Chapter 13
Preemptive Analgesia and Multimodal Pain Management for Temporomandibular Total Joint Replacement Surgery

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Introduction

Pain is not a single entity but a complex, multifaceted experience. Patients undergoing temporomandibular joint (TMJ) replacement are susceptible to postoperative pain for a number of reasons. Factors that may contribute to significant postoperative pain following TMJ replacement surgery include dense innervation of the face (Fig. 13.1) as represented by Penfield's homunculus on the postcentral gyrus of the cerebral cortex, dense innervation of the TMJ with substance P-secreting neurons, existing preoperative acute and chronic pain, psychological impact of preexisting pain, fear of postoperative pain, neurovascular tissue injuries from previous surgery, preexisting plasticity of the central nervous system, and extent of the surgery [1]. The typical surgical approach for TMJ total joint reconstruction involves a preauricular and a retromandibular approach to place the fossa and condylar components of the joint, respectively. Each of these approaches requires dissection through skin, subcutaneous tissue, fascia, and muscle layers as well as the removal of diseased condyle and a probable release of the temporalis tendon by coronoidectomy. Since many patients undergo simultaneous bilateral joint replacement, the sum of the surgical impact upon the tissues by the four incisions and dissections is considerable (Figs. 13.2 and 13.3). Contemporary patients are well informed and are interested in not only the risks and benefits of their proposed procedure but also the plan for their

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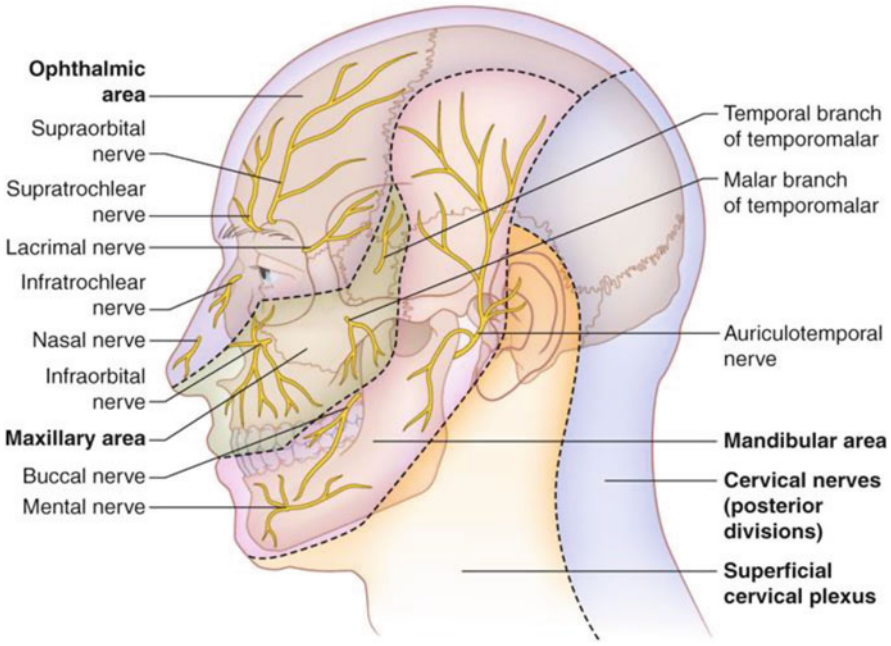

Fig. 13.1 Distribution of sensory nerves to the head (adapted from Gray's Anatomy, 1966)

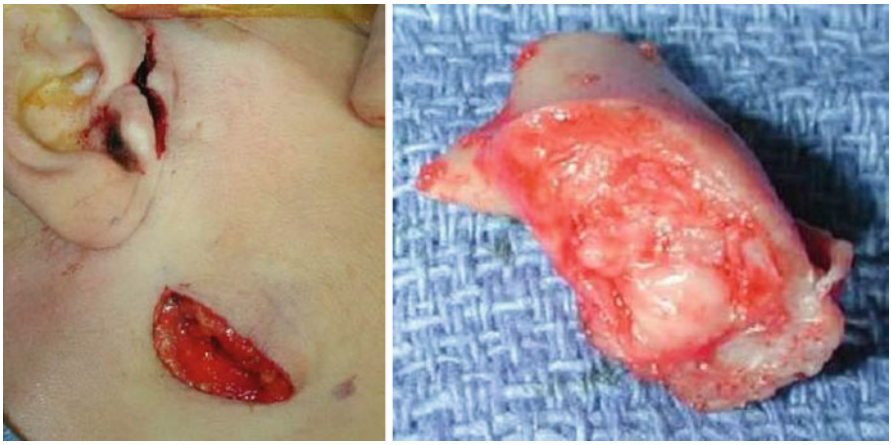

Fig. 13.2 (**a**) Preauricular and retromandibular incision. (**b**) Resected condyle with degenerative changes secondary to osteoarthritis

perioperative management, including pain control. The Joint Commission on Accreditation of Health Organizations has published standards for pain assessment and management, and within these guidelines it is stipulated that a surgeon should prospectively include within their operative plan a predesigned strategy for pain management which should be discussed with the patient [2]. Important concepts of

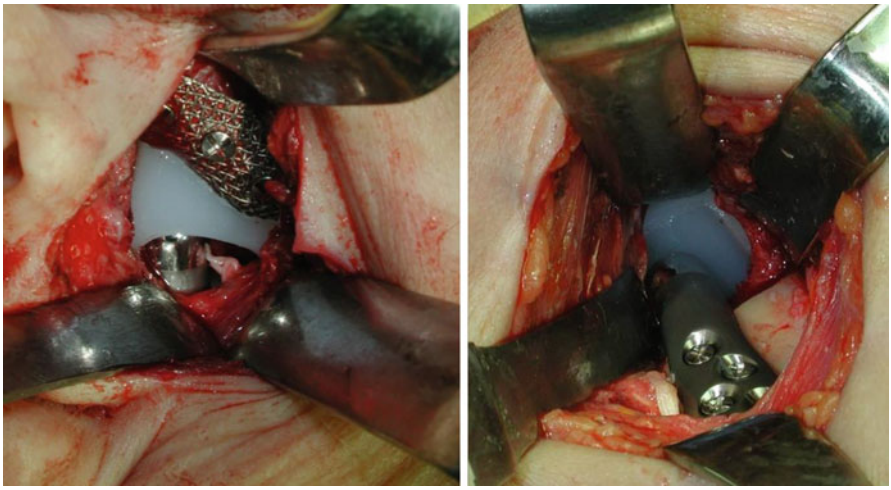

Fig. 13.3 Temporomandibular joint replacement viewed from preauricular and retromandibular perspectives (**a**, **b**)

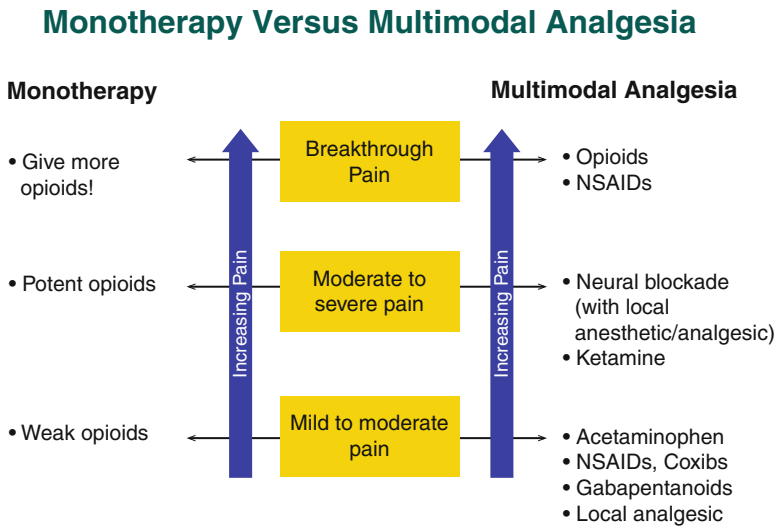

Fig. 13.4 Typical agents employed in multimodal therapy. Exparel™ educational slide set (modified). Modified from Awad IT, et al. Eur J Anaesthesiol 2004;21(5):379–83; Ashburn MA, et al. Anesthesiology 2004;100(6):1573–81; Gottschalk A, Smith D. Am Fam Phys 2001;63:1979–84; Iyengar S, et al. J Pharmacol Exp Ther 2004;311:576–84

acute and chronic pain related to trigeminal nerve pathways have been discussed in previous chapters of this text, although as noted above, patients undergoing joint replacement therapy may have a preexisting chronic pain component that is relative to their outcome. The focus of this chapter is on management of perioperative pain through preemptive analgesia and the neuroprotective benefits of multimodal pain management (Fig. 13.4).

Pain Pathways

Surgical pain is primarily nociceptive and considered to be a complex, unpleasant experience with emotional and cognitive as well as sensory features that occur in response to tissue trauma. Undertreatment of surgical pain can result in many potential consequences, including emotional and physical suffering, sleep disturbance, and respiratory, cardiovascular, gastrointestinal, musculoskeletal, and endocrine side effects, all of which can impact surgical outcome. Some of these include increases in ACTH, cortisol, catecholamines, and interleukin-1 and decreases in insulin levels. Water and sodium retention can occur; decreased mobility which can predispose to pneumonia; muscle splinting, which can result in cough suppression and the potential for hypoxemia and/or pneumonia; sympathetic mediated coronary vasoconstriction, which can result in ischemia, angina, and myocardial infarction; reduced limb blood flow and venous emptying, which can result in venous thrombosis/embolism; decreased intestinal motility and urinary retention; muscle spasm, muscle atrophy, impaired wound healing, and impaired muscle metabolism; increased nerve excitability, which can result in hyperalgesia and allodynia; and finally, sleep deprivation, anxiety, and depression.

Another important consideration regarding pain in the postoperative period is the impact on initiating physical therapy. Patients with uncontrolled pain struggle or avoid participation in physical therapy, whereas those with well-controlled pain, in general, participate in physical therapy within the first 24 h post surgery. To maximize short- and long-term benefits from multimodal pain management the plan should be initiated in the preoperative period continued intraoperatively and extended to the postoperative and post-discharge period.

Preoperative pain assessment for TMJ reconstruction patients is best performed by obtaining a patient history, completing a subjective patient interview, and correlation with a pain questionnaire including visual analog scores. Preexisting pain management should be maximized prior to surgery and may include basic strategies such as splint therapy, physical therapy, acetaminophen, and NSAID therapy, preferably with a COX-2 inhibitor. Acetaminophen, a very weak anti-inflammatory agent, inhibits both COXs by approximately 50 %. The lipoxygenase (LOX) pathway is not affected by any NSAIDs; therefore, leukotriene formation is not suppressed. If patients have chronic pain that requires narcotic therapy, we suggest referral to a pain specialist for management with extended-duration oral or transdermal opiates. If masticatory muscle myalgia and chronic muscle contraction do not respond to other conservative therapies, we recommend Botox treatment of the masseter and temporalis muscles prior to surgery [3]. Our method is the injection of 25 units of Botox A into each temporalis and masseter 2 weeks prior to surgery. Our experience has been that the Botox injections take 7–10 days to become fully therapeutic, and for those patients that require this treatment it not only reduces the muscular component of pain, but it also improves their response to physical therapy.

Table 13.1 Mechanisms of pain perception

Transduction: Activation of peripheral nociceptors.
Transmission: Propagation of action potentials from peripheral nociceptive endings to second-order cells in the dorsal horn.
Central facilitation: Activation of NMDA receptors associated with increased sensitivity and firing frequency of dorsal horn neurons.
Modulation: Different degrees of perception for similar stimuli.

Once a patient's condition is maximized, then they become a candidate for joint replacement therapy. Prior to surgery, we discuss our plan for perioperative and postoperative pain management and physical therapy.

Components of multimodal pain management for the TMJ reconstruction patient must be based upon the classic concept that pain is divided into four overlapping processes (Fig. 13.1, Table 13.1). These processes include *transduction* which is the conversion of energy from thermal, mechanical, or chemical noxious stimuli into nerve impulses by nociceptors; *transmission* of the signal from the nociceptors to the spinal cord and brain; perception or cognition of signals as pain; *modulation* of signals by descending inhibitory and facilitatory input from the cortex that modulates nociceptive transmission at spinal cord or in the case of the trigeminal nerve (Fig. 13.2), projections to the trigeminal brain stem sensory nuclear complex [4]; *central facilitation* involves activation of NMDA receptors associated with increased sensitivity and firing frequency of dorsal horn neurons (Table 13.1).

Surgical pain has incisional and inflammatory components. Incisional pain differs in its mechanism from other inflammatory or neuropathic pain states. Hyperalgesia in the region of the incision is thought to be mediated by sensitization of Aδ-fiber and C-fiber nociceptors and the conversion of mechanically insensitive or silent Aδ nociceptors to mechanically sensitive fibers. C-fiber nociceptors respond to thermal, mechanical, and chemical stimuli, and Aδ-fiber nociceptors respond to mechanical and thermal stimuli. A third system, the Aβ system, is primarily responsible for processing non-noxious mechanical stimuli and serves as a tactile discriminator, but it also plays a role in modulating nociceptive signals that enter the dorsal horn of the spinal cord. These fiber systems are supported by pseudounipolar cell bodies that, along with supportive satellite cells, are located in ganglia of spinal dorsal roots (DRG) and cranial nerves V, VII, IX, and X. The ganglia are located in or adjacent to intervertebral foramina of the spinal column or in or near boney canals and foramina of the skull, respectively. The intervertebral foramina and boney canals allow passage of elements of the peripheral nervous system into and out of the spinal cord and brain stem. The conducting elements of these fiber systems are composed of peripheral axons with free nerve endings or specialized receptor organs that are distributed in peripheral tissues and are contiguous with central elements that terminate either in the dorsal horn of the spinal cord or in the nuclei of the brain stem. They are connected to their respective pseudounipolar

perikarya by a T-segment of axonal membrane. No synapses occur between primary afferents in the peripheral ganglia, but the proximity of the neuronal perikarya affords the possibility for electrochemical cross-excitation between neurons to occur.

Transduction, or nociceptor activation, is chemically mediated by substances synthesized or released in association with cellular injury. Arachidonic acid metabolites, leukotrienes, and potassium are released by damaged cells; substance P stimulates nociceptors and also mediates vasodilation and the release of histamine from mast cells; bradykinin is released from plasma secondary to vascular injury, and serotonin is released from platelets. Thus, cellular, vascular, and neuronal injury leads to a rapid nociceptor-mediated pain response which is sustained by inflammatory mediators.

General Concepts and Typical Agents Employed

General Concepts

The rationale behind preemptive analgesia is that injury to nociceptive nerve fibers induces neural and behavioral changes that persist long after the injury has healed or the offending stimulus has been removed. This postinjury pain hypersensitivity can be due to posttraumatic changes in the peripheral and central nervous systems. The noxious stimulus-induced neuroplasticity can be preempted by administration of analgesics or by regional neural blockade.

The concept of multimodal therapies is that a combination of analgesic modalities in perioperative pain management results in better analgesia with a concomitant reduction in adverse effects.

Some established positive consequences of multimodal therapies are allowing for faster recovery and earlier hospital discharge. A component of multimodal therapy is rehabilitation. Generally, there are reduced doses of each analgesic with improved antinociception due to synergistic/additive effects. In theory, there is a reduction of severity of side effects of each drug.

Typical Agents Utilized

- Prophylactic antibiotic
  1. To reduce the risk of a potentially painful infection
- Pretreatment with a COX-2 inhibitor if not contraindicated
  1. To reduce the synthesis of arachidonic acid mediators which are involved with pain and inflammation

- Preoperative dexamethasone

  1. Pain reduction
  2. Nausea reduction
  3. Potent anti-inflammatory

- Balanced anesthesia, including:
- Opioid agent, typically fentanyl, morphine, or hydromorphone, to reduce acute pain. It is well understood that effective acute pain management reduces hospital stays, enhances recovery, and reduces the likelihood of developing chronic pain states.
- Ketamine can reduce opioid tolerance and decrease the dose of opioid required to treat pain. Ketamine possesses *N*-methyl D-aspartate (NMDA) receptor antagonist effects:

  1. NMDA is a receptor at the spinal cord or the trigeminal brain stem nuclear complex levels that facilitates pain sensitization and opioid tolerance. The NMDA receptor is part of a larger family of glutamate receptors, is involved in the processing of acute and chronic pain, and is an important mediator of rapid excitatory neurotransmission through the nervous system.
  2. Structurally, the NMDA receptor contains four transmembrane channels activated by both glycine and glutamate. Further, the NMDA receptor is divided into three subunits with the NR2B unit most involved in nociception and is thus the area of greatest study for pain-reducing modalities. Ketamine was first developed as an alternative to phencyclidine in 1962, is composed of a racemic mixture of *R*- and *S*-enantiomers, and is unique in that it is a central acting anesthetic and analgesic agent. Ketamine is known as the most complete anesthetic agent utilized today underscoring its intense analgesic, sedative, and amnestic properties [6, 7].
  3. Ketamine is ten times more lipid soluble than thiopental, and it is believed to exert its effects via NMDA receptors in addition to central and spinal opioid receptors, serotoninergic receptors, and norepinephrine receptors. Ketamine can be administered via multiple routes as a result of its high lipid solubility. The onset time for the intravenous and intramuscular route is 30–40 s and 3–4 min, respectively [6, 7].
  4. The bioavailability of ketamine after intramuscular administration is approximately 90 %. Ketamine is initially distributed to highly perfused tissues such as the brain, heart, and lung and undergoes redistribution much like thiopental [6, 7].
  5. The drug is metabolized in the liver by the P450 system to norketamine, an active compound which has one-third the activity of the parent drug. Norketamine is then further metabolized into water-soluble metabolites and excreted in the urine displaying an elimination half time of approximately 3 h. Ketamine is the only intravenous anesthetic displaying low protein binding [6, 7].

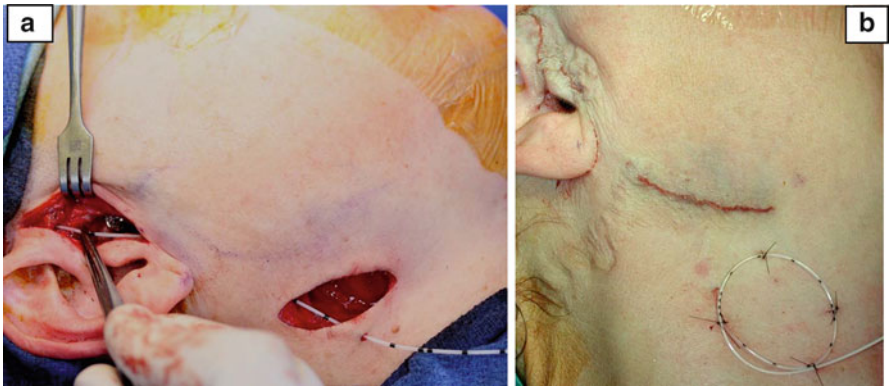

Fig. 13.5 Pain catheter is placed in a subcutaneous plane and sutured at the preauricular and retromandibular level (**a**), skin closure and stabilized catheter (**b**)

- Preemptive and intraoperative local anesthetic auriculotemporal nerve block and incisional infiltration.
    1. Bupivacaine delivered intravascularly can have significant morbidity and mortality.
    2. Ropivacaine has replaced bupivacaine as a preferred long-acting local anesthetic as it is a selective enantiomer that is one carbon different than bupivacaine. If injected intravascularly, it has significantly reduced cardiovascular side effects.
    3. Exparel™ is a novel long-acting liposomal bupivacaine injectable suspension, which was approved by the FDA in October 2011. The technology involves Depofoam, tiny lipid-based particles containing small discrete water-filled chambers dispersed through the lipid matrix. The particles are 10–30 μm in diameter, and the suspension can be injected through a fine needle. Levels persist for approximately 96 h.
- Layered precise dissection that is neurovascular protective.
- Diligent hemostasis to avoid hematoma formation.
- Placement of an I-Flow OnQ pain pump (270 ml, 2 ml/h REF: PM003) which provides local anesthetic 0.2 % ropivacaine for 5 days (Fig. 13.5).
    1. It is important to use the catheter with perforations in the distal portion and not a soaker catheter [8, 9].
    2. This technology allows for an extended delivery mechanism of local anesthesia and longer blockage of pain transmission.
- Continue dexamethasone for three postoperative doses.
- Continue NSAID (ketorolac) or COX-2 and acetaminophen:
    1. Control inflammatory mediators
    2. Control pain mediators

- Morphine, hydromorphone, or fentanyl (rarely utilized) patient-controlled analgesia (PCA) for opiate-dependent patients and for breakthrough acute pain.

  1. Typical PCA protocol; we prefer to use hydromorphone.
  2. Hydromorphone is five times as potent as morphine, has no metabolites, and possesses less side effects. Hydromorphone is very water soluble allowing for a very concentrated solutions.
  3. Morphine is glucuronidated to morphine-3-glucuronide (80 %) and morphine-6-glucuronide (10 %) and normorphine. Morphine-6-glucuronide is an active metabolite. Morphine-3-glucuronide is hyperalgesic.
  4. The continuous PCA setting is rarely utilized, with the exception of opiate-dependent patients.
  5. Typical bolus dose:

     Morphine: 1 mg (0.5–2 mg)
     Hydromorphone: 0.2 mg (0.1–0.4 mg)
     Lockout: 6 min (5–12 min)
     Hourly limit: Ten doses (5–10)
     Basal rate: 0 mg/h (0–2 mg/h)
     Clinician (nurse-activated) dose

- Continuous ice

  1. Decreased vasodilation and swelling and decreased pain transmission.

- Range of motion (ROM) exercise with Therabite or a similar device

  1. Typically start in the morning on postoperative day one.
  2. Improved distribution of medication to the tissue.
  3. Faster return of range of motion.

- Continue ice on discharge.
- Continue COX-2 and acetaminophen or oral hydrocodone.
- Continue ROM exercise.
- Formal physical therapy within 7 days.

In summary, preemptive analgesia and a multimodal approach to pain management, such as described in this brief chapter, can significantly reduce pain and the need to maximize the dose of a single therapy. One of the overlying concepts of multimodal therapy is a lower amount of any one given agent, in combination with others, which might impact pain through a different mechanism or process. Another overlying concept of multimodal therapy is that smaller amounts of each agent can reduce the risks of side effects from larger doses of any one particle drug (e.g., respiratory and/or central nervous system depression with large amounts of opiate). Poorly treated postoperative pain can lead to the chronic pain states which are much more difficult to suppress [10, 11].

In conclusion, multimodal therapy for TMJ replacement leads to improved patient satisfaction, reduced pain-related morbidities, reduced opiate side effects, earlier discharge, improved participation in physical therapy, and in many instances

a reduction in total cost. The development of new therapies such as extended-release bupivacaine (Exparel™) may eventually further simplify the administration of multimodal pain therapy, and the use of other analgesics such as gabapentin (a calcium channel blocker, now available in a gastroretentive formation that reduces overall side effects significantly (e.g., Gralise)) may eventually reduce or potentially replace opiates as the mainstay of postoperative pain management.

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Conflict of Interest None declared.

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