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Managing Pain in the Setting of Opioid Use Disorder

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ABSTRACT

Specific Clinical Issue: Healthcare providers are challenged with managing pain and minimizing morbidity and mortality associated with opioid use disorder.
Major Practice Recommendations Based on Best Evidence: The purpose of this article is to guide acute and ambulatory care clinicians in managing pain in patients with opioid use disorder. Included in this article is a review of medications used for opioid use disorder, a discussion of the management of patients with active opioid use disorder and acute or chronic pain, and a discussion of the management of acute and chronic pain in people in recovery both on and off medications for opioid use disorder.

In the United States, clinicians are faced with the significant challenges of managing pain and minimizing the morbidity and mortality associated with opioid misuse and abuse. Increasing numbers of people have both pain and opioid use disorder (OUD), and clinicians must be cognizant of these comorbidities while providing care. For this review, PUBMED, CINAHL, PsycINFO, and MEDLINE were searched using the following search terms: opioid use disorder, substance use disorder, addiction, postoperative pain, chronic pain. Filters included English language, human, clinical trial, or review for the years 2014-2019. Evidence for treatment based on high-quality studies is limited. The purpose of this review is provide a guide for acute and ambulatory care clinicians as they manage pain in patients with comorbid OUD based on current evidence and expert opinion.

Overview

In 2017, the opioid epidemic in the United States was declared a national public health emergency (U.S. Department of Health and Human Services [USDHHS], 2017). Prescribed opioids have been cited as one of the reasons for the multifaceted healthcare crisis of opioid misuse and abuse. Since the Centers for Disease Control and Prevention (CDC) guidelines for prescribing opioids were published (Dowell, Haegerich, & Chou, 2016), many social factors have influenced opioid prescribing and care for people in pain. These social factors include media coverage, blame placed on healthcare providers and on pharmaceutical companies marketing to healthcare providers and the public, changes in regulatory laws by states, changes in protocol in organizations, and changes in availability of prescription opioids to treat pain. The interplay of the opioid crisis and chronic pain creates an extremely complex healthcare problem. Chronic pain is estimated to affect 20% (50 million) of the U.S. adult population (excluding those in the military, in prisons, or in long-term care facilities), and 19. 6 million (8%) U.S. adults have "high-impact" chronic pain that limits life or work activities (Dahlhamer et al., 2018). These two public health crises require full attention by all clinicians.

Prevalence of OUD

The prevalence of morbidity and mortality related to opioids has dramatically increased in the past two decades (CDC, 2018a). It is very difficult, however, to accurately estimate the prevalence of OUD in individuals prescribed opioids for chronic pain owing to differences in definitions and heterogeneity of studies (Cheatle, 2015). One meta-analysis reported a 4.7% incidence of iatrogenic opioid abuse from prescribed opioids (Higgins, Smith, & Matthews, 2018), and another systematic review reported a prevalence range

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of 0%-31% (Minozzi, Amato, & Davoli, 2013). Overall, the true prevalence is unknown but may be higher than previously believed.

Deaths from prescription opioids are decreasing, but opioid deaths from illicitly manufactured fentanyl and fentanyl analogs rose 122% in 2016 (CDC, 2018b; Dai, Abate, Smith, Kraner, & Mock, 2019; National Drug Early Warning System, 2015). The rise in opioid deaths from illicitly manufactured fentanyl and fentanyl analogs is alarming. In a study of 10 states participating in enhanced overdose surveillance, fentanyl was found in at least 50% of overdose deaths in 7 of the 10 states (O'Donnell, Halpin, Mattson, Goldberger, & Gladden, 2017). Individuals may unknowingly use illicitly manufactured fentanyl or its analogs when these substances are added to heroin or other drugs, putting people who are misusing at increased risk for overdose (Cicero, Ellis, & Kasper, 2017; National Drug Early Warning System, 2015).

State and federal policies have been created to reduce the prescription of opioids for chronic nonmalignant pain. High-dose opioid prescribing has decreased 41% since 2010 (Guy et al., 2017; Piper, Shah, Simoyan, McCall, & Nichols, 2018). However, in 2015, the amount of opioids prescribed (in milligram morphine equivalent per person) remained approximately three times higher than it was in 1999 (CDC, 2017).

Description of Opioid Use Disorder

The term "addiction" has been replaced by "substance use disorder" (SUD). If the SUD involves opioids, the term used is "opioid use disorder"; if the SUD involves alcohol, the term used is "alcohol use disorder" (American Psychiatric Association Diagnostic and statistical manual of mental disorders, 2013). The characterizing criteria for all types of SUDs defined by the *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition; Diagnostic and statistical manual of mental disorders, 2013) include hazardous use, impaired control, social impairment, and pharmacologic criteria related to the substance. As with many chronic illnesses, SUD is characterized by periods of remission and exacerbation. OUD has become more prevalent with the increase in opioid-related morbidity and mortality. In the United States in 2017, an estimated 2.1 million people age 12 or older had an OUD (Substance Abuse and Mental Health Services Administration [SAMHSA], 2018a). Criteria for OUD include the continued use of an opioid for longer than intended, strong desire to use, inability to control or discontinue use, excess time spent involved with its use, interference with obligations, use that could result in harm, need for increased doses when the opioid is not used for legitimate medical use, and use to prevent withdrawal (Box 1). The degree of OUD severity ranges from mild (2-3 of the criteria items) to moderate (4-5 items) and severe (6 or more items) (Diagnostic and statistical manual of mental disorders, 2013).

In 2017, 2.5 million individuals in the United States aged 12 or older received treatment for SUD, which is much less than the estimated 20.7 million individuals who actually needed treatment (SAMHSA, 2018a). In the same year, 382,867 individuals were receiving methadone, 112,223 were receiving buprenorphine, and 23,065 were receiving naltrexone (SAMHSA, 2018b). The number of people receiving buprenorphine is expected to increase owing to the passage in 2016 of the Comprehensive Addiction and Recovery Act, which improved access to medication treatment. Nurse practitioners and physician assistants within an office-based setting are now permitted to become certified and registered to prescribe buprenorphine for OUD (Library of Congress, 2016).

Assessment of Withdrawal and Suicide Risk

There is a need to better understand the pertinent care for patients with OUD. Early interventions for withdrawal symptoms and screening for risk for suicide can facilitate appropriate patient care and support. In this review, the phrase "medications for opioid use disorder" (MOUD) is used as the accepted term rather than "medication-assisted treatment" because MOUD is more consistent with other chronic diagnoses where medications are used long term (Dr. Geetha Subramaniam, deputy director, Center for Clinical Trials Network, National Institute on Drug Abuse, personal communication, March 22, 2019).

Box 1
Criteria for Opioid Use Disorder

Opioid Use Disorder

Problematic opioid use with related impairment or distress with at least two of the following symptoms occurring in a 12-month period

1. Taking opioids in larger amounts or longer than intended
2. Persistent desire or unsuccessful efforts to control or cut down opioid use
3. Great deal of time spent in obtaining or using opioids or recovering from their effects
4. Craving, desire, or urge to use opioids
5. Opioid use that impairs ability to fulfill obligations at home, work, or school
6. Continued opioid use despite recurrent social/interpersonal problems caused by opioids
7. Opioid use results in giving up important social, occupational, or recreational activities
8. Recurrent opioid use in physically hazardous situations
9. Continued opioid use despite physical or psychological problems caused by or exacerbated by use
10. Tolerance—markedly diminished effect from opioids or need for increased amounts to obtain effect (not applicable to those taking opioids under medical supervision)
11. Withdrawal syndrome or taking opioids to avoid withdrawal syndrome (not applicable to those taking opioids under medical supervision)

Severity:
Mild—2-3 symptoms
Moderate—4-5 symptoms
Severe—6 or more symptoms

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders* (5th ed., pp. 541-542). Arlington, VA: American Psychiatric Association.

Screening for Withdrawal

Screening for withdrawal symptoms from opioids is within the scope of practice for pain management nurses (American Nurses Association & American Society for Pain Management Nursing [ASPMN], 2017). In adults, opioid withdrawal may occur when there is physical dependence and opioids are abruptly stopped; it does not always indicate OUD. Symptoms of opioid withdrawal are gastrointestinal distress, lacrimation, diaphoresis, rhinorrhea, piloerection, and shivering. The patient may also experience tachycardia, hypertension, myalgias, and insomnia. Irritability, restlessness, yawning, and dilated pupils may be apparent. Opioid withdrawal symptoms may occur within 6-12 hours after cessation of opioid use, and the duration of withdrawal is dependent on the pharmacokinetics

of the opioid. For example, withdrawal from opioids with long half-life, such as methadone, may be prolonged (Drew & Marie, 2011). The Clinical Opiate Withdrawal Scale has been used to assess withdrawal upon initiation of MOUD such as buprenorphine (Wesson & Ling, 2003). This 11-item scale can be administrated by nurses and physicians to measure opioid withdrawal symptoms. The nurses' knowledge of withdrawal symptoms will allow for enhanced recognition of withdrawal, early intervention, and expedited care.

Screening for Suicide Risk

There is concern that some overdose deaths may be a result of suicide. In 2017, more than 70,237 people died from drug overdoses (21.7 per 100,000) in the United States, as compared to 16,849 deaths in 1999 (National Institute of Health, National Institute on Drug Abuse, 2019). Sixty-eight percent of these deaths were attributed to opioids, including prescription opioids (n = 17,029), heroin (n = 15,482), and illicitly manufactured fentanyl and fentanyl analogs (n = 28,400) (National Institute of Health, National Institute on Drug Abuse, 2019). Some of these deaths were thought to be attributed to suicide related to either transition to heroin or increased pain when opioids were tapered (Demidenko et al., 2017). Similarly, within the background of reduced opioid prescribing and inadequately managed pain, a study of veterans indicated there were higher rates of suicidal ideation and suicidal self-directed violence after discontinuation of long-term opioids (Demidenko et al., 2017; Levi-Minzi, Surratt, Kurtz, & Buttram, 2013).

Screening for suicide intent is being overlooked in patients with OUD. A study from the National Emergency Department Sample between 2006 and 2011 found that of more than 250,000 adult opiate overdoses, 54% were categorized as "unintentional," 26.5% were "intentional," and 20% were "undetermined" (Oquendo & Volkow, 2018). Identifying patients at risk for suicide involves a comprehensive suicide risk screening tool that is validated and easily accessed in the electronic medical record, if available. Nurses are well positioned to ensure access to naloxone and to initiate screening for suicide risk in any clinical setting. Examples of screening tools are the Columbia Suicide Severity Rating Scale (Posner, 2008) and the Suicide Assessment Five-Step Evaluation and Triage (SAMHSA, 2009). A call to the National Suicide Prevention Lifeline (1-800-273-TALK [8255]) will also help guide the patient. Once screening is complete, a safety or crisis plan needs to be created to reduce access to lethal means. To reduce suicide risk and the negative impact of opioids and OUD, immediate access to OUD treatment programs and safe transition to behavioral healthcare providers are necessary. This support includes opioid tapering and access to MOUD (SAMHSA, 2019).

Nursing Care for the Patient With OUD

Physical Assessment

After the review of systems, assessment of pain, and assessment of withdrawal and risk for suicide, a physical examination is performed. The physical examination is essential to ensure that potential comorbidities related to OUD are adequately treated. In the physical examination, the nurse can identify abnormalities that may be related to drug use, such as signs of infection secondary to use or organ dysfunction as a result of use. The nurse may also identify signs of neglect or trauma that may accompany drug use (see Table 1 for Physical Assessment: Key Considerations).

Psychological Screening

Nurses play a vital role in supporting the psychological needs of patients with OUD. These needs often go unrecognized, even in the midst of improvements in medical and nonpharmacological management. As with other chronic diseases, the impact of OUD on a patient's life is great and can change the way the patient views himself or herself and the way friends and family view the patient. The nurse can explore changes the patient with OUD is experiencing and how these changes have affected the patient's lifestyle, relationships, ability to work, and the meaning of his or her life. The ability of nurses to understand the feelings of patients with OUD can be instrumental in allowing patients to talk about the impact OUD has had on their lives. Using open-ended questions and active listening can facilitate this communication. As nurses, we can borrow strategies from other nursing disciplines such as palliative care, postcardiac care, care of patients with chronic respiratory disease, and care of people with other chronic diseases and apply techniques that are empathetic, accepting, and holistic (Lynes & Kelly, 2003).

Managing the Patient With Pain and OUD

The recommended treatment for OUD is a concurrent program of MOUD, cognitive behavioral support, and counseling (American Society of Addiction Medicine [ASAM], 2015; Oliver et al., 2012). Table 2 presents a summary of MOUD. Multimodal analgesia utilizing medications and regional analgesia techniques (when appropriate) should always be part of the pain management plan for all individuals (Harrison, Kornfeld, Aggarwal, & Lembke, 2018; Kumar, Kirksey, Duong, & Wu, 2017; Thomas, Boominathan, Goswami, Mukherjee, & Vadivelu, 2018) and is especially important for OUD patients for whom the risks of opioid use may outweigh the benefits. Nonpharmacological approaches can be used to help patients manage pain in the context of OUD. Since its inception, the ASPMN has endorsed nonpharmacological approaches to pain (ASPMN, 2019). Nonpharmacological treatments are further endorsed by the National Pain Strategy (2012); the Joint Commission, Division of Healthcare Improvement (2018); the Agency for Healthcare Research and Quality (Skelly et al., 2018); and the Academic Consortium for Integrative Medicine and Health (Tick et al., 2018). Examples of nonpharmacological approaches with reported efficacy include cognitive behavioral therapy (Barry et al., 2019); mindfulness meditation (Khusid & Vythilingam, 2016); mindfulness-oriented recovery enhancement, a multimodal intervention (Garland, 2014; Garland et al., 2014); ImPAT, a combination of cognitive behavioral therapy and acceptance-based treatment (Ilgen et al., 2016); and an online pain self-management program (Wilson et al., 2018). In addition to these exercises, multidisciplinary rehabilitation programs, acupuncture, and mind–body practices may provide benefit (Skelly et al., 2018). Nonpharmacological approaches can be identified by nurses partnering with patients and endorsed as part of the multimodal treatment for pain (Dowell et al., 2016; Wenzel, Schwenk, Baratta, & Viscusi, 2016), and they may enhance medication interventions (buprenorphine, methadone, naltrexone) for OUD for acute and chronic pain.

Buprenorphine

Buprenorphine is a semi-synthetic partial mu agonist that has high affinity binding to the mu opioid receptors with only partial activation of the receptor. Formulations are approved for both pain management and treatment for OUD (SAMHSA, 2016). Formulations approved for pain management include transdermal buprenorphine in doses of 5-20 mcg/hr applied every 7 days and buccal buprenorphine in doses ranging from an initial dose of 75 mcg once a day, up to 450 mcg every 12 hours (Rauck, Potts, Xiang, Tzanis, & Finn, 2016; Silverman, Raffa, Cataldo, Kwarcinski, & Ripa, 2017). Formulations approved for the treatment of OUD include (1) sublingual or buccal buprenorphine (2 mg or 8 mg), which is combined

Table 1
Physical Assessment: Key Considerations

Eyes	Examine Pupil Size to Determine Pinpoint Vs. Dilated; Inspect Sclerae for Signs of Jaundice to Identify Potential Liver Dysfunction
Nose	Inspect for excoriation, perforation of nasal septum, and epistaxis, which may be signs of insufflation injury.
Ears	Inspect for ruptured tympanic membrane and signs of infection, which may be secondary to neglect/violence/trauma.
Oropharynx	Inspect teeth for poor repair, gum disease, and abscess. Assess oropharynx for signs of infection.
Cardiopulmonary	Evaluate for murmurs, arrhythmias, and pulmonary abnormalities.
Abdomen	Evaluate for hepatomegaly and hernia.
Extremities	Examine for musculoskeletal abnormalities such as fracture and traumatic amputations indicating trauma. Evaluate for edema, potentially indicating renal dysfunction.
Skin	Examine for abscesses, rashes, cellulitis, thrombosed veins, scars, track marks from injection, and burns.

with naloxone to minimize risk with tampering or injection, and (2) sublingual buprenorphine mono-products (2 mg or 8 mg) for use in pregnancy, because effects of naloxone on the fetus have not been well studied (ASAM, 2015; SAMHSA, 2016). The maintenance dose of these products will range from 2 mg to 24 mg daily, but occasionally patients will be maintained on 32 mg daily. The doses approved by the U.S. Food and Drug Administration (FDA) for pain management are much lower than the doses utilized for OUD. Clinicians may utilize buprenorphine approved for OUD to also treat pain by splitting the doses into every 8- or 12-hour doses; however, guidance from an experienced healthcare provider is required because the literature shows heterogeneous studies using variable dosing and formulations (Aiyer, Gulati, Gungor, Bhatia, & Mehta, 2018). Another OUD formulation that is available is monthly injection of buprenorphine (100-300 mg; Sublocade) (FDA, 2017). In addition, for those who can be maintained on buprenorphine 8 mg daily, a 6-month implant of four rods, each containing 80 mg of buprenorphine, is available (FDA, 2016). The partial mu agonist effect decreases the risk of respiratory depression unless there is concomitant use of other central nervous system depressants (Kelty & Hulse, 2017; SAMHSA, 2016). Buprenorphine may be a safer option than methadone owing to its ceiling effect (Sordo et al., 2017), decreased risk of QTc prolongation, and fewer clinically significant drug interactions (McCance-Katz, Sullivan, & Nallani, 2010).

Initiating Buprenorphine

Physicians, nurse practitioners, and physician assistants who have completed education and obtained a special waiver for buprenorphine treatment may prescribe buprenorphine to individuals in an ambulatory care setting (Library of Congress, 2000, 2016). Individuals initiated on buprenorphine must be abstinent from opioids or experiencing moderate opioid withdrawal symptoms (usually 24-72 hours after last opioid dose). Buprenorphine may trigger withdrawal symptoms due to its partial mu agonist effect if started when the individual is not already in moderate withdrawal (ASAM, 2015). Opioid cravings should diminish once the individual is on a stable buprenorphine dose. Buprenorphine is usually self-administered daily, although some suggest that every other day dosing may be effective (ASAM, 2015).

Acute Pain and Buprenorphine

Buprenorphine has a high affinity for the mu opioid receptor and thus can block the effects of other mu opioids for 24-72 hours. This creates challenges within that timeframe when treating acute pain with pure mu agonist opioids, such as morphine sulfate

Table 2
Medications for Opioid Use Disorder

Medication	Action	Usual Doses	How Obtained	Comments
Methadone	Full mu opioid agonist—can reduce craving for 24 hours	60-120 mg orally once daily (may be higher or lower)	Administered through a federally licensed opioid treatment program Daily observed dosing May graduate to take-home doses	Provides analgesia for 3-12 hours. Many drug–drug interactions Can cause electrocardiogram QTc prolongation
Buprenorphine/ naloxone Buprenorphine (pregnancy) Buprenorphine implants Buprenorphine (Sublocade) injection	Partial mu agonist—occupies mu receptors, reduces craving	8-24 mg sublingual or buccal daily. 320-mg implant every 6 months (i.e., 4 rods, each containing 80 mg buprenorphine hydrochloride equivalent). 100-300 mg monthly of the Buprenorphine (Sublocade) injectable.	Prescribed by physicians, nurse practitioners, and physician assistants in ambulatory office setting who have additional training and Drug Enforcement Administration waiver (starts with "X")	May provide analgesia if given in split doses (every 8 or 12 hours) Less risk for respiratory depression (unless administered with central nervous system–depressing medications) Fewer drug–drug interactions than methadone Implants can be removed before 6 months
Naltrexone (oral)	Full mu receptor antagonist	50 mg orally daily Three times weekly, e.g., Monday 100 mg, Wednesday 100 mg, Friday 150 mg	May be prescribed by anyone licensed to prescribe medications	Also used for alcohol use disorder Will block the effects of opioids
Monthly injection (Vivitrol)		380-mg monthly intramuscular depot injection	Injection administered by any clinician who is prescriber	

QTc = corrected QT interval.
American Society of Addiction Medicine, 2015; Salsitz & Wiegand, 2016; Substance Abuse and Mental Health Services Administration, 2018c; U.S. Food & Drug Administration, 2016.

(Bryson, 2014; Jonan, Kaye, & Urman, 2018). There are multiple protocols to manage acute pain in individuals who are treated with buprenorphine for OUD, and consensus on best practice has not been established or studied. The use of options of continuing or discontinuing buprenorphine during the perioperative period varies throughout the country. The risks for relapse and the risks for uncontrolled pain need to be individually determined (Bryson, 2014; Jonan et al., 2018; Sun, Mao, & Anderson, 2018). Interdisciplinary teams must work collaboratively to ensure appropriate treatment of pain and management of OUD.

The decision to continue buprenorphine throughout the perioperative course is based on realization that the perioperative timeframe is one of high risk for relapse, increased anxiety, and postoperative pain. Two methods for continuing buprenorphine in the perioperative period are currently utilized. One method is to continue buprenorphine and use patient-controlled analgesia (PCA) and multimodal analgesic approaches. A second method is to continue buprenorphine in divided doses every 6-8 hours while using adjuncts such as acetaminophen, nonsteroidal anti-inflammatory drugs, and opioids as needed (Harrison et al., 2018; Jonan et al., 2018; Lembke, 2018; Sun et al., 2018; Ward, Quaye, & Wilens, 2018). This second approach is gaining acceptance and is being adopted more widely as clinicians become more experienced with the use of buprenorphine.

The decision to discontinue buprenorphine throughout the perioperative course may be a result of poor pain relief from mu agonists when buprenorphine is continued during the postoperative course. If it is determined that discontinuing buprenorphine is advisable, there are two methods for discontinuing buprenorphine. One method is to stop buprenorphine more than 5 days prior to surgery and begin short-acting opioids prior to surgery. If buprenorphine is stopped prior to surgery and the risk for relapse is high, the expected duration of discontinuation of MOUD should be individualized. Another method is to stop buprenorphine the day of surgery, give single-dose extended-release/long-acting opioids before surgery, and continue the opioids as baseline analgesia using intravenous (IV) PCA bolus doses only or immediate-release/short-acting opioids (Harrison et al., 2018; Jonan et al., 2018; Sun et al., 2018; Ward et al., 2018). If buprenorphine has been discontinued during the acute pain event, it should be restarted once opioids are not needed and preferably during the hospital stay (ASAM, 2015). Restarting buprenorphine will prevent the risk of relapse and resulting morbidity (Bryson, 2014). In the cases where pure mu opioids may be required past the hospitalization period, coordination with the clinician prescribing buprenorphine is essential (Anderson et al., 2017).

In the future, there will be outcomes research evaluating these approaches. From these studies, expert consensus statements will emerge (ASAM, 2015; Bryson, 2014; Sen et al., 2016).

Outpatient Chronic Pain and Buprenorphine

When a patient is on buprenorphine therapy for OUD and has chronic pain, the clinician managing the pain should collaborate with the clinician managing the OUD. The buprenorphine dose may need to be adjusted to address the chronic pain, but this should be done only by the clinician treating the OUD. Buprenorphine can be administered in divided daily doses (every 8-12 hours) to a maximum of 32 mg daily. Buprenorphine in the formulations listed earlier are for treatment of OUD and are not approved by the FDA for pain management. However, there is emerging evidence that OUD and pain may be successfully treated with buprenorphine (Eilender, Ketchen, Maremmani, Saenger, & Fareed, 2016; Streltzer, Davidson, & Goebert, 2015). Although clinicians may treat pain with these formulations approved for OUD, the buprenorphine is prescribed off-label for pain (Rosen, Guitierrez, Haller, & Potter, 2014). FDA dosing approved for pain (e.g., buprenorphine transdermal and buccal) may be effective for pain but cannot be used to treat OUD. If the patient has worsening pain secondary to an aggressive disease process and the increased buprenorphine is not effective for pain, it may be necessary to transition the individual to methadone and provide additional daily doses of an opioid to provide adequate pain control (ASAM, 2015). Addiction medicine and pain management specialists should be involved if available.

Methadone

Methadone is a long-acting biphasic synthetic mu opioid that was first used as an analgesic in 1947 and first used for treatment of OUD in 1965 (ASAM, 2015; Salsitz & Wiegand, 2016). Methadone administered for the treatment of OUD can be provided only through a federally licensed opioid treatment program. Because of its long-half life, methadone is administered once a day to reduce opioid craving and can prevent withdrawal for at least 24 hours. The initial dosing of no more than 30 mg of methadone requires direct observation, and subsequent daily doses usually range from 60-120 mg. Dose adjustments are made based on cravings and withdrawal (ASAM, 2015). Methadone has more drug-drug interactions than other opioids due to its metabolism through the cytochrome P450 enzyme systems (Chou et al., 2014; McCance-Katz et al., 2010; Salsitz & Wiegand, 2016). In addition, methadone has been associated with higher risks of overdose during the first 4 weeks of treatment due to its long half-life and accumulation potential (Sordo et al., 2017). Methadone can cause electrocardiogram (EKG) corrected QT interval (QTc) prolongation, which can lead to increased risk for torsade de pointes, a potentially fatal arrhythmia. Thus, EKGs should be periodically monitored when the individual is taking methadone, with the frequency of testing determined by the baseline EKG QTc and concomitant use of other medications that can cause QTc prolongation (ASAM, 2015; Chou et al., 2014).

Acute Pain and Methadone

There is greater evidence and consensus on using methadone in the perioperative time period when patients with OUD are maintained on methadone. The recommendation is to continue the patient's usual daily methadone dose during the hospitalization while using multimodal analgesia including opioid and nonopioid analgesics (ASAM, 2015; Harrison et al., 2018; Sun et al., 2018). Another option is divide the total daily methadone dose into three times a day dosing and administer additional opioids and nonopioid analgesics for postoperative analgesia (Harrison et al., 2018; Taveros & Chuang, 2017).

Contraindications for methadone use in hospitalized patients are hemodynamic instability, increased sedation, and evidence of prolonged QTc on EKG. Upon patient hospitalization, hospital-based healthcare providers need to contact the outpatient treatment program provider to verify methadone dose (U.S. Department of Justice, 2018) because methadone administered for OUD does not appear in prescription drug monitoring programs. If the dose cannot be verified, methadone at a dose no more than 40 mg daily or in divided doses can be administered (ASAM, 2015) until the outpatient treatment program provider can be contacted. If the dose or schedule is changed during the hospitalization, the hospital providers must communicate that information to the outpatient treatment program provider (Sen et al., 2016).

Patients who cannot take oral medication can receive IV doses of methadone, with the conversion from oral to IV being 2:1 (Sen et al., 2016). If IV methadone is not available, the use of IV PCA with another mu agonist opioid can treat pain and decrease risk for opioid withdrawal. However, expert guidance should be sought because transition from methadone to other mu opioids has an

individual and variable response. As with any patient on opioids, patients receiving methadone should be monitored for poor analgesia and impending respiratory depression as part of routine care.

Outpatient Chronic Pain and Methadone

The outpatient healthcare provider managing pain must collaborate with the outpatient treatment program, especially regarding risk for drug–drug interactions with medications that can also prolong QTc (Chou et al., 2014; McCance-Katz et al., 2010). When the maintenance dose of methadone is not sufficient to manage pain, the clinician managing the patient's pain may not only continue that dose but also prescribe another opioid or a nonopioid medication such as a neuronal membrane stabilizer or a serotonin/norepinephrine reuptake inhibitor (ASAM, 2015; CDC, 2016). There is weak evidence to suggest that using methadone for the analgesia may be the best option, but one would have to consider whether the benefits outweigh the risks (Eilander et al., 2016; Taveros & Chuang, 2017). It is essential for the healthcare provider managing pain and the healthcare provider managing OUD to communicate and implement safety precautions and monitoring (Dowell et al., 2016).

Naltrexone

Naltrexone is a mu receptor antagonist that was approved for alcohol dependence in 1994 and for the prevention of OUD relapse in 2010 (SAMHSA, 2018c). Naltrexone blocks the euphoric effects of opioids and alcohol and is considered a good option for individuals with OUD and alcohol use disorder (Aboujaoude & Salame, 2016). Naltrexone can be initiated only after the individual has detoxified from opioids. Naltrexone can be prescribed by any healthcare provider with prescriptive authority. The dosage may vary depending on the product used. Oral naltrexone can be administered daily with a 50-mg dose; on a 3-day-a-week schedule, for example giving 100 mg on Monday, 100 mg on Wednesday, and 150 mg on Friday; or monthly with a 380-mg intramuscular depot injection (Vivitrol) (ASAM 2015; SAMHSA, 2018c). Naltrexone will not be identified in a prescription drug monitoring program, and there are no guidelines to alert the healthcare provider that a patient is prescribed naltrexone. Therefore, it is our recommendation to have naltrexone displayed on a patient's medic alert tag to ensure safe practice.

Acute Pain and Naltrexone

When an individual is going to have surgery, oral naltrexone should be discontinued 24-72 hours before surgery. The monthly depot injection should be discontinued 1 month before surgery (ASAM, 2015; Harrison et al., 2018; SAMHSA, 2018c). In the event of trauma or an acute pain event, 6-20 times the usual opioid dose may be required to overcome the naltrexone blockade (Bryson, 2014; Harrison et al., 2018). Even with high-dose opioids, analgesia may be suboptimal. The individual may need to be placed in a monitored setting owing to the risk for oversedation from the use of high-dose opioids needed to overcome the mu opioid receptor blockade and create analgesia (SAMHSA, 2018c). Liver function tests should be monitored owing to the risk of hepatotoxicity with naltrexone. Renal function also needs to be monitored owing to delayed renal excretion with renal impairment (SAMHSA, 2018c). Naltrexone cannot be restarted until a week to 10 days after the last dose of opioids (Harrison et al., 2018).

Outpatient Chronic Pain and Naltrexone

Naltrexone will not interfere with multimodal analgesia when nonopioid therapies are used. However, the patient and caregivers do need to be educated to avoid hepatotoxic medications such as acetaminophen and to monitor liver function tests (SAMHSA, 2018c). If mu opioids become a necessary part of pain management, the clinician should collaborate with the healthcare provider managing OUD to determine the best treatment alternative (ASAM, 2015).

Special Considerations

Active OUD With Acute Pain

Collaboration of clinicians must occur to treat pain and minimize withdrawal symptoms. In patients with opioid tolerance, multimodal analgesia must be considered (Dowell et al., 2016; Vadivelu, Kai, Kodumudi, Zhu, & Hines, 2017; Wenzel et al., 2016). Opioids should be considered for acute pain for short duration (Dowell et al., 2016), and when the patient is ready to treat the OUD, methadone or buprenorphine is beneficial (ASAM, 2015; Schuckit, 2016). For hospitalized patients, a waiver to prescribe methadone or buprenorphine is not necessary (U.S. Department of Justice, 2018). Upon discharge, if the patient and healthcare provider recommend continued use of MOUD for treatment of OUD or relapse prevention, referral to a waivered healthcare provider needs to occur. If the patient does not have a plan to continue MOUD in the outpatient setting and buprenorphine or methadone was administered in the acute care setting, the patient will need to be tapered off this medication before discharge, and continued discussions with the patient regarding referral to treatment should be documented.

If opioids are required for treatment of acute pain while a patient is hospitalized, IV PCA may be a viable option. This modality allows the individual to self-administer necessary doses of short-acting opioid for pain relief (Sen et al., 2016). Monitoring guidelines may need to be modified to minimize the risk of oversedation or of tampering with the IV PCA. Scheduled opioids rather than as-needed analgesics should be considered to manage ongoing pain (Vadivelu et al., 2016; Vadivelu et al., 2017). If the patient previously had been on high doses of opioids, he or she may still experience withdrawal symptoms even with opioids administered for pain. Withdrawal symptoms can be treated with medications such as clonidine and tizanidine (alpha-2 adrenergic agonists) to decrease symptoms of autonomic overactivity (Gowing, Farrell, Ali, & White, 2014).

There is a significant gap in care in the discharge plan of patients with active OUD and ongoing pain from acute injury, surgery, or medical disorder. Opioids may be the best analgesic option for the patient. Placement in an assisted living or skilled nursing facility may be the best transition for the individual, but this often is not feasible owing to insurance coverage or patient willingness. If the acute care clinician decides to discharge the individual with opioid medications, a clinician who will treat the pain must be identified before discharge. If the patient is not going to continue on MOUD therapy, the risk of overdose is high due to loss of opioid tolerance. Before discharge, the individual should be counseled about overdose risks and given a list of OUD treatment resources (ASAM, 2015) and a prescription for naloxone reversal (USDHHS, 2018). If possible, the patient's caregiver should be given instructions about naloxone reversal.

Active OUD With Chronic Pain

Pain management in patients with active OUD and chronic pain requires a dual focus—the assessment and management of pain and support for treating OUD. The use of nonopioid multimodal analgesia is the cornerstone of care. Opioids should not be a first line consideration for the management of chronic nonmalignant pain (Dowell et al., 2016). Additionally, the individual's comorbidities must be considered when prescribing commonly used nonopioid analgesics. Extenuating circumstances, such as a serious illness or end of life situations, may require the use of opioid therapy. A treatment plan must be developed with specific

communication with the healthcare team to ensure safety with opioid treatment. Urine toxicology screening and dispensing of a small amount of opioids with frequent visits can help detect misuse, overuse, and medication combinations that are high risk (Walsh & Broglio, 2016). Naloxone for opioid reversal should be prescribed as a safety precaution (USDHHS, 2018). Regular visits by home care nurses may be necessary to assess pain and adherence with prescribed opioid use. Reliable family or friends can be enlisted to help ensure adherence with appropriate and safe pain management (Walsh & Broglio, 2016). A careful assessment of the home situation is necessary because most opioids obtained outside a legitimate prescribing relationship are acquired by family or friends (SAMHSA, 2018a). Clinicians who specialize in pain and addiction medicine may be the best clinicians to manage these situations, but availability of these clinicians may be limited in many communities.

People With Acute Pain Who Are in Recovery for OUD and Not on MOUD

Individuals with OUD who are in recovery without the use of MOUD may face challenges in the setting of acute pain when opioid therapy may be necessary. Although the goal of multimodal analgesia is to target receptors at multiple sites through the use of different classes of analgesics and to minimize use of opioids, at times opioids may be the most effective medications for acute, severe pain. Clinicians should assess the patients' concerns about opioid use because some patients may have significant fears of relapse, especially those who have had previous episodes of relapse. The patient's wishes should be respected and efforts should be made to avoid opioid therapy if that is consistent with the patient's stated goals. If opioid therapy is the only viable choice to manage pain, the lowest effective dose should be used. A discharge plan should be developed in partnership with the patient. If the patient is discharged with opioids, naloxone for opioid reversal should be prescribed as a safety precaution (USDHHS, 2018). Caregivers should be instructed on the use of naloxone. Counseling and referral to appropriate psychosocial supports (e.g., Narcotics Anonymous) are important because individuals not receiving MOUD are at higher risk for relapse and resulting morbidity (ASAM, 2015; Connery, 2015).

People With Chronic Pain Who Are in Recovery for OUD and Are Not on MOUD

Individuals with OUD who are in recovery without the use of MOUD and who also have comorbid chronic pain will benefit from psychosocial support to prevent relapse. Pain should be treated with a multimodal approach maximizing nonopioid, nonpharmacologic therapies and supportive counseling. Ultimately, if opioids are started, the implementation of universal precautions for opioid prescribing (treatment agreements, urine drug screening, and so forth) with close follow-up may help support the individual (Gourlay, Heit, & Amahregi, 2005). Individuals should participate in psychosocial programs to prevent relapse (Vadivelu et al., 2016). In addition, naloxone for opioid reversal should be prescribed as a safety precaution (USDHHS, 2018) because the period of opioid abstinence may result in reduced tolerance to opioid doses previously used, and thus the risk of overdose is increased (ASAM, 2015).

Patient Acceptance of the Diagnosis OUD

A patient's acceptance of having OUD is thought to be foundational to successful treatment; however, many patients have difficulty with accepting the diagnosis of OUD. Even so, treatment does not have to be voluntary and accepted to be effective (National Institute on Drug Abuse, 2018). Acceptance of the diagnosis of OUD can be influenced by numerous variables, with the most important being the stigmatization that often occurs when patients with OUD encounter healthcare professionals. A systematic review found that many healthcare professionals expressed negative attitudes toward patients with SUD. With more specific education and training of healthcare professionals, these negative attitudes can be turned around to more accepting attitudes toward patients with SUD including OUD (van Boekel, Brouwers, Weeghel, & Garretsen, 2013). Strategies used in motivational interviewing have been shown to be successful in helping patients seek the care they need (SAMHSA, 2012). Counseling strategies to that end include cognitive behavioral therapy and acceptance commitment therapy, which may help patients accept their disease and commit to living a values-based life (Dindo et al., 2018). The nurse can assess the patient's level of understanding and acceptance of the OUD diagnosis in a nonjudgmental manner and offer referral into treatment.

Conclusion

Nurses who care for patients with OUD and comorbid pain must possess the skills to manage acute and chronic pain utilizing multimodal analgesia and nonpharmacologic modalities. In addition to comprehensive pain assessment, screening for suicide risk and signs of withdrawal are important components of assessment in patients with OUD. Although all types of pain can be treated with multimodal analgesia that may include opioids, special considerations are necessary in both the acute care and ambulatory setting for patients who have OUD. Nurses must balance the benefits of pain management that may include opioids with the risks for relapse, challenges with pain treatment in the ambulatory care setting, and risks for overdose when patients are discharged to the community. Through better understanding of the treatment of pain in this population, nurses can advocate for appropriate pain management and treatment for OUD.

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