Pain Management for the Otolaryngologist

Overview of Perioperative Analgesia and Introduction to Opioids

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KEYWORDS

- Perioperative analgesia • Pain management • Pain • Sinus surgery
- Head and neck surgery • Pre-operative optimization • Facial plastic surgery
- Non-opioid adjuncts and alternatives

KEY POINTS

- Nearly 50,000 US adults experience opioid-overdose deaths annually and 1.7 million experience a substance use disorder specifically from *prescription* opioids. Surgeons prescribe 36% of opioid medications in the United States.
- Opioids continue to be indicated to treat acute postoperative pain that cannot be expected to be well controlled with other modalities. There is a lack of dedication to prescribing education resources for surgical trainees.
- Excess opioids are prescribed following endoscopic sinus surgery despite the existence of efficacious alternatives.
- Controlled substance agreements set expectations as to the universal precautions providers should practice when prescribing chronic opioids. Standard practices include checking prescription monitoring programs, toxicology screens, and frequent assessment of ongoing risks versus benefits.

OVERVIEW

Educational societies, news media, and the political establishment have extensively reported on the recent upsurge in opioid misuse (**Table 1**). Furthermore, personal

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Table 1
Select local legislative initiatives targeting narcotic prescription

Max. # of Days[a]	States
14	NV
7	AK, CT, IN, LA, MA, PA, UT, WV
5	AZ, NJ, NC
4	MN
3	FL

[a] Referring to maximum number of days of supply allowed for prescription of initial pain prescription or acute pain prescription for adults.

Data from Prescribing Policies: States Confront Opioid Overdose Epidemic. NCSL 2019. Retrieved from https://www.ncsl.org/research/health/prescribing-policies-states-confront-opioid-overdose-epidemic.aspx.

and societal costs related to the US opioid "epidemic" have become more apparent to the lay public (Fig. 1), with multiple local legislative initiatives being passed and several landmark lawsuits making the news. In September 2019, OxyContin manufacturer Purdue Pharma reached a historical tentative settlement for several billion dollars with 23 state attorneys general and 2000 other local governments.[1] As part of the settlement, Purdue did not admit wrongdoing, but, assuming the deal goes through, will declare bankruptcy and reorganize as a company producing medications to fight the opioid epidemic. Proceedings such as these remain fraught with political and ethical considerations on both sides; nonetheless, they have been in the news recently amid the significant increase in opioid-related abuse and deaths in the United States. In 2017 alone, almost 50,000 US adults experienced opioid-overdose deaths (see Fig. 1) and 1.7 million experienced a substance use disorder specifically from *prescription* opioids.[2]

Evidence-based medicine plays an increasingly important role in contemporary practice. Notably, surgeons prescribe 36% of opioid medications in the United States.[3] Over the past several decades, there have been myriad studies examining perioperative analgesic regimens for otolaryngologic procedures. Many of these regimens have demonstrated the efficacy of opioid alternatives. Multimodal analgesia should be implemented whenever possible, but for surgeries where postoperative pain cannot be expected to be controlled with analgesic adjuncts, the surgeon must be versed in safe opioid prescription practices. There is a lack of dedicated opioid prescribing education (OPE) resources for otolaryngology and surgical trainees,[4,5] so many of these considerations are generally overlooked (Table 2). One of the main points of this issue of *Otolaryngologic Clinics of North America* is to summarize evidence-based cost-effective practices that can be used in many situations. To continue to progress as a specialty, otolaryngologists need to be educated about novel approaches to multimodal analgesia and be familiar with the literature.

Preoperative Optimization

Successful implementation of a perioperative analgesic strategy starts with preoperative planning. Regardless of preexisting comorbidities or analgesic history, there should be an agreed-upon-plan before every elective surgery. This can consist of a brief conversation between the patient, surgeon, and anesthesiologist in an uncomplicated case or range all the way to an involved multidisciplinary plan for a patient with chronic pain (Box 1). For patients with chronic pain, it is important to coordinate care with their outpatient provider preoperatively in order to set clear expectations and

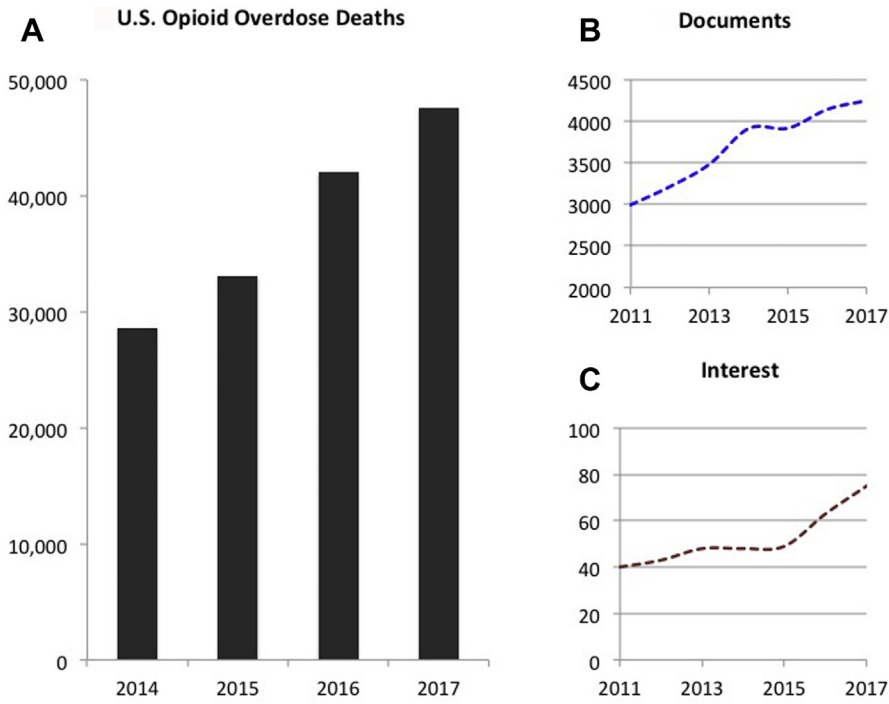

Fig. 1. (*A*) Bar chart: number of US opioid overdose deaths. (*B*) Upper right panel represents number of documents/publications by year on search for perioperative, surgical, surgery, otolaryngology AND analgesia, analgesic, opioid, and pain control. (*C*) Bottom right panel illustrates public interest via Google trends by year (January 1 of each year) for opioids as a class of prescription medications. (*Data from* [*A*] Drug Overdose Deaths. CDC 2020. Retrieved from https://www.cdc.gov/drugoverdose/data/statedeaths.html; and [*B*] Document search. Scopus, Elsevier 2020. Retreived from https://www.scopus.com/search/form.uri?display=basic&zone=header&origin=resultslist.)

goals for recovery. Notably, patients with substance use disorders require special attention. Postoperative pain control may be challenging, and discharge planning may be complex if postoperative opioids are indicated. Other issues integral to appropriate preoperative optimization include obtaining adequate nutrition and hydration, minimizing smoking, and providing appropriate deep vein thrombosis prophylaxis.[6,7] As this process is often underappreciated, the authors have dedicated a chapter entitled "Pre-Operative Optimization" in this issue to guide the surgeon in important questions to ask the patient preoperatively, optimization strategies, high-risk patients, and when it is necessary to consult a specialist.

Local Adjuncts

Regional anesthesia and local anesthetics can play a significant role in perioperative analgesia strategy when offered in appropriate circumstances. These agents can be used preoperatively and intraoperatively to minimize the need for postoperative "rescue." Their efficacy has been described for a variety of otolaryngologic surgeries and procedures, including nasal surgeries and thyroid surgery, and are further detailed and illustrated in the Elizabeth Boscoe and colleagues'article, "Local Blocks and Regional Anesthesia in the Head and Neck," in this issue.

Table 2
***Select* evidence-based recommendations for perioperative analgesia**

Reference	Surgery	# Studies/Patients	Highlights
Campbell 2019	Otologic Surgery	23 studies/1842 patients	Acetaminophen + Codeine superior to monotherapies; NSAIDs, a-agonists, and blocks are also viable monotherapies
Nguyen 2019	Septoplasty Rhinoplasty	37 studies	Preponderance of evidence for local anesthetics; NSAIDs decreased VAS scores and postop analgesic use; gabapentin and a-agonists are also evidence-based effective alternatives
Svider 2018	Endoscopic sinus surgery	32 studies/1812 patients	Acetaminophen reduced postoperative opioid requirements, as did NSAIDs (although beware of NSAID intolerance in sinus patients); gabapentin and a-agonists are also postoperative options
Sethi 2018	Endoscopic sinus surgery	155 patients (single-institution)	73.1% reported requiring no opioids; predictors of opioid use included concurrent turbinate reduction or septoplasty
Patel 2018	Rhinoplasty	62 patients (2 institutions)	Patients only used 40% of their hydrocodone/acetaminophen tablets

Abbreviation: NSAID, nonsteroidal antiinflammatory drug.

Perioperative Pain Management

Acute pain management following head and neck surgery represents a significant undertaking and certainly requires a preoperative plan as well as setting clear expectations. Local anesthetics may provide excellent coverage for some smaller head and neck cases, such as patients undergoing thyroid/parathyroid surgery, and there is evidence showing a preponderance of benefit over harm with the use of these

Box 1
Topics to address in order to optimize perioperative care

Analgesia Strategies

Issue
- Is the patient currently on any pain medications?
- Is the patient currently taking any illicit substances? Past use?
  - [a] Past pain medications?
  - [a] Medication requirements for prior surgeries/procedures
- Is the surgery elective? Inpatient? Outpatient?
  - What is the expected level of pain on discussion with the surgeon (ie, is this a small outpatient surgery or a major head and neck resection?)?
- What are the expected morbidities from this surgery?
- Are there any planned regional techniques or local blocks?
  - [a] Has a perioperative plan been discussed with the primary care provider?

[a] Particularly important for patients with chronic pain/prior history. Patients should be screened for whether they have chronic pain issues, and if so, there should be discussion with the outpatient provider. Considerations for patients on buprenorphine must occur in advance.

modalities.[8–11] However, depending on the extent of the surgery, some patients undergoing extensive head and neck resections require multidisciplinary care collaboration involving their operating surgeon, anesthesiology, and the pain medicine team. Involving the pain medicine team does not preclude the surgical team's participation in decision-making regarding analgesia, although all subsequent changes and plans should be taken forward together after discussion rather than a unilateral fashion. For physicians taking care of a patient following significant head and neck resection, nonenteral pain management takes on exceeding importance for patients unable to tolerate oral analgesics (see Katherine Tinkey and colleagues' article, "Non-enteral Pain Management," in this issue).

Beyond acute perioperative management following head and neck surgery, the close proximity of numerous critical structures in the head, neck, and skull base that may be affected may necessitate the need for a chronic pain plan. Extensive resection can harbor a wide variety of morbidities that may worsen pain, including those affecting speech, sight, swallowing, and airway patency.[12] Hence, keeping these patients comfortable while offering evidence-based practices can be important in minimizing superfluous subsequent narcotic prescription and decreasing hospitalization stays.[13] This also comes down to understanding the appropriate role of the otolaryngologist regarding interdisciplinary cooperation with pain and palliative physicians. Coming up with a "game plan" encompassing both anticipated immediate perioperative considerations as well as long-term postoperative recovery from an analgesic standpoint may facilitate the patient's suitability for planned adjuvant therapies, especially in patients who are undergoing extensive surgery.[14] In other words, many patients with extensive head and neck cancers may have significant pain before or after chemotherapy/radiotherapy, and all attempts should be made to minimize delays in the administration of adjuvant therapy. This includes ensuring that the patient has adequate pain control.

Obstructive Sleep Apnea and Perioperative Analgesia

Sleep apnea surgery represents a wide range of procedures. These involve inpatient endeavors as complicated as any oncologic surgery (base of tongue surgeries with airway concerns, maxillomandibular skeletal surgery) to more minor undertakings such as uvulopalatopharyngoplasty, nasal airway surgery, and limited palatal techniques. Regardless of surgical complexity, these patients are at greater risk with narcotic exposure due to their underlying obstructive sleep apnea (OSA) and may be more sensitive to the respiratory depressive impacts of opioids. This necessitates a special understanding of opioid alternatives and reinforces the importance of using these alternatives to decrease postoperative discomfort in the care of these patients. Patients with OSA, as previously discussed, benefit from preoperative optimization and have an appropriate anesthesia/analgesia plan; although there are not necessarily myriad studies specific to regimens following sleep surgery, there are evidence-based practices relating to throat surgery and other related techniques. Adverse events attributed to medications including narcotics have been cited in lawsuits related to patients with OSA perioperatively.[15] Appropriate level and duration of monitoring of these patients postoperatively must be ensured, especially for those patients requiring postoperative opioids.

Other Outpatient Perioperative Analgesia Considerations

Although seeking narcotic alternatives and applying appropriate postoperative monitoring is of utmost importance in patients undergoing sleep surgeries, other predominantly outpatient procedures in otolaryngology also warrant a discussion of outpatient

analgesic strategies. In an ideal preoperative informed consent process, perioperative quality of life should be discussed as well as long-term considerations; controlling pain in the immediate postoperative period minimizes the number of patients who are afraid of getting these surgeries in the first place. Otologic surgeries and sinus surgeries are generally outpatient and can be seemingly innocuous; however, a significant proportion of opioids prescribed in the United States is by surgeons for outpatient use; hence, there have been multiple papers demonstrating that many of the pills from these prescriptions are unused and in fact may be diverted, intentionally or not.[16] In one analysis of prescription patterns following sinonasal surgery, excess opioids were prescribed 85% of the time; for example, 25.3 tablets were prescribed per each postoperative patient, with a mean value of just 11.8 tablets reportedly being used.[17] Another study looking at opioid utilization following endoscopic sinus surgery also noted that most of the patients prescribed an opioid filled their prescriptions but did not use any opioids postoperatively for pain control.[18]

Perioperative analgesia following facial plastic surgery represents a primarily outpatient undertaking but with several unique considerations. Important differentiating factors include the type of surgery performed and the patient population being managed. There are different strategies and expectations based on whether a patient has undergone a cosmetic, elective procedure versus a reconstructive operation. Hence, setting realistic expectations particularly for aesthetic surgeries will play a significant role in patient satisfaction and the perception of success following a surgery. There may be a real and significant difference in how the elderly man who underwent a reconstruction of a branched-chain amino acid defect perceives their pain and satisfaction as compared with a younger woman undergoing a cosmetic rhinoplasty. Furthermore, psychiatric comorbidities may be far more prevalent in patients undergoing aesthetic procedures, and this can affect how pain is perceived. Considerations unique to pain perception and facial plastic procedures are further detailed in *Acute Pain Management following Facial Plastic Surgery.*

Special Populations

Several noteworthy populations should be considered in the context of providing high-quality evidence-based analgesia. Appropriately optimizing the chronic pain patient has been discussed earlier and also has its own dedicated Natasa Grancaric and colleagues' article, "Postoperative Analgesia in the Chronic Pain Patient," in this issue. Furthermore, although geriatric otolaryngology has been traditionally overlooked,[19,20] there are a whole host of considerations that can affect medication prescription in these patients. Older patients are undergoing surgery, including elective otolaryngologic procedures, in greater numbers than ever before.[21,22] Hence, close monitoring and judicious use of opioid alternatives in this patient population has never been more important, as narcotics have a high propensity to interact with other medications, and this population is characterized by polypharmacy.[23,24] Furthermore, unrecognized interactions with anesthetic agents and the greater potential for derangements of metabolism should prompt caution and really make one give second thought to using opioids in the elderly population until there is greater availability of dedicated high-quality studies exploring this topic.

Children also present a unique challenge, as they may not be able to appropriately communicate their pain in all situations. There are some evidence-based guidelines with regard to the use of nonsteroidal antiinflammatory drugs (NSAIDs), with controversy surrounding whether the use of these agents harbors an increased risk of potentially catastrophic postoperative bleeding. In addition, there is certainly evidence demonstrating the efficacy of narcotics in children, and as many of these opioids

are liquid rather than pills they are not necessarily thought of as substances used for misuse and diversion. Nonetheless, there are many surgeons who do not feel comfortable with prescribing narcotics to children, particularly younger ones or those with OSA, and evidence-based recommendations looking at alternatives exist. One analysis of 91 children younger than 10 years demonstrated combination ibuprofen/acetaminophen to provide effective posttonsillectomy analgesia; these patients did better and had fewer concerns compared with a posttonsillectomy morphine group, in which patients experienced a greater number of oxygen desaturation events.[25] Nonetheless, there is not a generalized consensus in the pediatric population, and evidence-based practices are further addressed in the Anthony M. Sheyn and colleagues' article, "Perioperative Analgesia in Pediatric Patients Undergoing Otolaryngologic Surgery," in this issue.

Opioid-Prescribing Education Among Otolaryngologists

Knowledge concerning the opioid "epidemic" is historically novel, as mass marketing of opioids and treatment of pain as a "fifth vital sign" did not show up until the turn of the century. Nonetheless, there have been paradigm shifts in resident education during this time period, including increased pressures regarding requirements that need to be learned in an increasingly limited amount of time. With no requirement for OPE, competing pressures and ignorance of evidence-based alternatives have contributed to the societal problems noted earlier. In one survey of 110 responding surgery program directors, only 22.0% of programs required OPE,[4] and most of these experiences are simply composed of 1 hour of OPE. These considerations, taken in conjunction with a lack of training covering nonopioid adjuncts and alternatives and poor knowledge of dealing with postoperative analgesia in the patient with chronic pain, harken back to the importance of appropriate preoperative optimization. Without specialty-specific educational resources such as those offered in this issue, this lack of familiarity promotes the situation for opioid misprescription, facilitating the opioid epidemic that our society has experienced. The authors hope that the foundational principles provided in the present issue are used to deal with doing their part to address the opioid epidemic.

Controlled Substance Agreements and Other Best Opioid Prescribing Practices

Controlled substance agreements (CSAs) are used for patients who are on chronic opioids and represent a nonlegally binding agreement the provider enters with the patient. These documents set expectations as to the universal precautions prescribing providers should practice. Standard practices include checking prescription monitoring programs and using toxicology screens. Although these are used frequently in nonsurgical settings such as primary care practices and pain medicine clinics, CSAs have invaluable features and can be helpful among patients experiencing chronic pain following surgery. The logistics of implementing CSAs are further discussed in *Controlled Substance Agreements*.

Pain Psychology

A basic understanding of pain psychology is important for providing context into patients with chronic pain or those who require dedicated attention. Surgeons in general have very little exposure to pain psychology despite being the practitioners who are most heavily exposed to pain prescribing practices in an acute setting. This section discusses the role of psychology and nonpharmacologic therapeutics in managing pain, including cognitive behavior therapies and pain-coping strategies. These outcomes can be affected by moods, behaviors, comorbidities, and extent of chronic

pain. The surgeon should be familiar with pain psychology in order to recognize when a patient would benefit from referral to a pain psychologist.

Sinus Headache

Sinus headache represents a unique consideration in this issue, in that the definition is not even widely agreed on. Patel and colleagues[26] explored sinus headache in a systematic review of the literature, focusing on standardizing results and definitions. Notably, in the setting of a comprehensive neurologic and ENT evaluation, most of the adults with sinus headaches are ultimately diagnosed with migraines and ideally treated with migraine therapy. Similar findings are noted on focusing on studies involving children and adolescents.[27] This section better organizes the considerations and controversies characterizing "sinus headache" and provides a practical approach for addressing symptomatic complaints.

Quality Improvement

Evolving pain paradigms represent a ripe target for quality improvement via the use of evidence-based practices. Over the past decade, there has been increasing recognition of the importance of quality improvement (QI) in medicine as a strategy for decreasing deleterious outcomes. QI differs from traditional human participant research in that its purpose is to assess an internal system, evaluate an established set of standards, and as a benefit, provide knowledge to directly benefit the process, program, or system. The objective of any QI project is to improve a process and/or system and then ultimately see whether that process can be transferred to another system with comparable standards and results. Several examples of QI in otolaryngology have been applied in recent years. For instance, Du and colleagues[28] implemented a multimodal analgesic protocol for all admitted head and neck patients and used these data to calculate average pain scores and opioid use, comparing results from before after protocol implementation. Implementation of their multimodal analgesia plan reduced opioid use immediately after surgery, demonstrating that such a plan is feasible (although opioid use was not reduced during the entire hospitalization course). Franz and colleagues[29] developed an opioid-sparing protocol following pediatric adenotonsillectomy at the University of Washington, identifying a feasible intraoperative anesthesia protocol that used dexmedetomidine and ketorolac and provided effective analgesia without lengthening recovery or increasing the need for reoperation. Although these studies represent an excellent approach toward tackling problems in an evidence-based manner, otolaryngology remains behind many other surgical disciplines when it comes to a discussion of pursuing QI practices, and further knowledge as to how to improve these trends is mandatory for our specialty to progress.

Introduction to Opioids

Opioids are potent analgesics that continue to be indicated for acute postoperative pain management as part of a multimodal analgesia strategy for surgeries with expected moderate and severe postoperative pain not controlled by other modalities. In addition, opioids are commonly used for cancer-related pain not controlled by other modalities, as well as in the palliative care setting. Nonetheless, opioids have the potential to cause serious adverse events. The otolaryngologist must be well versed in safe opioid prescribing in order to provide safe analgesia to the patient while minimizing side effects.

Opioids work by coupling to G proteins to cause membrane hyperpolarization. They act on the mu, kappa, delta, and sigma receptors.[30] The gold standard of comparing

opioids is in the form of oral morphine milligram equivalents (MME). The potency of commonly used opioids are listed in **Table 3**.[30] Opioid conversion is more of an art than a science, and there are interindividual variabilities. Hydrocodone (commonly combined with acetaminophen and branded as Norco and Vicodin) has the same potency as oral morphine. Oxycodone (commonly combined with acetaminophen and branded as Percocet) is approximately 1.5 times more potent than oral morphine. Oral hydromorphone (brand name Dilaudid) is approximately 4 times more potent than oral morphine. Codeine is an inactive prodrug that must be metabolized to morphine by enzyme Cytochrome P460 2D6 (CYP2D6) to produce analgesic effect. Common genetic variability in CYP2D6 may lead to lack of metabolism and no analgesic effect, or more dangerously, ultrarapid metabolism will lead to high morphine levels and potentially lethal overdose.[31] Because of similar concerns with tramadol, the Food and Drug Administration recommends *against* codeine or tramadol use in children younger than 12 years, recommends *against* codeine or tramadol use for posttonsillectomy and adenoidectomy pain, and recommends *against* codeine or tramadol use in children aged 12 to 18 years who are obese, have obstructive sleep apnea, or a weakened respiratory system. Tramadol is approximately 10 times weaker than oral morphine but also has serotonin reuptake inhibitor properties and so has the potential to cause serotonin syndrome when combined with other serotonergic agents.[30,32,33] Transdermal fentanyl may be delivered via fentanyl patch and acts as a long-acting analgesic. Fentanyl patch is administered as mcg/h and is exchanged every 72 hours. Conversion factor for mcg/h to MME over 24 hours range from 2 to 2.4.[30] Thus, a fentanyl patch at 25 mcg/h would be equianalgesic to 50 to 60 mg of oral morphine administered over the span of 24 hours. Analgesic onset time may take 12 hours, longer for maximum concentration, and offset after patch removal is also delayed. As a long-acting opioid, fentanyl patches are contraindicated in opioid naïve patients and contraindicated to treat mild, acute, intermittent, or postoperative pain. Methadone and buprenorphine are long-acting opioids that may be used to treat pain but also may be used to treat opioid use disorder.

To understand a patient's preoperative opioid use or to track the trend in the patient's postoperative opioid consumption, one calculates the patient's MME over 24 hours. This is helpful in several ways. If a patient is on chronic opioids preoperatively, the patient should generally be prescribed at least their preoperative MME in

Table 3
Opioid equianalgesic table

	IV (mg)	PO (mg)
Morphine	10	30
Hydromorphone	1.5	7.5
Oxycodone[a]	-	20
Hydrocodone[b]	-	30
Tramadol	-	300
Codeine	-	4.5[c]

Individual variation and variation in literature exist for opioid equianalgesic conversions.
Abbreviations: IV, intravenous; PO, oral.
[a] Brand name Percocet consists of oxycodone plus acetaminophen.
[b] Brand names Norco and Vicodin consist of hydrocodone plus acetaminophen.
[c] Abnormal metabolism of codeine can result in lower analgesic effects or higher analgesic effects leading to overdose. If converting from one opioid to another, account for incomplete cross-tolerance.

the postoperative period. For surgeries resulting in little to no pain, the patient's preoperative opioid regimen may provide adequate analgesia when combined with postoperative multimodal analgesia. For surgeries resulting in moderate to severe postoperative pain, it is likely that the patient will need their baseline MME plus supplemental opioid in the acute postoperative period. It is therefore important to know the patient's baseline opioid requirement. Postoperatively, a patient's opioid requirement may be tracked as MME to trend whether the patient's opioid requirements are overall decreasing as would be expected as the patient's pain improves while recovering from surgery.

MME is a useful way of thinking and comparing opioid doses. If converting the patient from one opioid to another, "incomplete cross-tolerance" must be taken into account if the patient has been on an opioid long enough to become tolerant to it. Incomplete cross-tolerance is a concept that notes if a patient is on one specific opioid (eg, hydrocodone) or the patient is more tolerant to hydrocodone than other opioids, so a dose reduction of 20% to 50% should be performed to account for the patient's relatively smaller tolerance to the new opioid (eg, oxycodone).[34] From a mathematical standpoint, the equianalgesic dose of hydrocodone, 30 mg, would be oxycodone, 20 mg. Because of incomplete cross-tolerance, prescribing oxycodone, 10 to 15 mg, would be more appropriate and would provide the same analgesia.

Table 4
Opioid side effects

CNS	Sedation Opioid-induced hyperalgesia Tolerance Assuming $Paco_2$ is maintained stable through artificial ventilation decreases cerebral blood flow, intracranial pressure, cerebral oxygen consumption Seizures (tramadol, meperidine)
Cardiovascular	Remifentanil (commonly used in TIVA) may cause bradycardia Morphine, hydromorphone, and meperidine cause histamine release
Respiratory	Respiratory depression $Paco_2$ increases Apneic threshold increases Hypoxic ventilatory drive decreases Large doses (fentanyl, sufentanil, remifentanil) may cause chest wall rigidity Blunt bronchoconstrictive response to airway stimulation Histamine release (see cardiovascular) may cause bronchoconstriction
Gastrointestinal	Stimulation of medullary chemoreceptor trigger zone → nausea/vomiting Delay gastric emptying time Constipation[a]
Genitourinary	Urinary retention
Endocrine	Attenuate stress response to surgery Decrease in testosterone, estrogen, cortisol, LH, GnRH

Abbreviations: GI, gastrointestinal; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; $Paco_2$, partial pressure of arterial carbon dioxide; TIVA, total intravenous anesthesia.

[a] Tolerance does not develop to constipation.

Opioids have potential to cause numerous adverse effects (Tables 4 and 5).[30,33,35] Cerebral effects include sedation. Opioid-induced hyperalgesia describes a state where patients become more sensitive to painful stimuli. Respiratory depression may occur, and there is higher risk for respiratory depression when opioids are combined with other sedating agents, such as benzodiazepines. Reversal agents, such as intranasal naloxone and subcutaneous naloxone, as well as intravenous naloxone are available. For *chronic* pain, the CDC recommends practitioners consider prescribing

Table 5
Special considerations for opioids

Medication	Consideration
Morphine	Avoid in patients with significant renal dysfunction. Metabolites morphine-3-glucuronide and morphine-6-glucuronide excreted renally can accumulate in renal dysfunction and lead to overdose
Meperidine	Avoid in patients with significant renal dysfunction due to accumulation of metabolites. Patients with renal dysfunction more prone to toxicity, including seizures. Avoid in patients taking MAOIs due to risk of hemodynamic instability, hyperpyrexia, coma, respiratory arrest, and death.
Tramadol	Has serotonin and norepinephrine reuptake inhibition properties. Caution with other serotonergic agents and MAOIs. Toxicity includes seizures Dose adjustment with renal dysfunction Contraindicated in patients younger than 12 years, patients younger than 18 years following tonsillectomy and/or adenoidectomy, and patients aged 12–18 years who have risk factors that may increase sensitivity to respiratory depression
Codeine	Codeine is a prodrug that must be metabolized by CYP2D6 to morphine for analgesia. Contraindicated in patients younger than 12 years, patients younger than 18 years following tonsillectomy and/or adenoidectomy, and patients aged 12–18 years who have risk factors that may increase sensitivity to respiratory depression
Methadone	Has NMDA antagonism properties Causes QTc prolongation on ECG, exercise caution with QTc prolonging medications Safe in renal dysfunction Long-acting Conversion factor varies based on dose, should only be prescribed by well-versed practioners
Fentanyl	Available in transdermal formulation (fentanyl patch) Transdermal formulation may take 12+ h for analgesic onset, longer for maximum analgesia Safe in renal dysfunction For opioid tolerant patients only Contraindicated for acute postoperative pain, intermittent pain, mild pain
Remifentanil	Intravenous opioid with fast onset and fast offset Commonly used as part of TIVA May cause bradycardia

Abbreviations: CYP2D6, cytochrome p450 2D6; ECG, electrocardiogram; MAOI, monoamine oxidase inhibitor; NMDA, N-methyl-D-aspartate; TIVA, total intravenous anesthesia.

home naloxone to patients at increased risk of overdose, including patients with history of overdose, patients with history of substance use disorder, patients concurrently taking benzodiazepines, and patients taking 50 MME daily or higher.[36] Gastrointestinal effects include nausea, vomiting, and delayed gastric emptying time. Patients do not develop tolerance to the constipating effects of opioids, and so patients should be placed on a bowel regimen. Peripheral opioid antagonists, such as methylnaltrexone, promote gastrointestinal motility by blocking peripheral opioid receptors without crossing the blood brain barrier and without reducing effectiveness of opioid analgesia.[35] Opioids may lead to urinary retention. Patients prescribed opioids should be educated regarding potential side effects.

SUMMARY

There has been increasing awareness of the role perioperative prescribing patterns have played in the increase of the opioid epidemic. The rising recognition of the impact that misuse and diversion of opioid prescriptions have played has facilitated a body of literature examining evidence-based alternatives and adjuncts to narcotic prescription in appropriate situations. Opioids are effective for breakthrough pain, but the decision to prescribe them should not be undertaken lightly, as there is myriad evidence supporting efficacious alternatives with regard to patients undergoing otolaryngologic procedures, including acetaminophen, NSAIDs, local anesthetics, and gabapentinoids. Further considerations should be given in order to enhance preoperative optimization regimens in unique populations, including patients with preexisting chronic pain issues, pediatric patients, and the elderly.

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