The role of buprenorphine in patients with opioid use disorder in need of acute or chronic pain management

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Purpose: The purpose of this review is to summarize and apply existing literature to acute and chronic pain management for patients using buprenorphine for opioid use disorder (OUD).

Summary: Pain management in patients taking buprenorphine for OUD presents many challenges for clinicians. Buprenorphine has unique pharmacological properties compared to full μ-opioid receptor agonists, including a strong affinity for and slow dissociation from the μ opioid receptor. Patients using buprenorphine have more pain than those not utilizing chronic opioid therapy, as occurs with most chronic opioid use. This may be due to the development of tolerance or hyperalgesia or may be part of the OUD process. Management of chronic pain should be approached the same as with any patient, focusing on nonpharmacological and nonopioid therapies, as opioid therapies have been shown to have very little efficacy for chronic pain. Management of acute pain is based on maintaining a stable dose of buprenorphine and supplementing with full μ-opioid receptor agonists, nonopioid analgesics, and nonpharmacological therapies. Transitioning to buprenorphine, in either the inpatient or outpatient setting, can be done with standard, low-dose, or high-dose induction based on the clinical situation. Transitions to and from the acute care setting require extensive communication and are enhanced by multidisciplinary teams.

Conclusion: It is imperative that providers be knowledgeable about buprenorphine and how to optimize it for OUD as well as pain. Pain management with buprenorphine can be tailored to the patient and clinical situation, but any therapeutic plan must contain a holistic approach and involve extensive communication that includes the patient and all relevant providers to achieve safe and effective care.

Keywords: acute pain, buprenorphine, buprenorphine induction, chronic pain, opioid use disorder, transitions of care

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As of 2019, opioid use disorder (OUD) was reported to affect 6.7 to 7.6 million Americans.[1] Federal and state legislation has increased access to buprenorphine over the past 25 years. The expanded use of buprenorphine offers significant benefit in treating OUD but also presents challenges in pain management. Many people develop OUD as they attempt to treat their pain, and both patients and clinicians may be hesitant to explore medication options due to stigma or fear of return to use. Buprenorphine, compared to most other μ-opioid receptor agonists, has a strong affinity for and slow dissociation from the μ-opioid receptor. This narrative review explores both acute and chronic pain management in patients using buprenorphine for OUD, highlighting some of the nuances in this population.

History and pharmacology of buprenorphine

Buprenorphine is a synthetic opioid with a pharmacological profile that makes it useful as an analgesic and as a medication for OUD (MOUD). It was introduced as an analgesic in the UK in 1977 for moderate to severe pain and in the US in 1985 as an injectable analgesic (Buprenex).[2] It was also studied for "narcotic addiction" in the 1980s and 1990s. This led to Food and Drug Administration (FDA) approval of both buprenorphine by itself (Subutex)[3] and buprenorphine/naloxone (Suboxone and Zubsolv)[4,5] for the treatment of "opioid dependence" in 2002. Concerns about adherence led to the development of a monthly subcutaneous product (Sublocade), approved in 2017.[6] A second sustained-release subcutaneous product (weekly or monthly dosing) was approved in 2023 (Brixadi)[7] (Table 1).

The pharmacology of buprenorphine is similar to that of other opioid agonists in that buprenorphine binds to the μ-opioid receptor; however, it is considered a partial agonist, which is a bit of a misnomer as it implies that buprenorphine has only weak analgesic activity.[8] Studies in the in vitro setting have indicated that buprenorphine does not produce full agonist effects. However, in the in vivo setting, particularly with regard to analgesic efficacy, this is not necessarily true.[9] Dahan et al[9] compared the proposed ceiling effect of intravenous buprenorphine in analgesia and respiratory depression. They found that respiratory depression reached a plateau as the dose increased but analgesia did not, demonstrating that receptor agonist activity is not the same as clinical efficacy, for pain management or for management of cravings in OUD. Comparative studies have shown equal efficacy with other full μ-opioid receptor agonists, including fentanyl, morphine, and sufentanil, in settings from acute postoperative pain to cancer pain.[10-14] This may be due to buprenorphine's complex pharmacology, with several theories exploring extra-receptor analgesic activity.[15] Pharmacodynamic effects like analgesia vary among patients across the opioid class, and buprenorphine is no different.

KEY POINTS

- Buprenorphine's unique pharmacological and pharmacokinetic properties make it ideal for opioid use disorder (OUD) and challenging in pain management. Chronic pain management includes addressing other comorbidities as well as pain.
- Acute pain management in patients taking buprenorphine is multimodal to manage pain, support OUD recovery, and prevent withdrawal.
- Transitioning to buprenorphine from full μ-opioid receptor agonists can be achieved in several different ways. Standard induction, low-dose induction, and rapid induction each have a role, depending on the clinical setting.

Buprenorphine is also an antagonist with high binding affinities at the δ- and κ-opioid receptors.[16] Antagonist activity at the κ-opioid receptor causes competition with spinal dynorphin. Spinal dynorphin levels usually increase following opioid exposure and may contribute to opioid-induced hyperalgesia.[17] Buprenorphine may, therefore, reverse or prevent hyperalgesia.[18,19] It may also reduce stress responses, dysphoria, and anxiety via this receptor activity.[17] Buprenorphine binds to opioid receptor–like 1 (ORL1 or nociceptin) with lower affinity.[16] Agonist activity at this receptor may have actions that oppose opioid-related analgesia.

One of the most unique aspects of buprenorphine is its high binding affinity for and slow dissociation from the μ-opioid receptor. Its μ-opioid receptor binding affinity is approximately 5 times as strong as that of morphine.[20] Buprenorphine exhibits dose-dependent attenuation of the effects of other μ-opioid receptor agonists, and the dose is inversely related to μ-opioid receptor availability. It displaces both endogenous and exogenous opioids when present. A dose of 24 mg is usually required to achieve enough receptor occupancy to meaningfully affect deterrence of illicit opioid use and suppress withdrawal and cravings. Only 5% to 10% receptor occupancy is necessary for analgesia.[21,22] Four hours after a single dose, 70% of receptors are occupied, while after 24 hours at least 50% are occupied, fading to 18% at 76 hours after the dose.[23] When enough receptors are occupied, buprenorphine also prevents any new opioid from binding, which makes it an effective agent for OUD but also presents challenges for pain management.

Pain management challenges

There are several challenges in managing pain in patients with OUD. One relates to the unique qualities of buprenorphine itself, as discussed above. The higher the dose of buprenorphine, the fewer opioid receptors are available. Another challenge is OUD itself. Several studies have shown that patients with OUD have an increased sensitivity to pain.[24,25] Even people who do not have pain upon initiation of an opioid-based MOUD therapy may develop chronic pain within 12 months (with a reported rate of as high as 45%).[26] This may be due to tolerance or opioid-induced hyperalgesia and may be why opioid-based OUD therapy is not as effective at providing analgesia in patients with acute and chronic pain compared to patients not on chronic opioid therapy (as an MOUD or for chronic pain).

Some of the challenges relate to patients and providers. Many patients develop OUD while attempting to treat pain. It has been estimated that almost 80% of people diagnosed with OUD had an opioid prescription before their diagnosis.[27] Given this risk, both providers and patients may be hesitant to utilize opioid medications due to the

Table 1. Buprenorphine Products Used for Opioid Use Disorder

Product	Indication	Route	Dose[a]
Buprenex	Acute pain	IM, slow IV	0.3-0.6 mg every 6 hours
Subutex	OUD	SL tab	Target dose of 4-24 mg SL daily, max daily dose of 32 mg
Suboxone (buprenorphine/naloxone)	OUD	SL tab, SL film, buccal film	Target dose of 4-24 mg SL daily, max daily dose of 32 mg
Zubsolv (buprenorphine/naloxone)	OUD	SL tab	Target dose of 11.4 mg/2.9 mg daily
Sublocade	OUD, already established on buprenorphine 8-24 mg/day for ≥7 days	SQ depot monthly	• 8-24 mg/day SL = 300 mg SQ 1 time then 100 mg SQ monthly • May titrate to 300 μg SQ monthly
Brixadi	OUD, already established on buprenorphine or received at least 1 dose	SQ depot weekly or monthly	• ≤6 mg SL = 8 mg SQ weekly • 8-10 mg SL = 16 mg SQ weekly or 64 mg SQ monthly • 12-16 mg SL = 24 mg SQ weekly or 96 mg SQ monthly • 18-24 mg SL = 32 mg SQ weekly or 128 mg SQ monthly

Abbreviations: IM, intramuscular; IV, intravenous; OUD, opioid use disorder; SL, sublingual; SQ, subcutaneous.
[a]Doses are not equivalent and products should not be interchanged without specific guidance. Refer to product package inserts.

risk of patient harm (respiratory depression, etc) or return to use.[28,29] Many times, these patients end up being undertreated for acute pain, as with surgery. There is a risk of return to use if the MOUD is stopped before surgery and a concomitant risk if opioids are prescribed upon discharge without the baseline MOUD present. There is also a greater risk of overdose after hospital discharge (planned or self-directed) if pain is undertreated, an MOUD is not adequate, or stigma is evident.[30] Several studies have found that, if MOUDs are continued with adequate supplemental analgesics, the risk of returning to use of other opioids, whether due to lack of OUD support or inadequately controlled pain, is diminished.[31]

Lack of knowledge and experience among providers is still a concern.[32] Providers fail to understand that buprenorphine, while preventing cravings and withdrawal, may offer a poor or varied analgesic effect.[32] Providers may also lack knowledge of buprenorphine's pharmacokinetic characteristics and potential for drug interactions. It is metabolized via the CYP3A4 enzyme and may interact with several other medications. There are also pharmacodynamic interactions, including additive respiratory depression when buprenorphine is used with other central nervous system depressants.

Wider societal and healthcare system challenges also exist, including a lack of trust. Patients may feel stigmatized or be afraid of having uncontrolled pain or that their stable MOUD will be stopped.[33] Providers may feel that when patients report pain they are just craving drugs. This leads to the discriminatory label of "drug seeking" instead of an honest report of pain.[32] Stigma and discrimination occur with all healthcare providers, including pharmacists, despite data showing that MOUD therapy decreases use of opioids and other illicit drugs, increases treatment retention, decreases criminal activity, improves individual function, and decreases HIV seroconversion.[32] Providers may judge that patients do not deserve to be given opioids. Providers are also concerned that, if patients are given opioids upon discharge, they may use these in a manner that would cause harm to themselves or others.

System issues arise with limited hospital formularies and lack of resources such as pain stewardship personnel and pain and/or addiction medicine services. Providers who manage patients with OUD may have their own protocols they follow perioperatively, such as switching to methadone or switching to a short-acting opioid for a short time before surgery. This variation in practice can cause confusion for patients and providers and ultimately patient harm. Algorithms and protocols should be developed, and open, frequent communication is necessary between inpatient and outpatient providers, along with the patient themselves.

Chronic pain management

Chronic pain management is complex, and each individual's experience is unique. Unfortunately, a lack of adequate resources and support systems (and payment for multi-resourced systems), industry-driven aggressive

marketing, and other factors have led to more opioid prescribing in the past 20 years and earlier.[34,35] The scaling back of opioid prescribing since 2012, with a persistent lack of management resources, led to a shift to illicit opioids and other substances.[36,37] As a result, a subpopulation of patients with OUD have inadequately managed chronic pain.

Because chronic pain may be present in those with OUD, patients should first be approached with pain management therapies used in the general population, including recommended first-line therapies (eg, for arthritis, low back pain, neuropathic pain, etc). Clinical guidelines for managing chronic noncancer pain recommend utilizing nonpharmacological and nonopioid modalities before considering opioids.[38,39] Nonpharmacological modalities such as physical rehabilitation and restoration, as well as cognitive behavioral and mind-body therapies, constitute the foundation for managing all types of pain and are also effective in patients concurrently taking opioids.[40] Interventional therapies (eg, steroid injections) may offer short-term relief and are intended to augment physical rehabilitation efforts. Analgesics of any kind may offer only modest pain relief, sometimes not better than placebo.[41] Neuropathic pain is managed with anticonvulsants (eg, gabapentin and carbamazepine) and analgesic antidepressants (duloxetine and tricyclics), as these are the most effective agent.[42] Chronic musculoskeletal pain is managed with anti-inflammatories.[38] Nociplastic pain arises from altered pain perception in the absence of clear evidence of actual or threatened tissue damage causing activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.[43] Such pain is managed mostly nonpharmacologically, as medications offer little efficacy. Opioids have very little efficacy for any type of pain with long-term use (more than 12 weeks).[44] Additive opioid therapy in the setting of an MOUD should be considered on a case-by-case basis to balance benefits and risks.

If an opioid is necessary, it should be used with caution. Screening tools to determine the risk of opioid misuse are only partially predictive and cannot be generalized to the OUD population. History of a substance use disorder or a psychiatric illness and concurrent use of certain psychiatric medications consistently correspond to risk.[45-47] If the patient is taking an MOUD, this will need to be continued to manage the OUD. There are mixed thoughts about the efficacy of buprenorphine for chronic pain. It may be less effective than in opioid-naive patients due to tolerance and possibly hyperalgesia. However, patients with chronic pain and OUD have also experienced a reduction in their pain when buprenorphine/naloxone was utilized.[48,49]

Many patients with concurrent chronic pain and OUD have a greater psychiatric burden (in one study, more than 92% had a long-term psychiatric diagnosis) compared to the general population with chronic pain.[24] Barry et al[45] reported that patients with both chronic pain and OUD commonly had comorbid psychiatric disorders, including post-traumatic stress disorder (21%), panic disorder (16%), mood disorders such as depression (40%) and anxiety (52%), and nonopioid substance use disorders (78%). These patients deserve a holistic and multidisciplinary approach.

Acute pain management

Postoperative pain. The recommendation for managing patients with OUD on buprenorphine (as an MOUD and not an analgesic) is to continue buprenorphine throughout the perioperative period to decrease overall opioid requirements, improve analgesia, and decrease the risk of return to use or failure to restart buprenorphine therapy.[50,51] Consider the case of a 55-year-old woman who is admitted for an elective knee replacement surgery and is on buprenorphine/naloxone. The patient has been in OUD recovery for 2 years. The care team would like a pain management plan for her elective surgery.

In this case, multimodal analgesia should form the backbone of the treatment plan.[50,51] The patient is opioid tolerant, and she will need additional opioids to effectively treat her pain. The total daily dose of buprenorphine/naloxone can be split into 3 or 4 doses to optimize the analgesic half-life.[32] For surgeries requiring admission to the hospital, the dose may be adjusted because no optimal approach has been recommended for postoperative pain.[52,53] Buprenorphine dosing should be adjusted back to the patient's home dose before discharge. Interventional therapies decrease the need for systemic opioid therapies. Thus, the regional anesthesia team could recommend a regional nerve block and an intraoperative periarticular injection.[54] Additional multimodal therapy can be added, including systemic opioids. Hydromorphone and fentanyl are preferred full agonist agents due to their affinity for the μ-opioid receptor.[50,51] Systemic nonopioid therapy should be scheduled, including acetaminophen alternating with a nonsteroidal anti-inflammatory drug (NSAID). Sub-anesthetic ketamine may be added for 24 hours to reduce overall opioid requirements.[55] For postoperative pain control, the patient could be sent home with a small supply of hydromorphone if needed. The decision of whether to send a patient home with opioids is patient specific, depending on who will be holding and managing the medications and the level of pain. MOUD, buprenorphine/naloxone in this patient, should be continued throughout the treatment course with a warm handoff back to the outpatient buprenorphine prescriber (Box 1).

Opioid-related adverse effects must be effectively addressed, including by scheduling a bowel regimen to prevent opioid-induced constipation. Opioid-induced pruritis may be managed with nalbuphine or ondansetron.[56,57] Intranasal naloxone should be co-prescribed for discharge. FDA recommends discussing the importance of intranasal naloxone with any

Box 1. Patient Case: Acute Postoperative Pain[32,50,51,54-59]

AJ is a 55-year-old woman with OUD on buprenorphine/naloxone 8 mg/2 mg sublingually twice daily as MOUD. She is admitted for an elective total knee replacement surgery. What would you do to manage her pain?

- Continue buprenorphine/naloxone 8 mg/2 mg twice daily; consider dividing this into 3 to 4 doses
- Multimodal analgesia
  - Regional anesthesia, including a combination of regional blocks and intraoperative peripheral arterial injection
  - Ketamine 0.1-0.5 mg/kg/h IV titrated as needed/tolerated
  - Ketorolac 15 mg IV every 6 hours for up to 5 days or ibuprofen 600 mg by mouth every 6 hours
  - Acetaminophen 1,000 mg by mouth every 6 hours
  - Hydromorphone 4 mg by mouth every 4 hours as needed
  - Ice, physical therapy, and other nonpharmacological interventions
- Manage adverse effects
  - Pruritus: nalbuphine 2.5-5 mg IV every 6 hours as needed
  - Nausea/vomiting: prochlorperazine 5-10 mg IV or by mouth every 6 hours as needed
  - Constipation: senna 2 tabs by mouth every night at bedtime; titrate as needed
- Prescribe intranasal naloxone on discharge

Abbreviations: IV, intravenously; MOUD, medication for opioid use disorder; OUD, opioid use disorder.

patient with an opioid in the home and strongly considering a prescription for intranasal naloxone in any patient at increased risk of respiratory depression, including in patients with a history of OUD on an MOUD.[58]

Nonpharmacological interventions, such as the use of hot or cold packs, aromatherapy, distraction, social and spiritual support, and any other forms of support the patient identifies, are also an important part of the care plan.[50,59] Institutions will have different resources, but the patient must be aware of the options available that can further decrease the painfulness of their experience. Patient education about expectations in the perioperative period helps with pain management and reduces anxiety.[60]

If a patient with OUD on an MOUD required an emergent surgery instead of planning an elective one, the principles and plan above would still apply. Additionally, assessment for recreational opioid use above and beyond the MOUD should be performed to ensure adequate opioid coverage and that the patient is not at risk of withdrawal. The admission assessment must include an opioid withdrawal assessment and, if the patient is taking buprenorphine, should determine when they last took a dose. If providers are not aware that a patient is taking buprenorphine, they may have a more difficult time controlling the patient's pain and there will be an increased risk of adverse effects once buprenorphine is no longer bound to the μ-opioid receptor.

Acute nonsurgical pain. For acute nonsurgical pain in a patient with OUD, as with surgical pain, an interdisciplinary, multimodal approach is recommended.[59] Consider the case of a 31-year-old man with a complex medical history including OUD on an MOUD presenting for treatment of acute cellulitis related to intravenous drug use after the death of his friend. In addition to treating his acute illness and pain, a priority for a patient who has active drug use is to assess for withdrawal and treat to prevent severe symptom burden.[59] Inadequate control of pain and withdrawal leads to patients leaving care before its completion and worse clinical outcomes.[61] In our case, the patient was using illicit fentanyl in addition to taking his MOUD, so he is at risk for significant withdrawal. Depending on where he lives, he may also be at risk for withdrawal from contaminants in the drug supply, such as xylazine or medetomidine, so targeted symptom assessment and treatment will be necessary.[62,63] Withdrawal should be assessed with the Clinical Opioid Withdrawal Scale (COWS), providing additional opioids in addition to nonopioid therapy such as antiemetics, antipsychotics, anxiolytics, and antidiarrheals if necessary to stabilize the patient's symptoms.[64] Methadone can be added to stabilize withdrawal.[64,65] Specific nonopioids should be scheduled for targeted symptoms. Pain is a part of this patient's clinical presentation and is part of the withdrawal picture, so the patient will benefit from the addition of full opioid agonists. Higher doses of

Box 2. Patient Case: Acute Nonsurgical Pain in a Patient With Active Opioid Use Disorder[52,53,59,61-67]

JH is a 31-year-old man with a complex medical history including morbid obesity, obstructive sleep apnea, anxiety, asthma, OUD on MOUD, and depression. He presents for treatment of acute cellulitis related to intravenous drug use. The cellulitis spans his arm from the shoulder to the elbow and is reported as a 9 out of 10 in pain severity on the visual analog scale. The patient is unable to move the arm without severe pain, limiting his ability to perform activities of daily living. The patient reports that he recently returned to using drugs when his best friend died unexpectedly 3 weeks ago and he has been using 6 bags intravenously daily. He has been on buprenorphine/naloxone 8 mg/2 mg twice daily for the past 2 years, plus lorazepam 1 mg by mouth every 12 hours as needed for anxiety, sertraline 100 mg by mouth daily, and an albuterol inhaler as needed. His goal is to return to recovery and to be able to get back to normal activities. The QTc interval on an electrocardiogram is 440 ms using Bazzett's formula. Vitals include a heart rate of 60 beats per minute, blood pressure of 150/90 mm Hg, and O_2 saturation of 97% on room air. How do you manage his pain while he is admitted to the hospital?

- Assess for opioid and potential polysubstance withdrawal
- Continue buprenorphine/naloxone 8 mg/2 mg sublingually twice daily; consider dividing into 3 or 4 doses
- Schedule hydromorphone 4-8 mg by mouth every 4 hours (for pain) with methadone 30-40 mg by mouth daily (for withdrawal)
- Multimodal analgesia
  - Gabapentin 300-600 mg by mouth every 8 hours
  - Ketamine 0.1-0.5 mg/kg/h IV or 1.5 mg/kg/day by mouth divided every 6 hours titrated as needed
  - Ketorolac 15 mg IV every 6 hours for no more than 5 days or ibuprofen 600 mg by mouth every 6 hours
  - Acetaminophen 1,000 mg by mouth every 6 hours
  - Nonpharmacological interventions
- Manage withdrawal and any adverse effects
  - Sympathetic symptoms: clonidine 0.1 mg by mouth every 6 hours; increase as needed/tolerated
  - Cramps: dicyclomine 10 mg by mouth every 6 hours as needed
  - Nausea/vomiting: ondansetron 4-8 mg IV/by mouth every 6-8 hours as needed
  - Constipation: senna 2 tabs by mouth every night at bedtime; titrate as needed

Abbreviations: IV, intravenously; MOUD, medication for opioid use disorder; OUD, opioid use disorder.

fentanyl or hydromorphone are recommended as he is also on buprenorphine and has a very high tolerance.[64] The patient may benefit from addition of adjuvants such as gabapentin, ketamine, and scheduled nonopioids such as NSAIDs and acetaminophen.[59,66] As when treating surgical pain, splitting the buprenorphine/naloxone dose is an option to maximize the analgesic half-life, and adjustment of the dose can also be considered.[52,53] During this admission and beyond, this patient may be more stable on an increased total daily dose of buprenorphine of 24 to 32 mg.[67] He may also be a candidate for long-acting injectable buprenorphine. Screening for risk of suicide and providing wrap-around care to address the patient's grief will decrease the risk of return to use, as will connecting with his outpatient buprenorphine prescriber[59] (Box 2).

Transitioning to buprenorphine

Transitioning to buprenorphine can seem like an insurmountable task, especially in settings of acute pain and concurrent medical problems. However, numerous studies have been published on transitioning patients from full opioid agonists to buprenorphine utilizing standard induction, low-dose induction, or high-dose induction protocols.[68-70]

Standard induction protocols utilize a process requiring patients to experience moderate to significant withdrawal before initiation of buprenorphine.[71] After a patient has reached a COWS score of 13 or higher, they can be started on buprenorphine with less risk of precipitated withdrawal than if they had a milder withdrawal score. Buprenorphine dosing varies in standard induction; however, most protocols utilize up to 8 to 12 mg on day 1, using a stepwise approach to target withdrawal. Some protocols give 2 mg sublingually every hour up to a total dose of 8 mg. Others utilize a larger initial dose of 4 mg sublingually with a repeat dose in 2 to 4 hours. On day 2, patients' doses are typically increased to a daily or split total daily dose of 12 to 16 mg. Patients are then maintained on this dose until follow-up, at which time the dose can be individualized for craving management. This process may be a barrier to starting patients on buprenorphine due to fear of

withdrawal and, in the case of acute pain, exacerbated pain and suffering.[72] Standard induction protocols are better equipped to help those acutely experiencing withdrawal due to abrupt or sudden cessation of opioids and are not often the best option in patients experiencing acute pain in the hospital setting.

Low-dose induction protocols continue full opioid agonist coverage while building up buprenorphine, resulting in a give-and-take pharmacological process. As buprenorphine, which has very strong affinity for the μ-opioid receptor, is started, it pulls other full opioid agonists off receptors. When done very slowly, this results in a slow buildup of buprenorphine to help limit severe withdrawal. As an analogy, starting buprenorphine at a low dose is like a child learning to walk vs hitting the ground running. By slowly pulling themselves up, the child learns to balance and get steady on their feet. If they were to run right away, there would be numerous falls. Depending on the protocol, buprenorphine is slowly added until the patient is on approximately 12 mg daily, resulting in more substantial saturation of opioid receptors. Full opioid agonists are then discontinued or tapered, and the buprenorphine dose can be optimized to target cravings and withdrawal symptoms. Low-dose inductions are better patient-centered options due to the patient not needing to enter withdrawal before starting buprenorphine, the ability to maintain adequate pain control during the transition, and the lower risk of withdrawal. This type of induction may be especially beneficial for individuals using illicit fentanyl, due to buprenorphine's high lipophilicity and tendency to redistribute into fatty tissues, which can complicate traditional induction approaches. Low-dose inductions have been utilized in both inpatient and outpatient settings as an alternative to standard induction.[69,73]

High-dose induction protocols are sometimes viewed as a more rapid alternative to low-dose and standard inductions. High-dose inductions typically use larger doses of buprenorphine during the first 24 hours of induction.[70] Once a patient has a COWS score of above 8, 4 to 8 mg of buprenorphine is administered with reassessment of withdrawal after 30 to 60 minutes. If the patient has improved, they can be transitioned to a more standard induction protocol. If the patient's withdrawal symptoms have not significantly improved or have worsened and they may have high opioid tolerance, a dose of 8 to 24 mg is given with ongoing withdrawal assessment. If withdrawal symptoms increase, a large dose of buprenorphine (eg, 24 to 28 mg) is utilized. These inductions have been shown to effectively transition patients via a more rapid protocol. High-dose inductions target μ-opioid receptor availability, which has been associated with worse withdrawal symptoms.[74] By targeting receptor availability and in a sense providing a loading dose of buprenorphine upfront, withdrawal and cravings may be targeted at a faster rate. While most of the literature has focused on utilizing high-dose induction in the emergency room, this strategy can also be utilized in outpatient ambulatory settings. However, there is very limited literature surrounding high-dose inductions in patients with chronic or acute pain.

The pharmacist and transitions of care

After starting a patient on buprenorphine, transition planning should occur to ensure access to follow-up care. Transitions of care can be complex due to an inability to connect patients with MOUD treatment clinics and lack of access to all forms of MOUD. In a study by Fockele et al,[75] major barriers to emergency room buprenorphine induction included physician comfort with MOUD practices and treatment access.

One possible way to improve transitions of care is through addiction medicine consult services. These services have shown benefit in initiating patients admitted to the hospital on MOUD.[76-78] Providers on these services are often aware of addiction medicine community partners, optimizing transitions to the community. Addiction medicine consult services may include physicians, advanced practice providers, clinical pharmacists, social workers, case managers, and peer recovery support specialists.[79] An interdisciplinary team will be well equipped to handle transition challenges as they arise, from medication management to housing support.

During transitions of care, proactive planning and implementation of strategies for risk reduction is essential. This may include educating patients on how to manage pain and preparing families to recognize signs of overdose and administer naloxone when necessary. Conducting thorough medication reconciliations can identify whether patients have been using buprenorphine or other forms of MOUD, which may complicate acute pain management. Clear communication among the patient, specialists, and opioid treatment programs is critical to ensure an accurate medication history and prevent complications.

Regardless of whether a patient in the hospital has OUD, good communication, from handoffs within the health system to patient discharge, is essential to effective healthcare.[80,81] For patients undergoing an unplanned or emergency procedure, consultation with addiction medicine and acute pain services may enhance care for patients with OUD. These services can help prevent unnecessary stoppage of MOUD while enhancing pain management. From an outpatient perspective, discussing pain management before a planned surgery may also enhance retention in treatment for people on MOUD while addressing acute pain concerns. For patients initiated on MOUD while hospitalized, communication with the patient and referral site may also affect treatment retention.

Discussion

Effectively managing pain for individuals with OUD requires a targeted patient-centered approach. Buprenorphine has a

unique pharmacology with its high binding affinity and distinct analgesic properties, presenting clinical challenges in acute and chronic pain settings. Pain management practices in patients with OUD often result in unnecessary patient burden; however, individualized multimodal strategies, continuation of MOUD, and perioperative planning can greatly improve outcomes.

System-level solutions are required to address pain in this patient population. Fragmented care, stigma, and misinformation are common barriers to effectively treating and managing pain while also helping those with OUD maintain recovery. These barriers could potentially be addressed through addiction medicine and pain management consult services and enhanced bidirectional communication between outpatient and inpatient groups. Enhanced continuity supports better pain and withdrawal management, smoother care transitions, and consistent access to MOUD, reinforcing long-term recovery efforts. This review highlights the importance of integrating pharmacological expertise into coordinated care to achieve compassionate and effective management of pain for individuals using buprenorphine for OUD.

Conclusion

Pain management with buprenorphine can be tailored to the patient and clinical situation, but any therapeutic plan must contain a holistic approach and involve extensive communication that includes the patient and all relevant providers to achieve safe and effective care.

Data availability

No new data were generated or analyzed in support of this work.

Disclosures

The authors have declared no potential conflicts of interest.

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