According to the Centers for Disease Control and Prevention, 47,600 accidental deaths related to opioid use occurred in 2017, representing a 12.0% increase from 2016.\(^1\) For the first time, the National Safety Council\(^2\) adjusted the lifetime odds of an American dying due to an opioid overdose to a 1 in 96 chance, surpassing the risk of dying in a motor vehicle crash. Despite these jarring statistics, preliminary data from 2018 suggest a slight decrease in drug-related deaths, although it is unknown if the decline is attributable to waning opioid consumption, greater availability of rescue medication (eg, naloxone), or a change in nonopioid substance use such as methamphetamines or cocaine.\(^3\) A concerted effort from government agencies, healthcare organizations, and clinicians to curb the opioid epidemic is under way, including the implementation of medication-assisted treatment (MAT), public health campaigns, and legislative and organizational policy. Certified Registered Nurse Anesthetists (CRNAs) have an essential role in controlling the opioid epidemic and must remain informed on opioid use disorder (OUD) diagnosis, treatment, and perioperative management, especially adapting the anesthetic plan for a patient who is prescribed MAT. Equally important, CRNAs should understand emerging trends and healthcare policy as they relate to the epidemic.

**Medication-Assisted Treatment and Anesthetic Care**

Medication-assisted treatment in the OUD population aims to prevent relapse and to increase the probability of successful recovery by preventing withdrawal symptoms and decreasing the euphoria associated with illicit opioid use. As one of the only safe and effective means of treating patients with OUD, MAT represents a unique set of psychosocial and pharmacologic considerations in anesthetic patient care. More than 400,000 Americans are in opioid treatment programs and nonopioid treatment programs nationwide, so it is not surprising that the CRNA will encounter this patient population during routine and emergent anesthesia.\(^4\)

Comprehensive understanding of the medications used in MAT as well as the implications for the anesthetic management of this population are paramount for the safe intraoperative care of these patients and for the prevention of preoperative and postoperative relapse.

Currently, the mainstay medications used in MAT treatment are methadone and buprenorphine, both of which have been shown to reduce opioid-associated mortality in the OUD population.\(^5\) Naltrexone, although used less often, will also be discussed. Regardless of the drug used in MAT, a consistent recommendation throughout the literature
champions multimodal analgesia for acute surgical pain treatment and collaborative, multidisciplinary care teams for relapse prevention. Multimodal nonopioid agents (acetaminophen, celecoxib, pregabalin, and gabapentin) for preemptive analgesia are advocated unless contraindicated. If opioids can be spared, patients receiving MAT should receive regional or local anesthesia with catheters placed for postoperative pain control when possible. Ketamine, dexmedetomidine, and lidocaine infusions are mentioned for intraoperative management of the MAT recipient. Postoperatively, if opioids are prescribed, MAT recipients should be dispensed a limited number of pills (according to the agreed-on plan between the patient and caregivers). There should be a return plan in place for any unused medication and a plan for transitioning to nonopioid analgesics when possible. Follow-up with addiction specialists should be encouraged, and support from family and/or the recovery community should be instituted as part of a comprehensive, multidisciplinary surgical plan.

Methadone

Methadone is a long-acting opioid agonist and N-methyl-D-aspartate (NMDA) receptor antagonist with a half-life of 1 day. Methadone is usually taken orally in doses of 40 to 60 mg/d, which should be continued through the perioperative course. The anesthetist should be aware that methadone in MAT does not function as an analgesic for the treatment of pain and should expect patients receiving methadone to exhibit opioid-induced hyperalgesia (increased sensitivity to pain) perioperatively. Methadone also causes QT interval prolongation on the electrocardiogram, so care should be taken when administering other drugs that have the same untoward effect. Patients receiving methadone may exhibit cross-tolerance to opioids, so they may require higher doses of opioids if used intraoperatively and postoperatively. Predictably, the literature advocates using nonopioid approaches for surgical analgesia and management, but if opioids are necessary for pain control, doses should be titrated as necessary to treat pain effectively because untreated pain is a predictor of relapse. Postoperatively, if an escalation of methadone is required for pain relief, the literature specifies that this is done concurrently with a plan to deescalate the methadone later with the assistance of additional pain management and substance use disorder specialists.

Buprenorphine

Buprenorphine is a semisynthetic mixed partial μ agonist/k antagonist that is available as buprenorphine only (Subutex) or in combination with naloxone (Suboxone). Buprenorphine is taken sublingually in 2-mg or 8-mg doses and is dosed less frequently than methadone. It exhibits less respiratory depression than methadone because of a ceiling effect that occurs at around 32 mg/d (thus less overdose potential), and its effects last 24 to 72 hours. When caring for the patient with OUD who is receiving buprenorphine for MAT, two management approaches can be taken: (1) buprenorphine can be discontinued preoperatively, or (2) it can be continued through the perioperative experience. If the patient and care team involved with the surgical experience collaboratively decide that the patient is a candidate for preoperative discontinuation of buprenorphine, it can be tapered off rapidly over 72 hours, or it can be discontinued gradually over several weeks (usually decreasing the dose 2 to 3 mg/d every 2 or 3 days). Keep in mind that rapidly tapering off the buprenorphine dosage has been associated with higher relapse rates. Regardless of how fast it is tapered in a cessation regimen, all buprenorphine should be discontinued 72 hours before surgery. If a patient is unable to discontinue buprenorphine therapy preoperatively, he or she can be converted to a methadone or opioid regimen. Postoperatively if a patient requires opioids or methadone, a buprenorphine reinstatement protocol can be initiated on an outpatient or inpatient basis. Anesthesia providers managing this patient population should be aware that before restarting any buprenorphine therapy postoperatively, acute surgical pain should be well controlled or dissipated, and the patient must be in mild opioid withdrawal. Buprenorphine displaces other opioid agonists from opioid receptors but as a partial agonist does not completely activate the opioid receptor. When given to a patient receiving opioid therapy, buprenorphine leads to acute withdrawal.

If buprenorphine cannot be discontinued preoperatively, or the care team collaboratively decides that continuation of buprenorphine treatment perioperatively is the best course for the patient, the anesthetist must know that higher doses of opioids will be needed to treat pain effectively. The literature advocates using opioids with higher μ receptor affinities (eg, fentanyl, morphine, and hydromorphone). Opioids such as codeine and hydrocodone should be avoided because of their lower affinity for μ-opioid receptors. If buprenorphine is continued during the perioperative surgical experience, it is recommended that the doses be divided into 6- to 8-hour increments to maximize the analgesic properties of the drug. If severe postoperative pain is anticipated, the literature suggests that it may be better to taper off buprenorphine therapy preoperatively and supplement with patient-controlled analgesia, regional anesthesia, and multimodal analgesia techniques in addition to opioids. If high doses of opioids are required for acute surgi-
Naltrexone

Naltrexone is a competitive μ-opioid receptor antagonist that renders opioid analgesia ineffective. Once metabolized, the anesthetist should be aware that it increases sensitivity to opioid side effects. It is available as a daily oral preparation or a monthly injection (Vivitrol). Patients receiving injectable naltrexone should schedule elective surgeries no sooner than 30 days after the last injection, and patients receiving oral naltrexone should be counseled not to take once-daily doses the morning of surgery. The key for successful and safe anesthesia in this population is judicious use of opioids. Some evidence shows that patients receiving naltrexone may exhibit upregulation of opioid receptors, resulting in an exaggerated response to opioid analgesia; the anesthetist should be exceedingly cautious of opioid dosing and should titrate opioids carefully. It is recommended that any outpatient oral opioid is reduced or restricted in favor of nonopioid analgesics (as soon as possible). During the perioperative period, patients are at increased risk of relapse, and the decision to delay naltrexone redosing until after surgery should be made with the consultation of the patient and addiction specialists.

Healthcare Policy Related to Medication-Assisted Treatment

The history of the opioid epidemic has been previously described in detail elsewhere but essentially is the complex interaction of limited research, misguided public campaigns, and a rapacious pharmaceutical industry. The opioid epidemic has had considerable societal effects, including an unprecedented drug-related death toll, $78.5 billion annual economic burden, and a transformed suburban demographic.

The Diagnostic and Statistical Manual of Mental Disorders Fifth Edition defines OUD as a problematic pattern of opioid usage that results in substantial impairment or distress. Data from the 2017 National Survey on Drug Use and Health show that approximately 2.1 million people aged 12 years and older met the diagnostic criteria for OUD. Equally concerning, the same national survey estimated that more than 10.5 million people aged 12 and older misused prescription pain relievers annually, which represents 92.8% of all opioid misuse. Data suggest that additional efforts should be explored to reduce opioid consumption and more effectively treat addicted individuals.

Although MAT is effective, numerous barriers prevent broader adoption. Some challenges include diagnosis-related stigmas, treatment misunderstandings, and access to practitioners who are qualified to prescribe MAT. Historically, MAT has been underutilized, with one study finding that less than half of private-sector OUD treatment programs offered a medication option and only one-third of eligible patients received medication.

The federal government has responded to the epidemic with policies aimed at increasing access to MAT care, educating at-risk populations, and supporting new research into pain management. While US Health and Human Services Secretary, Thomas Price detailed a 5-point strategy to control the opioid epidemic: 1. Improve access to treatment and recovery services. 2. Encourage the broader use of rescue medication (eg, opioid antagonists). 3. Increase data through expanded public health surveillance.

4. Expand on the research for pain and addiction health. 5. Promote best practices in pain management.

Although federal guidance is valuable, controlling the opioid epidemic requires a more comprehensive approach and robust collaboration between states, local communities, healthcare organizations, and clinicians.

In October 2018, the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act was signed into law. While broad in scope, the SUPPORT Act has many Medicaid-related provisions to help states provide better coverage and to improve services to the OUD-affected individual. Section 3201 identifies CRNAs explicitly in states with prescriptive authority as being qualified to prescribe MAT, an acknowledgment of the CRNA’s clinical expertise in pain management. The time-limited legislative changes are important to states, Medicaid participants, and healthcare providers because Medicaid covers 4 in 10 nonelderly adults with OUD.

In addition, the federal government is embracing systematic approaches previously used in other public health epidemics (eg, AIDS). The Cascade of Care for OUD is an integrated public health framework that follows a progressive, 4-stage process. As described by Williams and colleagues, the model begins with patient engagement either through an initial OUD diagnosis or a recent opioid-related overdose. The second stage involves prescribing appropriate MAT (eg, buprenorphine), and the remaining 2 stages focus on retaining the patient in treatment and undertaking efforts to induce lifelong remission. Additionally, the comprehensive framework addresses many system-level practice issues while simultaneously delivering care
continuity and sustainable patient outcomes.

Community health centers (CHCs), which are primarily located in medically underserved rural and urban areas and receive funding through Medicaid, have been instrumental in addressing the opioid epidemic. In a recent survey, CHCs reported a 70% increase in patients with a diagnosis of OUD seeking a prescription for MAT as compared to the previous year.24 The same survey also found that 48% of all CHCs responded to the epidemic by expanding care to include medication as part of their OUD services. Predictably, the authors reported that CHCs in Medicaid expansion states were significantly more likely to offer comprehensive MAT services compared with centers in nonexpansion states (54% vs 38%).24 Despite CHCs having an essential role in the opioid crisis, several challenges threaten their continued role, including reaching maximum service capacity, potential eligibility changes to the Medicaid system (eg, work requirements, Section 1115 demonstration waivers), and ongoing financial challenges. Nonetheless, CHCs continue to offer access to MAT, and CRNAs should be familiar with their role as a primary treatment source for patients with OUD.22

Role of the Nurse Anesthetist

As prescribed medication increasingly becomes first-line therapy for OUD, CRNAs must be prepared to deliver anesthesia care to patients receiving MAT. Patients who are participating in MAT require individual perioperative planning. All CRNAs must be familiar with their organization’s policy and available resources, as well as the state of the science, epidemiology, and fundamental health policy related to OUD and MAT. Moreover, the CRNA should regard the care of this patient population as an opportunity to champion a clinical pathway or other change initiatives. As part of an interdisciplinary team, CRNAs should collaborate with other specialty professionals to establish institutional policy and evidence-based protocols. As the opioid epidemic expands, CRNAs will continue to have a sizable role in delivering care to patients with an OUD and must be proactively creating solutions.

REFERENCES

8. Myers J, Compton P. Addressing the potential for perioperative relapse in those recovering from opioid use disorder.
19. Price TE. Secretary Price announces HHS

30. Price TE. Secretary Price announces HHS


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