



Perioperative Considerations for the Patient with Opioid Use Disorder on Buprenorphine, Methadone, or Naltrexone Maintenance Therapy

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KEYWORDS

- Buprenorphine • Methadone • Naltrexone • Perioperative
- Multi modal pain management • Opioid use disorder • Addiction • Relapse

KEY POINTS

- Buprenorphine and methadone for the treatment of opioid use disorder (opioid addiction) should be continued in the perioperative period for most patients.
- Oral naltrexone should be discontinued 2 days before surgery and resumed once additional opioids are no longer needed.
- Extended-release injectable naltrexone is active for 28 days with peak at 7 days.
- Multimodal pain management is critical for patients on chronic opioid therapy. Regional anesthesia, ketamine, nonsteroidal anti-inflammatory drugs, acetaminophen, dexamethasone, lidocaine, magnesium, gabapentinoids, dexmedetomidine, esmolol, and mindfulness relaxation training have all been shown to reduce opioid use and decrease postoperative pain.

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INTRODUCTION

The United States is facing the worst drug crisis in US history, with more than 63,600 drug overdose deaths in 2016, almost double the deaths caused by traffic accidents or gun violence.¹ Two-thirds of drug overdose deaths are opioid related. Furthermore, overdose death is only 1 metric by which to measure the impact of the epidemic. By conservative estimates, 2.5 million people in this country are addicted to opioids (prescription and illicit), and more than 11 million people in the United States are misusing prescription opioids obtained directly or indirectly from a doctor's prescription (according to the 2016 National Survey on Drug Use and Health).² Prescription opioid misuse, addiction, and overdose cost the US more than \$78 billion annually.

MEDICATION-ASSISTED TREATMENT OF OPIOID USE DISORDER

The Food and Drug Administration (FDA) has approved 3 medications to target opioid use disorder/addiction:

1. Methadone (generic oral and injectable forms, Dolophine, or Methadose)
2. Buprenorphine alone (generic sublingual tablets or Probuphine intradermal implant) or combined with naloxone (Suboxone, Zubsolv, Bunavail, or generic sublingual tablets)
3. Naltrexone (generic tablets, ReVia, or Vivitrol long-acting injectable form)

The first 2 fall into a category called opioid agonist treatment, because they are both long-acting opioids that are believed to decrease the physiologic cravings that drive drug-seeking behavior. The third, naltrexone, acts as a deterrent by blocking the opioid receptor, preventing other opioids from binding. It may also reset the reward pathway through an opponent process mechanism.

All 3 of these medications, methadone maintenance, buprenorphine products, and naltrexone (oral or injectable), comprise in part what is called medication-assisted treatment of opioid use disorder. Medication-assisted treatment is defined by the Substance Abuse and Mental Health Services Administration as the use of medications in combination with counseling and behavioral therapies for the treatment of substance use disorders.

Multiple placebo-controlled trials across continents and decades demonstrate the effectiveness of opioid agonist treatment (methadone and buprenorphine) in opioid use disorder.³⁻⁵ Both methadone and buprenorphine result in significant reductions in overdose death, illicit drug use, criminal activity, and HIV and hepatitis C incidence. These treatments are also associated with improved health status and overall improved quality of life. By contrast, short-term use of opioid agonist therapy as part of a "detoxification protocol" is rarely effective.^{6,7} Patients randomized to placebo withdrawal, compared with methadone or buprenorphine maintenance treatment, are 2 times to 4 times more likely to be dead at a year.^{3,8}

A Cochrane meta-analysis of oral naltrexone showed no difference compared with placebo when comparing retention in treatment, use of illicit opioids, or side effects, a year after initiating treatment.⁹ However, 2 recently published studies comparing injectable extended-release naltrexone (XR-NXT) to buprenorphine-naloxone found comparable rates of retention and abstinence from heroin and other illicit drugs at 12 weeks¹⁰ and 24 weeks,¹¹ respectively. The latter study¹¹ showed that initiating patients onto injectable naltrexone was more difficult than on buprenorphine, which may have significant real-world implications, despite comparable efficacy in this study.

BUPRENORPHINE

Pharmacology

Several decades after the development of methadone, buprenorphine—a synthetic analog of the opium poppy constituent thebaine—was discovered and introduced into clinical practice in Europe in 1978 for acute and chronic pain.¹² In the United States, the FDA approved buprenorphine for (1) acute pain in 1981 as a parenteral injection; (2) opiate use disorder in 2002, as a sublingual tablet; and (3) chronic pain in 2010, as a transdermal patch. Buprenorphine is available in many different formulations, including parenteral, sublingual tablet, sublingual film, transdermal patch, mucoadhesive film, and implant.¹³ In 2017, several FDA advisory committees voted to recommend approval of an additional dose form, once-monthly and once-weekly injections of a depot form of buprenorphine for the treatment of opioid use disorder.

Although prescribing buprenorphine for addiction requires special registration (Drug Enforcement Agency Prescriber identification number X), any physician with a Drug Enforcement Agency license can prescribe it for pain. Buprenorphine retains abuse liability and thus is a Schedule III controlled drug. The range of buprenorphine doses is more than 2 orders of magnitude, with the lowest dose of the mucoadhesive form (Belbuca) at 0.075 mg (75 µg) and the highest dose of the sublingual film (Suboxone) at 12 mg (12,000 µg). This reflects the potency of low-dose forms of buprenorphine for pain, particularly in patients who are not opioid dependent, compared with the higher doses used for patients with opioid use disorder. The high-dose forms of buprenorphine are available as a monoprodut containing only buprenorphine but also in a form combined with naloxone in a 4:1 ratio. The addition of naloxone helps prevent misuse because it induces withdrawal symptoms when injected intravenously (IV).

Buprenorphine is unique in that it acts as both an agonist and antagonist at different opioid receptors. Buprenorphine has a high binding affinity at the mu receptor but only partially activates it compared with other opioids. Despite partial activation, buprenorphine still provides analgesia but has a ceiling effect on respiratory depression, conferring significantly less risk of respiratory compromise and overdose compared with opioids, such as morphine and fentanyl.¹⁴ Unique to buprenorphine is its antagonism of the kappa opioid receptor, which, along with its agonist action at the nociceptin opioid receptor (ORL-1), may confer several advantages over other opioids. These advantages include improved respiratory safety and attenuated euphoria and may contribute to its role in managing neuropathic pain, opioid-induced hyperalgesia, and psychiatric syndromes.¹⁵

As a result of its extensive first-pass metabolism, oral bioavailability is poor and buprenorphine is often given via the sublingual (or transmucosal) routes. Due to its lipophilic nature and potency, buprenorphine is remarkably well suited to transdermal delivery.

Respiratory depression can occur when buprenorphine is used along with central nervous system sedating agents, including alcohol, sedative-hypnotics, and neuroleptic drugs, or in fragile, young, or elderly populations. Reversal requires greater than the usual dose of naloxone: a 2-mg bolus is usually recommended in adults followed by 4-mg per hour infusion under close observation.¹⁶

Buprenorphine is primarily metabolized in the liver by phase I reactions (*N*-dealkylation) through the cytochrome P450 Cyp 3A4 enzyme to norbuprenorphine. Both buprenorphine and norbuprenorphine are conjugated by uridine 5' diphosphoglucuronosyltransferase (UGT), in phase II reactions to their glucuronide forms. Buprenorphine and norbuprenorphine are primarily eliminated through bile and feces. Only a small amount of the glucuronide metabolites are excreted in the kidney. These

pharmacokinetics confer relative safety compared with other opioids, when buprenorphine is used in patients with moderate to severe hepatic failure or in renal insufficiency. Due to little influence of buprenorphine on the activity of the cytochrome p450 Cyp 3A4 enzyme, drug-drug interactions are usually not a significant concern.¹⁷

Due to its tight binding and attenuated intrinsic activity at the mu receptor, parenteral or sublingual (but not transdermal) buprenorphine can precipitate withdrawal symptoms in patients who are dependent on other opioids. Therefore, an induction process involving early opioid withdrawal before introduction of sublingual buprenorphine is required.

Perioperative Use

Buprenorphine's ability to tightly bind to the mu receptor and potentially block additional opioids from binding has created a concern that additional opioids are less effective in the presence of buprenorphine, thus reducing the analgesic efficacy. Clinical research conducted early in the history of buprenorphine development¹⁸ and multiple investigations and clinical practice in more recent years,^{19,20} however, provide strong reassurance that standard opioids given to buprenorphine maintained patients are effective and additive to the baseline analgesia associated with the buprenorphine.

Clinical guidelines issued in 2004 by the Center for Substance Abuse Treatment,²¹ despite acknowledging lack of evidence, set into motion a misconception in the United States, widely quoted, that perioperative analgesia is difficult to achieve with standard opioids in buprenorphine-maintained patients and that buprenorphine in most cases should be stopped and converted to methadone preoperatively. This misunderstanding may stem from addiction research, which did not assess analgesia but rather demonstrated that buprenorphine in higher doses blocked the euphoric and reinforcing effects of subsequently administered heroin.²²

Case studies have been published describing difficult to control pain in postoperative buprenorphine-maintained patients.^{23,24} Other cases, however, have been published describing adequate management, particularly when combined with multimodal analgesia.^{22,25}

Extenuating circumstances, including intraoperative nerve injury, nonoptimal dosing of buprenorphine, and failure to use multimodal analgesia in a timely way characterize the published cases reporting difficult postoperative analgesia.²² Furthermore, difficult postoperative analgesia is a common occurrence in patients who are preoperatively dependent on opioids of any type.

The experience in Australia established opioids were effective in hospitalized and postsurgical patients maintained on buprenorphine.^{26,27} This was confirmed by US obstetricians, who did discontinue buprenorphine in pregnant patients for either vaginal deliveries or planned caesarean sections and reported adequate pain control.²⁸⁻³⁰

Stopping buprenorphine in stabilized opioid use disorder and/or chronic pain patients confers medical risk, discomfort, and logistical burden on patients, their prescribing clinicians, and the health system. A significant opioid debt will exist that will need to be filled with another opioid, risking over-dosing or under-dosing, and reinduction can be clinically and symptomatically problematic in the immediate postoperative period and can also prolong hospital stays.

Optimal use of buprenorphine in the perioperative setting has not been established. Whether to continue a patient's current dose or wean the dose down but not off to provide more mu receptor availability has not been studied. Nonetheless, receptor binding studies using radiolabeled carfentanil and PET scans to identify available mu receptors in buprenorphine-treated heroin-addicted persons confirm a

dose-response curve of reduced but conserved receptors available for additional analgesia, even at high sublingual doses of buprenorphine.³¹ Which opioid to use for additional analgesia has not been studied, but using opioids that have higher mu receptor affinity, such as sufentanil, fentanyl, or hydromorphone, should be considered. Increasing the buprenorphine as the primary opioid analgesic has also been advocated by some investigators as well as dividing the daily dose into 3-times-daily dosing because a daily dose may not provide adequate analgesia throughout the entire 24-hour period.^{32,33} Finally, patients who have stopped buprenorphine postoperatively and are still taking additional opioids potentially could be restarted on buprenorphine by using a daily microdose escalation known as the Bernese method without precipitating withdrawal. Once a sufficient dose of buprenorphine is reached, patients can discontinue their additional postoperative opioids.³⁴

METHADONE

Pharmacology

Methadone is a full mu opioid receptor agonist. It is a racemic mixture with the R enantiomer responsible for the opioid effect and the R and S enantiomers having *N*-methyl-D-aspartate receptor (NMDA) antagonist activity. Oral administration has a moderate bioavailability approximately of 70% to 80% and is 90% bound to plasma proteins. Peak plasma levels are reached within 2 hours to 4 hours. Methadone undergoes a biphasic pattern of elimination— α -elimination (8–12 hours) and β -elimination (30–60 hours). The α -elimination is associated with analgesia and the β -elimination with withdrawal suppression. Methadone is metabolized in the liver and eliminated through renal and fecal routes. Hepatic metabolism is through the cytochrome P450 system, and coadministered medications that induce or inhibit the cytochrome P450 system can dramatically alter the metabolism, resulting in lower or higher systemic levels for the same dose of methadone. Methadone binds approximately 30% of the mu receptors allowing for additional activity from both endogenous and exogenous mu opioid agonists.^{35,36}

Sedation, respiratory depression, and death can occur with increasing doses of methadone. The toxic dose can be difficult to predict secondary to long half-life, changes in metabolism, and variable tolerance profile at higher doses. Methadone can also increase the QT interval and has been associated with sudden cardiac death. Prolongation of the QT to greater than 500 milliseconds is associated with arrhythmias, including torsades de pointes.³⁷

Perioperative Use

Patients should take their usual dose of methadone on the day of surgery. Patients are opioid tolerant; thus, additional opioids likely are needed. Patients should be continued on their home maintenance dose throughout the perioperative period. Because the α -elimination (8 hours) is associated with the analgesic component of methadone, dosing a patient's daily dose in 3 divided doses might improve pain control.³⁸ It is important to confirm a patient's home dose with the methadone prescriber. If there is concern about what the actual dose is, the methadone can be administered in divided doses throughout the day, monitoring for sedation and respiratory depression. Patients unable to take their oral dose should be given IV methadone. The IV dose should be reduced by one-half to two-thirds and be given in divided dose every 6 hours to 8 hours. Oral to IV conversion can be difficult, especially at higher doses, so consulting with a pharmacist or the methadone prescriber may be warranted. Up-titration of methadone in the perioperative period is not advised secondary to

the long half-life. If any up-titration occurs, it should be in consultation with a patient's methadone prescriber or expert on the use of methadone. If a patient's methadone dose has been interrupted for more than 5 days, restarting should be in consultation with a provider who is experienced in methadone maintenance induction.³⁹ Documenting the contact number of the methadone prescriber is important so appropriate follow-up at discharge can be arranged.

NALTREXONE

Pharmacology

Naltrexone is a semisynthetic opioid antagonist derived from oxymorphone via substitution of the *N*-methyl group with methylcyclopropyl group. It is a competitive antagonist at mu opioid receptors and partial agonist at kappa receptors and has minimal activity at delta receptors.⁴⁰ In oral formulation, it has rapid absorption, with peak concentration at 1 hour, undergoing first-pass hepatic metabolism.⁴¹ After continuous administration for 7 days, the half-life is approximately 10 hours with renal excretion.⁴² XR-NXT, a biodegradable microsphere matrix embedded with naltrexone, was introduced in 2010 as a 380-mg gluteal intramuscular injection to yield opioid antagonism for 28 days.⁴² Pharmacokinetically, XR-NXT peaks at 7 days and avoids first-pass hepatic metabolism.⁴³ Opioid antagonist effects of XR-NXT decrease over the course of a month. Although currently there are no published data determining exactly when opioid antagonism can be overcome, case reports suggest it can be achieved during the fourth week postinjection.⁴⁴

Perioperative Use

With a 10-hour half-life, oral naltrexone should be discontinued approximately 2–3 days before surgery in close coordination with the patient and prescribing physician, accounting for 5 half-lives. For XR-NXT, there is less guidance; however, a balanced risk-benefit decision of need for surgery and ability to use opioid-sparing techniques, including regional and neuraxial anesthetics, needs to be considered. Successful pain management has been reported starting in the fourth week of treatment, with complete lack of analgesia to opioids in the first 2 weeks of treatment.^{43,44} Close monitoring may be required, however, if patients receive opioids postoperatively because variable responses have been observed, including both attenuation and enhancement; in some animal studies, levels 6 times to 20 times typical doses of opioids have been needed to achieve analgesia.^{45–47} Restarting naltrexone requires patients to be free of opioids to avoid acute withdrawal. FDA-approved prescribing information advises patients to be abstinent from opioids for 7 days to 10 days prior to induction.⁴⁸

MULTIMODAL PAIN MANAGEMENT

Multimodal pain management is important to improve efficacy and minimize side effects. Multimodal therapies are even more important for the opioid use disorder patient because these patients are opioid tolerant but often pain intolerant ([Table 1](#)).

Opioids	Acetaminophen	Gabapentinoids
Regional anesthesia	Dexamethasone (>0.1 mg/kg)	Dexmedetomidine
Ketamine	Lidocaine infusion	Esmolol
NSAIDs	Magnesium infusion	Mindfulness relaxation

Opioids

Opioids are still an important component of multimodal pain management; however, doses need to be increased in opioid-tolerant patients. The degree of tolerance can be difficult to predict and patients are still at risk for respiratory depression from increasing doses of opioids. Continuing the preoperative dose of opioids is important to prevent withdrawal. Early withdrawal is subjective and often results in increased pain, but as it progresses physical signs of withdrawal become evident (sweating, gastrointestinal upset, tremor, restlessness, anxiety, yawning, gooseflesh, and runny nose/tearing). As with all patients receiving perioperative opioids, careful monitoring for sedation and respiratory depression is critical.^{49,50}

Regional Anesthesia

Regional anesthesia is vital to anesthetic management of opioid-tolerant patients. Neuraxial anesthesia or use of peripheral nerve blocks reduces both pain and opioid requirements and improves patient satisfaction.^{51–53} Single-injection spinal with opioid (morphine or hydromorphone) with or without local anesthetic has been associated with lower pain and decreased systemic opioid requirements.⁵⁴ Thoracic epidural anesthesia is associated with decreased pain and reduced opioid requirements.⁵⁵ Transversus abdominis plane blocks provide superior pain control and lower opioid requirements for abdominal surgery compared with opioids alone.^{56–58} Continuous peripheral nerve blockade is associated with improved pain control, lower opioid requirements, and greater patient satisfaction compared with single injection.⁵⁹

Ketamine

Ketamine is an IV anesthetic and NMDA receptor antagonist. It has been shown to improve postoperative pain control as well as decrease opioid consumption in both opioid-naïve and opioid-tolerant patients. Several different dosing protocols have been studied but low-dose ketamine (0–1 mg/kg bolus and infusion of <1.2 mg/kg/h) is safe and effective at reducing both opioid consumption and time to first opioid request.^{60,61} Ketamine administered at 0.5 mg/kg IV at induction and at an infusion of 10 µg/kg/min until skin closure decreased both reported pain scores as well as morphine consumption in opioid-tolerant patients at 48 hours and at 6 weeks.⁶² One case report suggests potential for ketamine misuse and addiction when initiated as an analgesic alternative in a patient with opioid use disorder on buprenorphine.⁶³

Lidocaine

Perioperative use of lidocaine has been shown to reduce pain scores and opioid use in the immediate postoperative period up to 24 hours. The analgesic effects were most apparent after laparoscopic and open abdominal surgery. It has also been shown to reduce ileus, postoperative nausea and vomiting, and hospital length of stay. Common dosing for perioperative lidocaine infusion is 1.5 mg/kg/h to 3 mg/kg/h after a bolus of 0 mg/kg IV to 1.5 mg/kg IV. It can be run in the immediate postoperative period usually at a lower dose. There are no data for use greater than 24 hours. Lidocaine has a narrow therapeutic index, with therapeutic levels occurring at 2.5 µg/mL to 3.5 µg/mL but with central nervous system toxicity occurring at 5 µg/kg and cardiovascular toxicity at 10 µg/mL. Lidocaine toxicity should be treated 20% lipid emulsion and supportive care.^{64–67}

Magnesium

Magnesium is an often overlooked adjunct in acute pain management. A meta-analysis of 1200 patients showed IV magnesium reduced both early and late pain at rest and late pain with movement. Magnesium has also been shown to have a large effect on reducing perioperative opioid use. The usual dose range is 30-mg/kg to 50-mg/kg bolus followed by a 10-mg/kg infusion intraoperatively. Several studies continued the infusion for 24 hours to 48 hours at a reduced rate. Continuing the infusion may provide additional benefit compared with intraoperative use only.⁶⁸ Magnesium may also help prevent opioid-induced hyperalgesia.⁶⁹

Acetaminophen

Acetaminophen can be administered orally, rectally, or IV. The exact mechanism of action is unknown but it is believed to inhibit cyclooxygenase (COX) enzyme in the central nervous system.⁷⁰ A meta-analysis showed that 36% of patients receiving IV acetaminophen experienced at least a 50% reduction in pain and used 26% less opioids in the first 4 hours postoperatively.⁷¹ Oral and IV administration seem to have similar efficacy.⁷² Combining acetaminophen with nonsteroidal anti-inflammatory drugs (NSAIDs) confers additional analgesic efficacy over either drug alone.⁷³

Gabapentinoids

Gabapentinoids (gabapentin and pregabalin) are a class of drug that bind to the $\alpha 2\delta$ subunit of the voltage-dependent calcium channel, thus inhibiting the opening of the calcium channel and reducing release of excitatory neurotransmitters. Gabapentin and pregabalin have been shown to reduce postoperative pain and reduce opioid consumption; however, they have been associated with an increase in sedation and dizziness.^{74,75} When gabapentin was added to a methadone⁷⁶ or buprenorphine-assisted detoxification program, it reduced withdrawal symptoms.⁷⁷

Nonsteroidal Anti-inflammatory Drugs

Nonselective NSAIDs (eg, ibuprofen, naproxen, and ketorolac) inhibit both the COX-1 and COX-2 isoforms whereas celecoxib is selective for the COX-2 isoform. COX inhibitors decrease conversion of arachidonic acid to prostaglandins and thromboxane, thus reducing pain and inflammation. NSAIDs have been shown to reduce pain and decrease opioid use postoperatively. Caution should be used in patients with cardiovascular disease, renal insufficiency, and gastrointestinal bleeding. The risk is increased with long term use however the risk of brief postoperative use is unclear.^{70,78–81}

Steroids

Dexamethasone is a corticosteroid that has been shown to reduce pain and opioid use. A meta-analysis of 2500 patients showed that intermediate dose of dexamethasone (0.11–0.2 mg/kg) had opioid-sparing effects as well as reduced early and late pain at rest and movement. Low dose (less than 0.1 mg/kg) was not effective. Dexamethasone is more efficacious if it is administered preoperatively. Rapid administration of a small volume of dexamethasone can cause perineal pain. This risk can be reduced by giving the dose over 10 minutes and in a larger volume (50 mL). Wound infections or delayed wound healing did not seem associated with the intermediate dose. The risk-benefit analysis of perioperative blood glucose control versus pain control should be considered. The effects on blood glucose were not addressed in the meta-analysis.⁸²

Dexmedetomidine

Dexmedetomidine is an α_2 -adrenergic receptor agonist, which has sedative, anxiolytic, sympatholytic, and analgesic properties. When used intraoperatively, it can reduce the need for opioids and decreases pain intensity. The degree of opioid sparing is stronger than acetaminophen but weaker than ketamine or NSAIDs. Dexmedetomidine can cause hypotension and bradycardia.^{83–85}

Esmolol

Esmolol is an ultra–short-acting β_1 -receptor antagonist. It has been shown to decrease intraoperative and postoperative opioid consumption when used intraoperatively.⁸⁶

Drug	Preoperative	Day of Surgery	Postoperative
Buprenorphine	Continue daily dose. Document buprenorphine provider's contact information for postoperative follow-up.	Patient should receive usual daily dose. Plan for multimodal pain management.	Continue daily dose but consider switching to TID dosing. Consider increasing buprenorphine to target pain. Continue multimodal pain management. Arrange for follow-up with buprenorphine provider early in the postoperative period. Discharge with the lowest dose and shortest duration of additional opioids as possible.
Methadone	Continue daily dose. Document methadone dose and methadone provider's contact information for postoperative follow-up.	Patient should receive usual daily dose. If unable to take PO, give IV (reduce dose by 1/2 to 2/3 and split into TID dosing). Plan for multimodal pain management.	Continue daily dose but consider switching to TID dosing. Continue multimodal pain management. Arrange for follow-up with methadone provider early in the postoperative period. If daily dosing patient may need to go to methadone clinic postoperatively. Discharge with the lowest dose and shortest duration of additional opioids as possible.
Naltrexone	Oral—discontinue >48 h preoperatively. XR-NXT—discontinue 30 d preoperatively.	Confirm last dose >48 h for oral and >30 d for implanted XR-NXT. Plan for multimodal pain management.	Continue multimodal pain management. Patient may be more sensitive to opioids. Resume after patient has been off opioids for 7 d.

Psychological

Psychological factors affecting pain include general anxiety, depression, posttraumatic stress disorder, pain-related anxiety, and pain catastrophizing.⁸⁷ A single scripted 15-minute session of mindfulness training or hypnotic suggestion delivered in a hospital setting has been shown to reduce pain intensity by up to 30% in one-third of patients who were reporting severe pain. Preoperatively addressing a patient's risk of pain catastrophizing can also help decrease postoperative pain.⁸⁸

SUMMARY

The appropriate use of buprenorphine, methadone, and naltrexone in the perioperative period, for patients with opioid use disorder on maintenance therapy, is an increasingly important part of modern medical treatment (**Table 2**). Buprenorphine and methadone should be continued in the perioperative period for most patients. Oral naltrexone should be discontinued 2 days before surgery and resumed once additional opioids are no longer needed. Multimodal pain management is critical for patients on chronic opioid therapy. Regional anesthesia, ketamine, NSAIDs, acetaminophen, dexamethasone, lidocaine, magnesium, gabapentinoids, dexmedetomidine, esmolol, and mindfulness relaxation training have all been shown to reduce opioid use and decrease postoperative pain.

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