. The overall evidence quality is low to moderate and limited as it relates to trauma pain.

Special Populations

Crucial to the discussion of trauma pain is an examination of special populations that could confound some of the aforementioned therapies and strategies, such as the patient acutely intoxicated, the patient with opioid tolerance, and the patient with prior substance abuse and addiction.

Alcoholic patients The patient with acute or chronic alcohol exposure presents a unique challenge to pain management during trauma. This is a high-risk population with intoxicated trauma victims known to have more severe injuries and higher mortalities. Additionally, chronic alcoholism is associated with coagulopathies, liver disease, and poor physiologic status [65]. Askay described several concerns with trauma pain management and alcoholism. The patient acutely intoxicated can yield questions about the interaction between opioids and alcohol, the belief that ethanol can affect the binding of opioids to its receptors. The effects of opioids and alcohol together are believed to be additive. The chronic alcoholic introduces tolerance and pain thresholds as therapeutic roadblocks [66]. This may require increasing dosage of analgesics with caution that those with liver disease may show a decreased hepatic metabolism and increased sensitivity and duration of action to opioids [12]. In the patient with an addiction to alcohol but in a recovery state, there is a mixed opinion and, at times, confusion as to the best course of action to prevent a relapse [66]. Ultimately, pain should be treated with the chronic alcoholism in mind with realistic expectations at the initial encounter.

Opioid-tolerant patients The benefits of opioid agonist therapy, such as methadone and buprenorphine, in the patient with opioid tolerance are far-reaching and include decreased drug abuse, improved functioning, decreased criminal activity, and decreased infectious disease transmission. There are several misconceptions contributing to the treatment of the opioid-tolerant patient in pain including the use of opioids in analgesia will result in relapse, they will cause severe respiratory or nervous system depression if doses are increased, and the provider is being manipulated by drug-seeking tendencies [67]. The best treatment strategy starts with partnering with the patient and discussing the pain management plan and realistic expectations. In addition to opioids, multimodal analgesic medications that include acetaminophen, NSAIDs, TCAs, and SNRIs should be used [68]. To treat the injury, use conventional opioids, often times higher doses at shorter intervals given the increased pain sensitivity. Patients receiving methadone should be continued on their maintenance dose with addition of short-acting opioids [67]. Patients taking buprenorphine can either be continued at maintenance dose with addition of short-acting narcotics, continued at divided doses, discontinued and started on short-acting opioids with re-start upon discharge, or discontinued and started on methadone and short-acting opioids with re-starting buprenorphine on discharge [67].

Substance abuse and addicted patients Patients with a history of other substance abuse and addictions during a traumatic episode require careful assessment of the injury and associated pain physiology. Sympathomimetics such as methamphetamine can cause tachycardia just as the compensatory mechanism of hemorrhagic shock does [65]. It is important to assess for historical and physical signs and symptoms of substance abuse to best ascertain the severity of the injury and which analgesics may interfere with the drug of abuse. Furthermore, patients with a history of trauma-related pain, such as a TBI, may have long-term cognitive impairments and psychosocial difficulties, contributing to the potential for substance abuse [69].

Summary of Treatments for Trauma Pain (Tables 1.1, 1.2, 1.3, and 1.4)

Table 1.1 Evidence-based treatments for trauma pain

Intervention	Pain phase	Studies	Study features
Propofol-fentanyl	Acute	Aminiahidashti et al.	RCT (n = 136)
Fentanyl	Acute	Haske et al.	SR/MA (n = 69 K)
Ketamine (bolus, PCA)	Acute	Haske et al. Majidinejad et al. Takieddine et al. Losvik et al. Tran et al.	SR/MA (n = 69 K) RCT (n = 126) RCT (n = 20) Cohort (n = 1876) RCT (n = 298)
Morphine-ketamine	Acute	Jennings et al. (2011)	RCT (n = 135)
Morphine	Acute	Haske et al. Majidinejad et al. Farsi et al.	SR/MA (n = 69 K) RCT (n = 126) RCT (n = 200)
Epidural	Acute	Galvagno et al. Jensen et al. Simon et al.	Guidelines RCR (n = 1347) Guidelines
Acetaminophen	Acute	Craig et al.	RCT (n = 55)
Perineural steroids	Chronic	Bhatia et al.	SR/MA (n = 353)

Table 1.2 Emerging or promising treatments for trauma pain

Intervention	Pain phase	Studies	Study features
Vitamin C (prophylaxis of CRPS-1 after wrist fracture)	Chronic	Aim et al.	SR/MA (n = 875)
Paravertebral	Acute	Galvagno et al.	Guidelines

Table 1.3 Accepted but unproven treatments for trauma pain

Intervention	Pain phase	Studies	Study features
Morphine-ketamine	Chronic	Jennings et al. (2013)	Cohort (n = 135)
Ketamine (low-dose infusion)	Acute	Carver et al. Wiel et al.	RCT (n = 91) RCT (n = 44)
Intrapleural analgesia	Acute	Galvagno et al.	Guidelines
Intercostal analgesia	Acute	Simon et al.	Guidelines

Table 1.4 Disproven treatments for trauma pain

Intervention	Pain phase	Studies	Study features
Midazolam	Acute	Auffret et al.	RCT (n = 91)
Opioids (high dose)	Acute	Shenk et al.	Cohort (n = 268)

Pain Management for the Burn Patient

Introduction

Despite the historical prevalence of burn injury, medical literature is limited with regard to the proper management of adult victims' pain and secondary psychiatric comorbidities. Much of the evidence available as of now is through smaller randomized controlled trials or extrapolation through other populations. This chapter defines burn injury, its pathophysiology with regard to pain evolution, and available evidence for pharmacological and non-pharmacological treatments for the varied types of burn pain.

Burn Insult Classification

In order to effectively manage burn pain, one must first identify the severity and degree of burns involved. Although the same injury has a markedly variable pain response depending on patient characteristics, attention must be given to the type of burn as management will vary [70]. Additionally, the heterogeneity of sensory innervation between epidermal and dermal layers leads to important implications in both the acute and chronic process evolutions of pain after a noxious insult [71].

The traditional classification of burns as "first-, second- or third-degree" was formulated by Peter Lowe in 1597 and modified by Guilielmi Hildani Fabricii in 1610 [72]. Clinical classification of burns currently based on the International Society for Burn Injuries (ISBI) originates from Douglas Jackson in 1953 [73]. This classification system of burn insult includes superficial, moderate, and deep partial thickness as well as full thickness. An alternative classification, from superficial to deep, is epidermal, superficial epidermal, mid-dermal, deep dermal, and full thickness [71]. Traditionally, pain is more severe in more superficial burns due to searing of afferent nerve endings with deeper insults. However, this has not proven to be the case in all patients [74]. This is because pain from burns incorporates a complex interplay between psychological and somatic factors, thus requiring individualized, patient-centered management and monitoring (Fig. 1.1).

Mechanism of Burn Pain

Thermal insult (above 42 °C) to the skin results in an amalgam of downstream nociceptive pathway activation. Thermosensitive channels on afferent sensory C- and A-delta fibers promote calcitonin gene-related peptide (CGRP) and transitively significant transmission of nociception to the dorsal horn of the spine [75]. Tissue necrosis also stimulates sensory fibers via P2X and toll-like receptors (TLRs) on

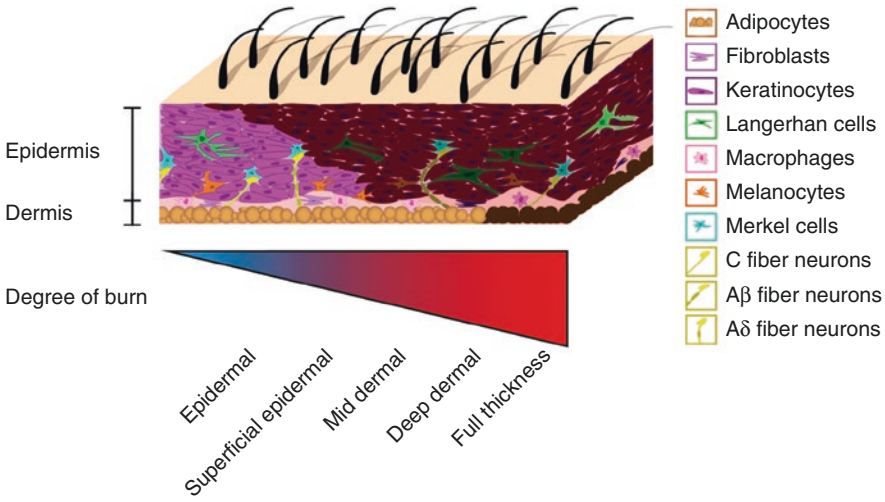

Fig. 1.1 The severity of a burn injury is determined by the depth of tissue injury. The skin is intensely innervated with many morphologically and functionally distinct sensory nerve endings that respond to a multitude of non-noxious and noxious stimuli. Noxious heat stimuli are generally conducted to the dorsal horn of the spinal cord via nociceptive Aδ and C- fiber neurons. Only the epidermis is affected in epidermal or superficial epidermal burns, while increasing damage to the dermis occurs in mid-dermal, deep -dermal, and full-thickness burns (Morgan et al. [71])

recruited leukocytes, with downstream effects of significant cytokine, bradykinin, and prostaglandin release [71]. PGE2 stimulates mast cells to release histamine, responsible for the significant pruritis associated with burn injury [71].

Understanding neuropathic mechanisms that evolve in burn pain facilitate management of postburn distress, sedation, and long-term morbidity [73]. Primary (pain in affected tissue) and secondary (pain in unaffected tissue) hyperalgesia and allodynia (pain without noxious insult) are common in burn injury and facilitated through multiple mechanisms. Immediately after insult, primary hyperalgesia and thermal allodynia are mediated via activation of voltage-gated sodium channels on sensory afferents [76]. Soon after injury, inflammatory cytokines IL-1B, IL-8, and TNF-α as well as platelet-activating factor are released from neutrophils, all contributing as well to primary hyperalgesia. Nerve growth factor (NGF), released into regenerating skin, contributes to systemic hyperalgesia and allodynia via downregulation of lumbar spinal μ-opioid receptors and upregulation of NMDA receptors in the same location [71].

Central neuronal adaptations in the burn patient have been found to involve the phenomenon described as windup and central sensitization. The windup phenomenon is an etiology for the evolution of background, breakthrough, procedural, and chronic pain in the setting of continuous, low-frequency activation of C-fibers. These depolarizations appreciate exponentially in the dorsal horn of the spinal cord, leading to hypersensitivity to pain (primary and secondary hyperalgesia) mediated by the NMDA receptors [77].

Central sensitization, often confused for windup, is a downstream effect of windup occurring at a cellular level. Central sensitization involves increased intracellular calcium in dorsal horn neurons. This increased intracellular calcium decreases threshold for depolarization, causing secondary hyperalgesia and allodynia via myelinated Aβ mechanoreceptors [77, 78].

Acute Management of Burn Pain

The mechanisms described above manifest in burn patients in the form of four variable types of pain: background, breakthrough, procedural/postoperative, and chronic pain [79]. Background pain serves as a low-grade, continuous stimulus stemming directly from thermal insult. It contributes significantly to windup and central desensitization. Breakthrough pain in the burn patient is defined as pain at rest piercing the efficacy of the analog-sedative regimen. Wound debridement, dressing changes, and therapy all cause bouts of brief, severe pain known as procedural pain. Chronic burn pain, primarily neuropathic, is pain beyond 6 months of injury [71]. Management of each type of pain is summarized in Tables 1.5, 1.6, 1.7, and 1.8.

Direction of analgesic therapy should be governed by pain institutionally approved scoring systems, preferably with a focus on patient self-reporting [73]. The numerical rating scale (NRS) has been found to be an accurate standard for assessment of pain in the non-sedated patient, although confounded by pain interference [80]. There does not appear to be a significant difference in validated pain scales for sedated patients, and all have similar efficacy [81].

The ideal approach to managing burn pain invokes a multimodal and systematic regimen [73]. Interestingly, management of acute psychological comorbidity has been shown to decrease acute pain, and management of acute pain, specifically through early opiate administration, has been shown to decrease the incidence of chronic psychiatric comorbidity [70, 82]. This interplay is significant in the burn patient, as the rehabilitative aspect of burn medicine is what necessitates multimodal therapy.

Opioids

Opiates are the foundation of burn pain management due to their accessibility and studied pharmacokinetics in the setting of the two phases of burn physiology – burn shock and hypermetabolism [74, 83, 84]. They should be employed in the treatment of background, breakthrough, procedural, and even chronic pain. For the most extreme acute cases, continuous intravenous infusion of morphine or fentanyl for those in the intensive care unit is appropriate, thanks to the regular monitoring

capacity for opioid-induced respiratory depression [76]. In less critical inpatient settings, patient-controlled analgesia (PCA), when feasible, of morphine or fentanyl is considered ideal and carries minimal risk of respiratory depression when administered without background infusions of opioids or benzodiazepines [79, 85]. Given that fentanyl has a shorter duration of action and longer elimination half-life than morphine, it is preferable for procedural burn pain [86]. A 30 mcg PCA bolus dose of fentanyl is optimal in burn patients [87]. Additional benefit to fentanyl over morphine is its stronger association with significant histamine release than other opioids, theoretically exacerbating pruritis and hypotension in the susceptible burn population [86]. Intravenous boluses of fentanyl, hydromorphone, or morphine administered by nurses are an alternative to PCA but are more labor intensive, and the patient may have to wait on pain control depending on staffing.

Breakthrough pain can be managed with a mix of opioid and non-opioid analgesia [71, 74, 75]. An appropriate opioid option for breakthrough pain consists of short-acting (not ultra-short-acting) opiates such as hydromorphone and fentanyl [78]. Non-opioid analgesics that have proven to synergize well with opioids for breakthrough pain include clonidine and ketamine [75, 78, 88]. These options carry over into management of procedural pain as well [87]. Chronic pain, to be discussed later, should involve management of neuropathic and psychiatric comorbidities to minimize opiate requirement due to the known long-term repercussions of chronic opiate therapy.

Opioid-induced hyperalgesia (OIH) has become an increasing concern in burn patients, as patients' hypermetabolic state and variable level of pain requirements invoke significant opioid burden. OIH manifests as paradoxical primary and even secondary hyperalgesia most commonly observed in the setting of high-volume, short-acting parenteral opioids such as remifentanil [89, 90]. Studies are limited, but OIH is thought to be mediated by peripheral (nociceptive receptor) and central sensitization [76]. Clinical manifestations of OIH can be confused with opioid tolerance, as both involve increased analgesic consumption and pain scoring [90]. The most robustly studied treatment for OIH is the potent NMDA receptor antagonist ketamine, with other options including non-steroidal anti-inflammatory drugs (NSAIDs), opioid switching, α2 agonists, buprenorphine, and methadone [74, 76, 89, 90].

While some side effects of opiates are well documented, such as pruritus, nausea/vomiting, opioid-induced bowel dysfunction, and respiratory depression, there are emerging studies demonstrating novel short-term and long-term complications of this drug class. Opioid-induced hypogonadism and adrenal insufficiency have been confirmed to have significant and lasting impacts on psychiatric well-being in patients on acute and chronic opioid therapy [22, 23]. Monitoring for these endocrine aberrancies should be implemented in the correct setting in any and all patients on chronic opiate therapy. Finally, burn patients often fall into the at-risk categories for overdose and addiction as many are Caucasian, middle-aged males with histories of mental illness and cardiopulmonary comorbidities [91].

Non-opioid Analgesics

While an appropriate opiate base is necessary for burn pain management, non-opioid analgesia is necessary for mitigating opioid-induced sequelae, providing potentiation of analgesia, and controlling psychiatric comorbidity.

Acetaminophen

Acetaminophen is an antipyretic and analgesic without anti-inflammatory properties and provides minor background pain relief for low-to-moderate pain as a combination agent [76]. Although the mechanism of action remains elusive, it is believed to inhibit cyclooxygenase-3 after crossing the blood-brain barrier, thus decreasing central PGE3 [79]. It has demonstrated efficacy in preventing central sensitization and is opiate-sparing [70, 76]. Given the commonality of liver dysfunction in the burn population, full-dose acetaminophen should be avoided for more than 4 days [78].

Non-steroidal Anti-inflammatory Drugs

NSAIDs inhibit prostaglandin synthesis with downstream effects involving inhibition of central sensitization and opiate-sparing by up to 30–50% (without opiate side effect profile) while providing synergistic analgesia with acetaminophen and opiates [33, 76, 78, 89, 92]. As such, they have been implemented early in management of background and postoperative pain to alleviate central adaptations contributing to hyperalgesia and allodynia [33, 73]. Studies have demonstrated maximum efficacy of preventing central sensitization with administration about 30 minutes prior to opiate administration [89]. Risk of renal dysfunction, gastric ulceration, and bleeding should be assessed on an individual level, with attention in elderly patients. Gastrointestinal prophylaxis with H-2 blockers and proton pump inhibitors is recommended in burn patients receiving NSAID therapy.

Antidepressants

While antidepressants do not have robust evidence in the acute management of burn patients, many sources have extrapolated their efficacy in management of chronic pain due to significant neuropathic and pruritic sequelae from burn injury. Neuropathic analgesia provided by tricyclic antidepressants (TCAs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have demonstrated modest outcomes [8]. Analgesia from these drugs takes less time than mood modification, but limited titratability makes them inappropriate for acute management of burn pain [76, 93]. However, given the importance of managing potential for PTSD, neuropathic pain development, and significant pruritus, TCAs and SNRIs have efficacy in subacute and chronic burn

pain management [74, 76, 93]. The US Food and Drug Administration (FDA) has approved duloxetine (SNRI) and amitriptyline, nortriptyline, desipramine (TCAs) for the treatment of neuropathic pain [94]. Duloxetine has the most robust evidence for this patient population and should be considered a first line. Caution should be used with TCAs, specifically in the older population, due to increased risk of cardiac arrhythmia, anticholinergic, and antihistaminergic effects [8].

Antiepileptics

The most robust evidence for antiepileptics in burn pain as of now involves gabapentin and pregabalin. Gabapentin and pregabalin, although structurally like the GABA neurotransmitter, have primary action at the α2-δ subunit of voltage-activated calcium channels. This class of medications is thought to decrease substance P and glutamate while increasing norepinephrine release in certain areas of the nervous system [8]. Gabapentin has been found to have little opioid-sparing effect in the immediate postburn period; however, both gabapentin and pregabalin remain efficacious in neuropathic pain management postburn [71, 76, 95].

Local Anesthetics

Topical bupivacaine and lidocaine, specifically in the postoperative period, have demonstrated modest efficacy for procedural pain [78]. While concern for systemic toxicity has limited the use of lidocaine in burn patients, lidocaine-prilocaine cream (5 g to 25 cm^2 for a 30-minute interval) has been identified as an appropriate option for debridement of partial-thickness burns [76, 96]. Use of IV lidocaine for background or procedural burn has not been adequately assessed as of now, but its use is becoming more prevalent with the current movement to utilize opioid-sparing techniques for acute pain management [97].

α2-Adrenoreceptor Agonists

Clonidine and dexmedetomidine have favorable analog-sedative effects with peripheral and central mechanisms that mitigate a myriad of mechanisms in the evolution of burn pain. They are sympatholytic via inhibition of the hypothalamic-pituitary-adrenal axis [78]. Clonidine provides central analgesia in dorsal horn neurons, promotes release of peripheral enkephalins, blocks C-fiber activation at high concentrations, and inhibits OIH when co-administered with opiates [89]. Dexmedetomidine, studied less extensively in this population, has a similar mechanism of action. Favorability in management with dexmedetomidine comes from opioid-sparing effects, lack of tolerance, and amelioration of respiratory depression and need for propofol- and benzodiazepine-induced sedation [74, 76, 78]. Dexmedetomidine is only available in the intravenous form, whereas clonidine is available in both intravenous and oral forms.

Both clonidine and dexmedetomidine are viable options for management of background, breakthrough, procedural, and chronic pain, particularly in combination with ketamine and opiates [76, 89]. Side effects include hypotension, bradycardia, and rebound hypertension with abrupt discontinuation.

Benzodiazepines

Benzodiazepines are $GABA_A$ agonists that provide anxiolytic, sedative, hypnotic, and amnestic effects. They are the mainstay of sedation in burn patients for breakthrough and procedural pain. They can be co-administered with ketamine to reduce dysphoria and potentiate analgesia from opiates [71]. Per the ISBI, they should be minimized to prevent delirium, oversedation, and respiratory depression, all of which prolong ICU stay and increase mortality.

Ketamine

Ketamine is a phencyclidine derivative that antagonizes the NMDA receptor and serves as a potent analgesic and dissociative anesthetic [75]. It prevents windup (when administered with morphine), central sensitization, and OIH while also providing opioid-sparing analgosedation with relative preservation of cardiopulmonary function [70, 74–76, 78]. As a result, it is the most common deep sedative employed for procedural and, occasionally, background pain via infusion [71, 75, 98]. Ketamine used intravenously has been shown to reduce secondary hyperalgesia when compared with placebo [75]. The option of oral ketamine (5 mg/kg) has been explored in the adult population with better procedural analgosedation compared to dexmedetomidine (4 mg/kg) [99]. In fact, 20 mg ketamine/0.5 mg midazolam PCA has demonstrated efficacy in controlling procedural pain with the only side effect being hallucination [75]. Controversy with ketamine use in burn injury involves its dose-dependent dysphoric, hallucinatory, and delirium-induced effects, often minimized by concomitant dexmedetomidine or benzodiazepine administration [70, 74–76, 78, 99]. There have been no long-term studies on the effects of regular ketamine use in the adult burn population.

Periprocedural and Intraoperative Management of Burn Pain

Burn injury patients require frequent dressing changes, skin grafting, and other medical interventions that are accompanied by a significant amount of anxiety and pain. Appropriate pharmacological intervention is integral to managing procedural pain. Multimodal pain regimens are key to management of procedural pain in order to prevent severe anxiety and the stress response that can accompany dressing changes.

Conscious procedural pain should be managed with a foundation of opioids (PCA or continuous infusion) alongside short-acting opioids such as dilaudid or fentanyl [70, 71, 76, 87]. Agents utilized solely for sedation include benzodiazepines (midazolam or lorazepam) and first-generation antipsychotics, specifically haloperidol [71, 74, 76, 78]. Per ISBI recommendations, non-benzodiazepine sedatives should be employed before benzodiazepines. As mentioned previously, analgosedation has been proven in dexmedetomidine, propofol, and ketamine boluses or infusions, with the added benefit of prevention of OIH and central sensitization [71, 75–77, 89, 90]. Although ketamine has an unfavorable profile with regard to emergence delirium, dysphoria, increased respiratory secretions, hypertension, and tachycardia, these are seen at anesthetic doses [75, 76]. Utilization of ketamine for conscious sedation at rate of 0.15–0.3 mg/kg/h provides synergistic analgesia with opioids, maintains airway patency, and prevents chronic pain [70, 75, 76, 78, 89]. Additionally, dexmedetomidine has a favorable hemodynamic profile and does not exhibit tachyphylaxis, making it ideal for burn patient management when available. Subanesthetic nitrous oxide-oxygen mixture has also proven efficacious in analgosedation with a manageable side effect profile [16, 71, 93]. Propofol is commonly utilized for dressing changes due to its amnestic effects. It is commonly given with an opioid or ketamine secondary to the fact that it does not possess any analgesic properties. Propofol has been found to have increased clearance and volume of distribution in the burn population, requiring doses that may be overly sedating upon emergence [74, 78]. With regard to pain, propofol may increase sensitivity to thermal stimuli [78]. Co-administration with ketamine for prevention of these effects has had mixed evidence [70, 78].

When possible, regional anesthesia consisting of single-shot nerve blocks and peripheral nerve catheters (PNCs) should be incorporated in order to avoid risks of general anesthesia [76]. PNCs allow for continuous infusion of local anesthetics, leading to decreased systemic opioid requirements and improved patient satisfaction [70, 71, 74, 76]. Neuraxial anesthesia has generally been avoided due to risk of sepsis and coagulopathy in burn patients.

Non-pharmacologic Management of Burn Pain

Non-pharmacological treatments have increasing efficacy in the adult burn patient [73]. The goal is to incorporate these treatments early on during hospitalizations in order to reduce agitation, anxiety, and sedation – all of which have proven to increase ICU stay and mortality [73, 100].

Hypnosis (via Barber's *Rapid Induction Analgesia* method [101]) for procedural analgosedation has been moderately researched in the burn population. The method employs a set of suggestions for facilitating rapid comfort, relaxation, and dissociation [101]. A meta-analysis of six studies demonstrated improved pain intensity and anxiety without change in medication usage [102]. Hypnosis and distraction

techniques such as virtual reality and sensory focusing interventions appear to efficacious in pain relief secondary to utilization of the gate control theory of pain, whereby attention dictates conscious interpretation of pain severity [103].

Music therapy has been studied in burn patients as well, demonstrating pain alleviation, anxiety reduction, and heart rate reduction [46]. Other promising non-pharmacologic management of burn patients include deep breathing, virtual reality, guided imagery, mindfulness meditations, cognitive behavioral therapy, extracorporeal shockwave therapy (ECSWT) for scar pain, and transcutaneous electrical nerve stimulation (TENS) [4, 103, 104].

Outpatient Management of Chronic Burn Pain

Chronic postburn pain is primarily neuropathic in nature and can be challenging to treat, requiring the use of a multitude of analgesic agents concurrently. Multimodal analgesia allows for better analgesic outcomes while concurrently permitting opioid sparing and limiting medication-related side effects. Optimal chronic pain therapy for burn pain should include not only opioids but other adjuvant and neuropathic medications. Some of the most commonly used neuropathic pharmacologic agents include antiepileptic medications (gabapentin, pregabalin, topiramate), TCAs (amitriptyline, desipramine, nortriptyline), SNRIs (venlafaxine, duloxetine), as well as other adjuvant medications such as acetaminophen and non-steroidal anti-inflammatory drugs. Some opioid medications such as methadone, tramadol, and tapentadol possess both opioid and non-opioid qualities, making them particularly useful in the treatment of neuropathic pain [24].

Opioids

Opioids are considered the cornerstone of therapy for moderate-to-severe acute pain or pain of similar intensity due to life-threatening illnesses, but their long-term use in non-cancer pain is controversial. Opioids provide analgesia by binding to opioid receptors of the mu and kappa class and blocking the release of neurotransmitters such as substance P. Opioid receptors are expressed both centrally and peripherally (during the inflammatory response in injured tissue) [105]. Based on their mechanism of action, it has been postulated that methadone, tramadol, and tapentadol have been thought to treat neuropathic pain.

Methadone is metabolized in the liver via the cytochrome P-450 system and is excreted via the kidneys and intestines. Dosage adjustment is not required in renal or hepatic insufficiency or in hemodialysis. Additionally, methadone does not appear to produce active, potentially toxic metabolites. Methadone has a long, biphasic elimination half-life. It may take up to 10 days to reach steady-state serum levels. It is inherently long acting and is significantly less expensive than opioids

that are pharmaceutically manipulated into controlled-release formulations. Its slow onset and offset is also thought to confer methadone a lower risk of addiction in comparison with other opioids. Methadone is also a N-methyl-D-aspartate (NMDA) receptor antagonism. Activation of the NMDA receptor by excitatory amino acids, such as glutamate, has been implicated in the development of neuropathic pain and appears to have a role in the development of opioid tolerance and opioid-induced hyperalgesia. In 2017, a Cochrane review was done to assess whether there is evidence for using methadone to treat neuropathic pain in adults. According to the review, there was very low-quality evidence regarding the efficacy and safety of methadone for chronic neuropathic pain, and there were too few data for pooled analysis of efficacy or harm or to have confidence in the results of the individual studies. No conclusions can be made regarding differences in efficacy or safety between methadone and placebo, other opioids, or other treatments [105].

Tramadol and tapentadol are short-acting, mixed opiates found to have mechanisms like methadone but with varied degree of affinity for the serotonin (5-HT3) and NMDA receptors. They have minimal efficacy in the treatment of chronic neuropathic pain based on limited existing literature [106].

More than half of trauma and burn patients are discharged from the hospital with an opioid prescription. The question remains as to whether long-term use of opioids leads to a transformation of acute to chronic pain. With increased scrutiny from the Drug Enforcement Agency and growing concerns regarding opioid use, dependence, and abuse, there has been a push in the healthcare field toward greater regulation for the chronic prescribing of opioid pain medications. The current paradigm for chronic opioid therapy is to limit opioid dosing to the lowest necessary amount to control pain symptoms in combination with non-opioid analgesic supplementation and multidisciplinary pain management [26].

Summary of Treatments for Burn Pain

Table 1.5 Evidence-based treatments for burn pain

Intervention	Pain phase	Studies	Study quality
Opioids	Procedural Breakthrough Background Chronic	Faucher (2006) [86] ISBI Yang (2018) Prakash (2004)	Guidelines Guidelines SR/MA ($n = 9$) RCT ($n = 60$)
Ketamine	Procedural Background	Kundra (2013) [99] McGuinness (2011)	RCT ($n = 60$) SR ($n = 4$)
Non-steroidal anti-inflammatory drugs	Procedural Background	Marret (2005)	MA ($n = 22$)
Benzodiazepines	Procedural Background Breakthrough	Zor (2010) [107] Patterson (1997) [108]	RCT ($n = 24$) RCT ($n = 79$)

Table 1.6 Emerging or promising treatments

Intervention	Pain phase	Studies	Study quality
Peripheral nerve blockade	Procedural Procedural Procedural	Cuignet (2004) [109] Cuignet (2005) [110] Shtyenburg (2013) [111]	RCT (n = 20) RCT (n = 81) RCT (n = 16)
α2-Agonists	Procedural Breakthrough Background	Asmussen (2013) [16] Kundra (2013) Kariya (1998) [88]	MA (n = 4) RCT (n = 60) RCT (n = 100)
Antidepressants	Chronic	Finnerup (2015)	SR/MA (n = 229)
Antiepileptics	Procedural Chronic	Gray (2011) [112] (pregabalin) Finnerup (2015)	RCT (n = 90) SR/MA (n = 229)
Virtual reality	Procedural Background	Scheffler (2018) Sharar (2007) [113]	MA (n = 21) RCT (n = 88)
Hypnosis	Procedural Background	Scheffler (2018) Provencal (2018)	MA (n = 7) MA (n = 18)
Music therapy	Background	Li (2017) Scheffler (2018)	MA (n = 17) MA (n = 5)
Nitrous oxide	Procedural	Li (2017) do Vale (2014)	RCT (n = 240) RCT (n = 15)
EMLA cream	Procedural Procedural	Lillieborg (2017) Jellish (1999) [114]	RCT (n = 8) RCT (n = 60)

Table 1.7 Accepted but unproven treatments

Intervention	Pain phase	Studies	Study quality
Acetaminophen	Procedural Breakthrough Background Chronic	Koppert (2004) [115] Koppert (2004) [115]	RCT (n = 14) SR/MA

Table 1.8 Disproven treatments

Intervention	Pain phase	Studies	Study quality
Gabapentin	Background (non-neuropathic)	Wibbenmeyer (2014)	RCT (n = 53)

Conclusion

Pain is among the most common causes of distress during the first year after recovery from trauma and burns. Early pain treatment is assumed to effectively reduce pain in patients and improve long-term outcomes. Despite advances in the various areas of trauma and burn care, control of pain is often inadequately managed during the acute and chronic rehabilitation phases of treatment. In the past, opioids have been the first-line treatment for acute pain following trauma; however, increased regulation and a lack of data for long-term opioid use for the management of chronic non-malignant pain in trauma and burn patient have created a need for creation of multimodal pain management treatment algorithms designed to minimize opioids and their side effects. Current evidence has shown that the most advantageous

methods for treatment of pain associated with trauma and burns incorporate both pharmacologic (opioid and non-opioid analgesics) and non-pharmacologic therapies targeting the specific clinical pain settings unique to the patient and hospital system/institutional capabilities.

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