



# Perioperative Approach to Patients With Opioid Abuse and Tolerance

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Substance abuse in the United States is increasing. Most of the rise in illicit drug use has been attributed to marijuana, with the use of heroin remaining relatively stable over the past 10 years. Yet although heroin use has plateaued, overall use of opioid analgesics has increased dramatically.<sup>1</sup> Sales of prescription opioids quadrupled between 1999 and 2010.<sup>2</sup>

Enough of these substances were prescribed in 2011 to medicate every American adult with a standard dose of 5 mg of hydrocodone every 4 hours for a month. In 2010 alone, 12 million Americans reported nonmedical use of prescription pain killers in the past year.<sup>2</sup> As the use and abuse of opioids increases, the likelihood of an anesthesiologist encountering these patients during clinical practice also will increase.

The anesthetic and analgesic implications of increased opioid use are 2-fold. First, as both illegal and prescription use of opioids increases, anesthesiologists will encounter more patients exhibiting opioid tolerance. Second, as abusers of opioids seek treatment for their addiction, the numbers of patients receiving long-term opioid therapy for their addiction also will increase. Long-term medical therapy for opioid dependence introduces several issues in the management of patients that clinicians must consider when forming an anesthetic and analgesic plan.

All anesthetic and analgesic plans can be divided into preoperative considerations, intraoperative management, and postoperative recovery and analgesia. For patients with known or suspected opioid abuse, this strategy is no different. Optimal patient care always begins in the preoperative period with the patient assessment. Obtaining information about patient drug use and potential ongoing treatment is critical in constructing an appropriate plan. If the patient's history with opioids is limited or unknown to the anesthesia care team, patient care and satisfaction are likely to be compromised. Understanding and performing appropriate screening and assessment is paramount in these cases.

### Patient Evaluation

Screening and assessment of opioid use can be broken down into 2 main categories: subjective and objective data. Subjective data are gathered by the practitioner at time of interview, either in preadmission

testing or in the preoperative holding area. Objective data largely are related to urinalysis and blood testing.

The interviewing clinician will benefit from realizing that many patients with a history of abuse of or dependence on prescription opioids—including oxycodone, hydrocodone, fentanyl, and other drugs—will be evasive about that history or will attempt to minimize their use of these drugs. A helpful strategy when collecting the patient history is to focus on specific questions while preserving a nonjudgmental environment. For example, “What is the most you have ever used in a day,” can provide more useful information than simply asking about average daily use.

Whenever possible, the interviewer should determine the time of the last dose of opioids and, if applicable, who is prescribing these medications. To help with this difficult task, several drug screening questionnaires have been developed. Some of these validated screening tests can involve many questions, which may be impractical for daily use by anesthesiologists, who must make efficient use of their limited time. However, 2 such questionnaires are short enough to be practical for everyday use by anesthesiologists.

### CAGE-AID

The CAGE-AID (Adapted to Include Drugs) is a modification of the common 4-question tool used to detect potential alcohol abuse (Table 1).<sup>3</sup> A second, and perhaps easier, validated screening test is the single question: “How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?”<sup>4</sup> Regardless of which strategy anesthesiologists use in their own practice, most patients are unlikely to volunteer this important information without direct questioning.

Drug screening, specifically urine drug screening (UDS), is an important tool in obtaining objective information about a patient’s use of opioids. However, these tests have several important limitations (Table 2).<sup>5</sup> Immunoassay screening, which is the most common UDS, can detect the presence of specific opioids and their metabolites but frequently returns false-positive results and typically findings must be confirmed by gas

chromatography-mass spectroscopy—a time-consuming process. Also, a UDS, and even serum testing, have difficulty detecting fentanyl use. Finally, UDS cannot detect past abuse. Nevertheless, drug testing can provide useful objective information as long as clinicians are aware of these limitations.

### Long-Term Opioid Therapy

When collecting patient information in the preoperative period, the clinician likely will encounter patients who have been taking opioids chronically. These include the opioid agonists methadone and buprenorphine-naloxone (Suboxone, Reckitt Benckiser), as well as the opioid antagonist naltrexone (Vivitrol, Alkermes). Having at least a working knowledge of these medications is helpful in understanding their anesthetic and analgesic implications.

#### METHADONE

Methadone is by far the most commonly used long-term opioid treatment and has been widely available since the 1960s. Methadone is a long-acting opioid agonist with some activity as an *N*-methyl-*D*-aspartate antagonist. The major function of methadone is to suppress withdrawal symptoms, which in most patients can be achieved with as little as 30 to 40 mg per day. It is only available in outpatient treatment programs and is dispensed on a daily basis.

If a patient reports having received methadone, clinicians should verify the dose by contacting the methadone clinic by telephone. The verified dose then can be administered. Administering methadone without the supervision of a methadone clinic is illegal. For that matter, treating opioid withdrawal with opioids is against guidelines from the Drug Enforcement Administration. The administration of opioids, including methadone, by an anesthesiologist or other clinician is reserved exclusively for treating pain and must be thoroughly documented in patients’ medical records.

#### BUPRENORPHINE

Unlike methadone, buprenorphine is a partial opioid agonist. Buprenorphine relieves drug cravings without producing the “high” and dangerous side effects of other opioids. Suboxone is a combination of buprenorphine and naloxone that received FDA approval in 2002.<sup>6</sup> If Suboxone is injected intravenously, the naloxone component will precipitate withdrawal symptoms. Its increased therapeutic window and deterrence of IV use allow Suboxone to be prescribed by certified physicians outside the context of a specialized treatment clinic and without the need for daily supervision. Given its relative ease of use for those seeking treatment, prescription use of this medication has been increasing steadily in recent years.

Although opioid agonists, whether full or partial, are the most commonly used treatment modality by far, some opioid-dependent patients opt for therapy with an opioid antagonist. Historically, the main treatment was naltrexone, similar to naloxone. As a once-daily treatment, poor patient compliance limited the effectiveness of this

**Table 1. The CAGE-AID Questionnaire**

Have you ever felt that you ought to Cut down on your drinking or drug use?

Have people Annoyed you by criticizing your drinking or drug use?

Have you ever felt bad or Guilty about your drinking or drug use?

Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover (Eye opener)?

Brown RL, Rounds LA. Conjoint screening questionnaires for alcohol and other drug abuse: criterion validity in a primary care practice. *Wis Med J.* 1995;94(3):135-140. Adapted from reference 3.

agent. However, Vivitrol, an extended-release form of naltrexone, has gained acceptance as treatment for patients with dependence on alcohol, opioids, or both. Given as a monthly injection, this medication has clear advantages over once-daily dosing in terms of patient compliance.

### Intraoperative Management

With appropriate data collection and assessment in the preoperative period, intraoperative management of patients with opioid dependence or abuse relies heavily on 3 areas: managing intoxication, preventing or treating withdrawal, and achieving effective analgesia. Although many patients will not present for elective surgery when they are acutely intoxicated, urgent or emergent situations involving these patients often occur. In these incidents, monitoring respiratory rate and oxygen saturation is critical. Antagonist therapy should be reserved for patients with potentially life-threatening respiratory depression, as precipitating withdrawal in such a patient may make both anesthetic and analgesic management more difficult.

Although patients not receiving established agonist therapy, like methadone, cannot be given opioids to treat withdrawal symptoms directly, they can be managed in other ways. First, patients on long-standing prescription opioids can be directed to take these medications as they normally would on the morning of surgery. Second, patients at risk for or entering withdrawal can have their symptoms managed. Clonidine commonly is used to treat symptoms of opioid withdrawal and can be given at a starting dose of 0.1 mg twice daily. Other medications, such as loperamide, also can be administered to target specific withdrawal symptoms.

Analgesia strategies for patients with significant histories of opioid use should focus less on opioids as a foundational, single-agent therapy and more on opioid-sparing or multimodal techniques with nonopioid agents such as IV acetaminophen (Ofirmev, Cadence Pharmaceuticals) or liposomal bupivacaine (Exparel, Pacira Pharmaceuticals). Many of these agents can be initiated in the preoperative or intraoperative phases and continued into the postoperative period. Nonopioid analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs, regional anesthesia when possible,  $\alpha_2$  agonists, and ketamine can have profound analgesic effects, particularly when used in combination.

Pregabalin (Lyrica, Pfizer) and gabapentin also can be useful for managing neuropathic pain, which often is poorly controlled by opioids in general. An emphasis on multimodal analgesia is paramount in these patients and should be continued through surgery and into the postoperative period.

Goals for the postoperative period can be divided into 2 main categories: comfort and safety. Patient comfort consists of providing adequate analgesia and continued prevention or management of opioid withdrawal. Patient safety is equally important, as this population typically manifests significant opioid tolerance. Patients with opioid tolerance generally will require at least 2 to 3 times

**Table 2. Potential Limitations Of Urine Drug Screening for Opioids**

Standard UDS and tests used for pain management differ greatly in complexity
Standard UDS frequently reported only as positive for opiates
Oxycodone, oxymorphone, methadone, and buprenorphine often must be checked specifically
Fentanyl: cannot be detected in-office

UDS, urine drug screening

more opioids than an opioid-naïve patient. Yet despite their analgesic tolerance, they appear to be at risk for respiratory side effects.

During the postoperative period, clinicians must continue to manage both a patient's potential withdrawal symptoms and his or her analgesic needs. For opioid-dependent patients, these 2 aspects often intersect. Opioid withdrawal, either real or potential, can complicate pain assessments; patients may overreport pain to obtain increased opioid dosages.

Reassuring patients that their withdrawal symptoms will be managed, either with their current opioid agonist or by easing of their symptoms, is a good first step. Even patients on high doses of opioids in the postoperative period may suffer intermittent withdrawal symptoms given the waxing and waning effects of short-acting opioids. If appropriate, combining a long-acting opioid analgesic with shorter-acting agents, such as hydromorphone by patient-controlled analgesia during periods of breakthrough pain may help to alleviate patients' withdrawal fear or symptoms. However, this strategy can be used only when treating pain and not for the management of withdrawal symptoms, which are not life-threatening.

In addition to managing a patient with opioid tolerance, patients on some type of long-standing opioid medical therapy require modifications to the analgesic plan. For those receiving methadone maintenance, management is relatively straightforward. After verifying the dose with a methadone clinic, the drug can be continued during the postoperative period. The dose can be divided into a 3-times-daily regimen to take advantage of methadone's analgesic properties, which are much shorter than its withdrawal-preventing effects.

Management can be significantly more complicated for patients receiving buprenorphine-naloxone therapy. As a partial  $\mu$ -opioid agonist, buprenorphine has what is known as a ceiling effect. Similar to full agonists, morphine, or methadone, initially increasing buprenorphine dosage will heighten both its analgesic properties and its unwanted side effects. Unlike full agonists, as the dose of buprenorphine increases, the effects will plateau, at which point further doses have no effect<sup>7</sup>—widening the drug's therapeutic window by broadening its safe dosing range. Coupled with its long half-life, these attributes help

to make buprenorphine both relatively safe and effective in managing long-term opioid dependence.<sup>8</sup>

In the context of managing acute pain, however, buprenorphine is more difficult.

The drug has a high affinity for  $\mu$  receptors, about 1,000 times higher than that of morphine.<sup>9</sup> With its long half-life and high receptor affinity, buprenorphine will persist on the receptor even when more potent, short-acting opioids are introduced in an attempt to provide analgesia. And because buprenorphine is only a partial agonist, effective analgesia will be difficult to provide.

Given this profile, 4 recommendations for acute pain generally exist when dealing with buprenorphine.<sup>10</sup> First, maintenance therapy can be continued and short-acting opioids can be titrated to effect.<sup>11</sup> One must recognize that with buprenorphine present on the receptor sites, the patient likely will require higher than usual doses of a short-acting opioid to achieve an expected effect.

A second option is to divide buprenorphine into 3-times-daily dosing to take advantage of its inherent analgesic properties in much the same way as methadone.<sup>12</sup> This strategy may be helpful if the surgery or procedure is not likely to be particularly invasive or painful.

A third option is to discontinue buprenorphine therapy and treat the patient with full opioid analgesics, while being mindful of potential withdrawal.<sup>11</sup> A caveat here is for the clinician to realize that buprenorphine can continue to be present on the receptor up to 5 days after the last dose.

Finally, a fourth option with buprenorphine is to convert to methadone at 30 to 40 mg per day. This total daily dose is usually sufficient to prevent withdrawal symptoms.<sup>13</sup> However, because methadone cannot be prescribed for withdrawal outside a methadone clinic, this strategy requires the standard 3-times-daily dosing of methadone, and its primary purpose would need to be documented as treating pain, not managing withdrawal.

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