Nonopioid Adjuncts and Alternatives

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KEYWORDS

• Nonopioid • Pain control • Postoperative care

KEY POINTS

- Multi-modality non-opioid analgesia can be effective for pain control.
- Otolaryngologists should be well versed in the role of non-opioid analgesia based on surgical subsite.
- Balancing risks and benefits of treatment can help cater to the appropriateness of opioid versus non-opioid pain control.

INTRODUCTION

Opioid use in the United States of America has become an epidemic, affecting approximately 2.5 million adults and resulting in close to 50,000 deaths in 2017 alone.[1] The opioid crisis has garnered significant attention in the past decade, leading to increased oversight and monitoring of physician prescribing patterns in an attempt to quell the surge of prescription opioid drug addiction and abuse. This escalating health crisis and the increased attention to prescribing patterns have led to the need for otolaryngology providers to consider nonopioid adjuncts and alternatives for pain management. Otolaryngologists frequently employ the use of medication for pain control after surgical intervention, and adjunctive treatment options for these patients potentially can decrease opioid prescriptions provided while optimizing patient analgesia.

The concept of perioperative multimodal opioid-sparing pain control starts in the preoperative period, includes intraoperative pain management, and extends to the acute postoperative period. Effective adoption of these methods requires communication and collaboration with the anesthesiologist providing care during the surgical period. Administration of therapy prior to the start of surgery, preemptive analgesia, is intended to prevent sensitization of the nervous system to the subsequent noxious

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Otolaryngol Clin N Am 53 (2020) 831–842
https://doi.org/10.1016/j.otc.2020.05.012
oto.theclinics.com

stimuli during surgery that can amplify pain. Commonly employed nonopioid preemptive analgesic drugs that have been investigated in otolaryngologic procedures include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, ketamine, corticosteroids, and dexmedetomidine. Intraoperative use of topical and infiltrated local anesthetic medications has been employed in several otolaryngologic procedures to decrease the need for postoperative pain control. Finally, postoperative use of gabapentinoids, acetaminophen, and NSAIDs has been reported in multiple otolaryngologic procedures. **Table 1** summarizes the types of drug classes and their mechanisms of actions discussed throughout this article. This article highlights the role of nonopioid pain management throughout the different subspecialties of otolaryngology–head and neck surgery.

HEAD AND NECK SURGERY

Head and neck surgery comprises the largest and most extensive array of surgical procedures performed in the field of otolaryngology. Pain management, however, is not isolated to postsurgical patients with head and neck cancer but also is an issue for those patients who receive radiation and chemotherapy as well as patients with chronic pain after completion of treatment. One study demonstrated that 13% of patients with head and neck malignancies who received radiation treatment of curative intent had prolonged opioid use 6 months after treatment.[2] Another study demonstrated that more than 50% of oropharyngeal squamous cell carcinoma patients treated with radiation became chronic users of opioid medications.[3]

Immediately after surgical intervention, many patients receive scheduled opioids but also are treated with patient-controlled analgesia (PCA) devices to give low dose boluses of opioids on demand. In this group of patients, the current management goals are to provide opioid-sparing multimodal analgesia and to focus on reducing opioid use with nonopioid adjuncts while preserving patient analgesia.[4] Smith and colleagues[5] examined the utility of regularly scheduled intravenous (IV) acetaminophen in addition to the standard PCAs given to head and neck cancer patients in the first 24 hours after surgery. This study found significantly decreased total narcotic requirement, a reduction in the need for PCA, and a significantly decreased length of stay. Another study examined the use of the NSAID celecoxib, a selective cyclooxygenase (COX)-2 inhibitor, for the treatment of postoperative pain management in head and neck cancer patients undergoing surgical resection and free flap reconstruction. NSAIDs that are nonselective inhibit COX-1 and COX-2, whereas selective COX-2 inhibitors do not affect platelets in the same manner, and this theoretically reduces the risk of bleeding. This study determined that there was a significant decrease in oral, IV, and total opioid requirements without increasing surgical-related or flap-related complications.[6] Currently, there are open trials examining the utility of IV lidocaine administration as a means to reduce opioid consumption postoperatively after major head and neck cancer surgery.[7]

Mucositis is a common side effect after treatment of head and neck cancer patients with chemotherapy and/or radiation therapy and results in tremendous discomfort. A recent systematic review examining treatment of mucositis pain with nonopioid adjuncts demonstrated significant pain relief compared with placebo with topical doxepin, amitriptyline, diclofenac, and benzydamine.[8]

SLEEP SURGERY

An additional area of concern with postoperative opioid use in the field of otolaryngology is the potential acute complications of narcotics. Opioids can cause respiratory

Table 1
Nonopioid drug classes used for pain in otolaryngology

Drug Class	Examples	Mechanism of Action	Common Side Effects
NSAID	Aspirin Ibuprofen Naproxen Ketorolac Diclofenac Celecoxib	COX-1 inhibitor → inhibits prostaglandin production COX-2 inhibitor → inhibits prostaglandin production	Gastric ulcers, platelet dysfunction, nephrotoxicity, cardiovascular events Fewer gastric side effects
	Acetaminophen	Exact mechanism unclear, prevents central prostaglandin synthesis	Liver toxicity
Muscle relaxants	Cyclobenzaprine Tizanidine Baclofen Diazepam	Centrally acting, mechanism varies by drug	Drowsiness, dizziness, drug-drug interactions, respiratory depression
Antidepressants	Amitriptyline Nortriptyline Duloxetine	Tricyclic antidepressant SNRI	Blurred vision, dry mouth, orthostatic hypotension, urinary retention, prolonged QTc, drug-drug interactions
α-Agonists	Dexmedetomidine Clonidine	α_2-Aadrenergic receptor agonist	Hypotension, bradycardia, sedation
Gabapentinoids	Gabapentin Pregabalin	Calcium channel blockade	Dizziness, somnolence, peripheral edema, blurred vision Pregabalin is a controlled substance
Corticosteroids	Prednisone Methylprednisolone Triamcinolone Cortisone	Inhibition of phospholipase	Mood changes, hypertension, increase in glucose, adrenal suppression, osteoporosis

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Drug Class	Examples	Mechanism of Action	Common Side Effects
Local anesthetics	Lidocaine Bupivacaine Ropivacaine	Sodium channel blockade	Local anesthetic system toxicity, including tinnitus, perioral numbness/ tingling, altered mental status, seizures, cardiac arrhythmias, and cardiac arrest
Other anesthetics	Ketamine	NMDA receptor antagonist	Hallucinations, increased oral secretions, sympathomimetic effects, direct myocardial depression, increased intracranial pressure, increased pulmonary hypertension

Abbreviations: NMDA, *N*-methyl-D-aspartate; SNRI, serotonin norepinephrine reuptake inhibitor.

depression and increased upper airway collapse. Patients with severe obstructive sleep apnea undergoing sleep surgery, therefore, are particularly vulnerable to this potential complication. Surgeries for obstructive sleep apnea, such as uvulopalatopharyngoplasty, are known to be painful, with reported 20% of postoperative return visits to the hospital for inadequate pain control. Additionally, there is a high rate of postoperative bleeding, accounting for up to 40% of unplanned revisits.[9] Therefore, it is important to develop analgesic protocols that provide adequate pain relief while minimizing opioid use and risk of bleeding in this population of surgical patients. There have been numerous studies demonstrating the effectiveness of perioperative regional anesthesia in the form submucosal infiltration of long-acting local anesthetic in the oropharyngeal region prior to incision. These interventions at the time of surgery can provide effective postoperative analgesia in the immediate postoperative period.[10,11] Ayatollahi and colleagues[12] found that the administration of IV vitamin C intraoperatively during uvulopalatopharyngoplasty reduced postoperative pain, both in overall severity and duration, prior to requesting analgesic, without side effects.

THYROID AND PARATHYROID SURGERY

Sensitivity of the anterior neck from thyroid and parathyroid surgery can result in significant postoperative pain. A national survey examining trends in pain management after thyroid and parathyroid surgery demonstrates that there is significant variability in practice patterns and that only 35% of practitioners do not utilize opioids.[13] There have been several studies that sought to reduce postoperative opioid consumption

with the use of various perioperative adjuncts. In a metanalysis of 14 randomized controlled trials (RCTs), Mayhew and colleagues[14] demonstrated the analgesic efficacy of bilateral cervical plexus block in the early postoperative period with significant reduction in analgesic requirements and decreased length of hospital stay. Another study examined the use of preemptive IV ibuprofen preoperatively and found there was a significant reduction in visual analog scale (VAS) for pain as well as reduced opioid consumption and use of rescue analgesia.[15] Preoperative administration of gabapentin also has been shown to have similar effects in decreasing pain scores and opioid consumption postoperatively.[16] One of the arguments against using NSAIDs in thyroid and parathyroid surgery is the risk of postoperative hematoma. A study by Chin and colleagues,[17] demonstrated an increased incidence of hematoma in patients who received ketorolac perioperatively (2.7% vs 1.3%); however, there were low number of hematomas and these findings were not statistically significant. Studies have demonstrated that the implementation of protocols utilizing multimodality analgesia (preoperative acetaminophen, NSAIDs, and gabapentin with postoperative acetaminophen and ibuprofen) can help decrease prescriptions for postoperative opioid analgesics for patients undergoing thyroid and parathyroid surgery.[18]

SINONASAL SURGERY

Postoperative opioid analgesics are prescribed by up to 95% of providers after sinonasal surgery, according to a recent national survey.[19] Some studies, however, have demonstrated that patients utilize only a small number of pills and a majority of the medication remains unused.[20,21] Therefore, the judicious prescribing of opioids after rhinologic surgery coupled with adjunctive nonopioid use represents a practical opportunity for otolaryngologists to reduce the possibility for abuse by patients and opioid diversion. Acetaminophen is a mainstay for analgesia after sinonasal surgery, but there also have been several RCTs examining perioperative IV acetaminophen dosing prior to the start of surgery, which led to reduction of immediate postoperative pain and decreased opioid requirements.[22–24]

There have been several double-blind RCTs for NSAID use for septoplasty, rhinoplasty, and endoscopic sinus surgery.[25–30] Moeller and colleagues[27] demonstrated that IV ketorolac is a safe analgesic in the setting of septoplasty and sinus surgery. Ozer and colleagues[28] determined that administration of IV dexketoprofen provides good postoperative analgesia in septorhinoplasty patients irrespective of intraoperative versus postoperative administration. Turan and colleagues,[25] meanwhile, showed that rofecoxib, a COX-2 inhibitor, demonstrated decreased pain scores, reduced rescue analgesia, and prolonged times to first analgesic requirement. Rofecoxib was pulled from the market due to adverse cardiovascular events. Celecoxib currently is an available COX-2 inhibitor with safer side-effect profile.

Pregabalin and gabapentin are new-generation anticonvulsants with antihyperalgesic and antinociceptive properties. These drugs were initially used for the treatment of neuropathic pain, but their use has been expanded to treat multiple types of acute and chronic pain. The use of preemptive gabapentinoids in nasal surgery has also been well documented in several RCTs, with a majority reporting significantly lower VAS pain scores compared with placebo.[31–36]

Local anesthestic agents also have been explored as a means to provide analgesia after sinonasal surgery. Several studies reported that the use of local anesthetics, including lidocaine and bupivacaine, either as injection or infusion in postoperative nasal packing, led to decreased VAS scores and lower analgesic requirements.[30,37] Other studies have utilized a sphenopalatine ganglion block or

infraorbital nerve block to provide analgesia by targeting the sensory innervation of the nasal mucosa.[38,39]

Dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, has been utilized more frequently in the practice of anesthesia because it produces sedation, anxiolysis, and analgesia without causing respiratory depression. Administration prior to sinonasal surgery was found to result in significant reductions in VAS pain scores compared with placebo-saline solutions in 1 study.[40]

FACIAL PLASTIC SURGERY

Distinct from septorhinoplasty surgery, there are a variety of procedures in facial plastic surgery that require consideration with respect to the type of analgesia utilized, including rhytidectomy, brow-lift, and blepharoplasty. Studies have reported the use of a multimodality approach to pain control for facial rejuvenation procedures, balancing the use of intraoperative tumescence with dilute local anesthesia and nerve blocks at the completion of surgery as well as supportive wraps and cold compresses postoperatively.[41] Rhytidectomy is an important procedure in facial rejuvenation, and hematoma is considered the most dreaded complication, which has limited the study of postoperative pain control that increases the risk of bleeding. One study demonstrated that perioperative celecoxib use was associated with reduced opioid use, nausea, and later sedation without any adverse side effects, including bleeding.[42]

OTOLOGIC SURGERY

Otologic surgery can be divided into myringotomy and tube (MT) surgery versus more involved ear surgery, such as middle ear or transmastoid surgery in regard to perioperative pain control. MT surgery has been studied extensively, with a majority of studies reporting acetaminophen, NSAIDs, or both for effective analgesia.[43] The addition of ketorolac or codeine, while providing superior analgesia, were not found cost effective or necessary for this limited surgery.[44–46] Nonpharmacologic adjuncts also have been examined, with acupuncture therapy diminishing pain and emergence agitation after MT placement.[47] For more extensive otologic surgery, Suresh and colleagues[48] showed the benefit of a greater auricular nerve block performed intraoperatively during transmastoid surgery to provide superior analgesia and a reduction in overall postoperative opioid requirement. Another analysis examined intramuscular NSAID injection after mastoidectomy, which did not lead to any major adverse events, such as hematoma.[49] These findings taken together indicate that the use of postoperative opioid analgesia likely can be reduced with judicious local anesthetic infiltrate at the time of surgery and the use of NSAID and acetaminophen in the postoperative period.

PEDIATRIC SURGERY

Some of the most common procedures performed in pediatric otolaryngology practices include MT surgery and adenotonsillectomy. Although these procedures also are performed in adult patients, pain management in the pediatric population requires separate evaluation for several reasons. The assessment of postoperative pain is challenging in children due to their lack of understanding and of ability to verbalize the degree of pain being experienced. VAS systems have been validated for children to help explain their experience and this can be utilized to improve their ability to communicate with practitioners.[50] One of the most basic steps in the management of pain and anxiety in children is to utilize cognitive behavioral strategies, such as distraction

(music or video), positive reinforcement, and environment optimization (not performing procedures inside a hospitalized patient's bedroom).[51] These steps, when combined with topical anesthetic, allowed for the placement of tympanostomy tubes in awake pediatric patients ranging from age 8 months to 17 years.[52] Local anesthetics also can be used to perform blocks of the auricular branch of the vagus nerve to facilitate tolerance of MT placement in children.[53] Infiltration of local anesthetic after tonsillectomy also has been studied extensively, with a metanalysis demonstrating it to be a safe and effective method to treat pediatric post-adenotonsillectomy pain.[54]

Given the potentially significantly morbid side effects of respiratory depression associated with narcotic use in pediatric patients undergoing tonsillectomy, the use of nonopioid adjuncts has received significant attention. Evidence has demonstrated the most effective first step in management for pain control after tonsillectomy includes the use of acetaminophen with or without ibuprofen. This treatment regimen has demonstrated similar efficacy to opioid analgesics without the added risk of oxygen desaturations from respiratory depression.[55] Although many practitioners worry that the use of NSAIDs could lead to increased post-tonsillectomy hemorrhage, a Cochrane review demonstrated postoperative ibuprofen was not associated with increased bleeding risk.[56] Literature on the usage of ketorolac in the setting of tonsillectomy has been less clear with respect to its effect on bleeding. Some studies suggest that post-tonsillectomy ketorolac is safe in children but can increase the bleeding up to 5-fold in adults.[57] Other reviews have concluded that risks and benefits should be considered before routinely using ketorolac for tonsillectomy.[58]

The intraoperative usage of dexamethasone during tonsillectomy has been endorsed by the American Academy of Otolaryngology–Head and Neck Surgery guidelines for its analgesic and antinausea properties.[59] Postoperative dosing also has shown improved outcomes, with recent literature demonstrating the effectiveness of oral steroids for improvement in pain, diet, activity, re-epithelialization of tonsillar bed, and sleep disturbance.[60] Another study examined the utility of a short course of steroid, 3 doses of dexamethasone, which decreased pain-related postoperative phone calls as well as hemorrhage rate.[60,61] In addition to steroids, a low dose of IV ketamine after tonsillectomy also has been reported to effectively reduce pain without side effects, such as nausea, vomiting, and agitation.[50,62]

EMERGING TECHNOLOGY

Some of the most difficult patients to treat are those with chronic pain. A specific category that can be encountered in otolaryngology practice is atypical facial pain. These patients often are comanaged with neurology or pain medicine specialists, and newer options for nonmedical therapy are being developed in the field of chronic pain. When medical management with neuromodulating agents (amitriptyline, gabapentin, and pregabalin) fails, additional adjunct interventions, such as botulinum toxin injections, can be attempted. Nonpharmacologic approaches, such as acupuncture and biofeedback, have been shown to have mixed results in this patient population.[63] Transcutaneous electrical nerve stimulation (TENS) has been shown to relieve chronic pain from facial myalgias.[64] This technology has recently been applied to patients with sinus pain—with an RCT indicating that microcurrent-treated patients had a significantly greater reduction in pain compared with placebo controls.[65] Future studies will investigate the reliability and durability of these findings, but TENS does show promise in alternative nonopioid therapies for patients with chronic pain in the head and neck.

The continued expansion of app development for smartphones has spilled over into assessment of postoperative pain. The utilization of patient-reported outcome

measures has become an important tool for clinical research, quality improvement, and optimization of patient care. A recent study examined the use of a mobile health platform to assess functional outcomes and pain after endoscopic sinus surgery and rhinoplasty. The study found that there were high response rates with this digital engagement platform, demonstrating that it can be an effective approach to assess postoperative outcomes, including pain control.[66] The implementation of these platforms has been useful particularly in the pediatric population, where the ability to communicate pain control may be difficult.[67]

SUMMARY

Across all subspecialties of otolaryngology–head and neck surgery, multimodality nonopioid analgesia is an effective way to control postoperative pain without causing increased morbidity. Pain is multifactorial, and clinical judgment should be made when choosing between opioid versus nonopioid adjuncts.

DISCLOSURE

Financial Disclosures: None.
Conflicts of Interest: None.

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