Navigating the Continuing Opioid Epidemic: Managing Acute Pain in Patients Taking Buprenorphine

by Alexandra Beckmann, PharmD

Question

How can health-system pharmacists take a proactive role in managing patients with opioid use disorder, specifically managing acute pain in patients taking buprenorphine?

Imagine that you are an acute care clinical pharmacist, managing patients on a general medical unit. You are rounding with the interdisciplinary healthcare team on a newly admitted patient. The 38-year-old female patient was in a motor vehicle accident and sustained multiple broken bones. The patient has a past medical history notable for opioid use disorder, for which the patient currently takes buprenorphine/naloxone 16 mg/4 mg sublingually once daily. The patient is in extreme pain, but the team is unsure of how to treat the patient's acute pain and looks to you for guidance. Given that the patient is taking buprenorphine/naloxone, what will you recommend for acute pain management?

In the late 1990s, opioid prescribing increased due to pharmaceutical companies reassuring the medical community that opioid analgesics were not addicting. Due to increased prescribing, it was not long before there was widespread misuse and abuse of both prescription and non-prescription opioids. With the increased misuse and abuse, opioid overdose deaths rose to epidemic proportions.[1] Since 1999, the number of drug overdose deaths in the United States have quadrupled. Between 1999 and 2019, nearly 500,000 people died from opioid overdoses.[2] In 2017, the U.S. Department of Health and Human Services declared a public health emergency to address the national opioid crisis. Under this public health emergency, a five-point opioid strategy was developed. The priorities for combatting this epidemic include improving access to prevention, treatment, and recovery support services; improving the availability and distribution of overdose-reversing drugs; strengthening public health data reporting and collection; supporting cutting-edge research on addiction and pain; and advancing the practice of pain management.[3]

It is estimated that opioid use disorder (OUD) affects over 16 million people worldwide, with over 2.1 million people affected in the United States.[4] One of the leading causes of preventable mortality in the United States is opioid-related overdose. From 2019 to 2020, the rate of drug overdose deaths involving synthetic opioids increased 56%.[5] The Wisconsin Department of Health Services (DHS) reported that, during the COVID-19 pandemic, the state's opioid epidemic has worsened.[6] After a steady increase in opioid overdose deaths before 2018, the deaths in Wisconsin had dropped by 10% to 839 that year. However, the numbers have increased since then, with 916 deaths in 2019 and 1,227 deaths in 2020. As opioid overdose deaths continue to rise in the state, the Wisconsin DHS has recommended multiple measures to continue to combat the opioid epidemic. These recommendations include continuing to train healthcare professionals on best practices for opioid prescribing and OUD treatment.[7] Pharmacists can play a key role by providing education to patients and recommendations to other healthcare providers, including recommendations for managing acute pain in patients with OUD.

The strong stigma associated with all substance use disorders creates a barrier between patients and healthcare providers. Some of those stigmas—inaccurate perceptions—include that people with

OUD are dangerous, are to blame for their condition, or are incapable of managing treatment and maintaining recovery. These perceptions are rooted in the antiquated idea that addiction is a moral failing. However, OUD is a chronic, treatable disease from which patients can recover. For healthcare providers, there should be a continual goal to address and change stigmatizing behavior (Table 1).[8] For situations where patients with OUD need inpatient acute pain management, both patients and providers might have concerns. For the patients, concerns may include: potential withdrawal symptoms, especially if usual maintenance medications are not given on schedule; fear that pain is not being taken seriously by healthcare providers leading to restricted access to proper analgesia; fear of discrimination, which can lead to distrust of healthcare providers; and fear of relapse if they are exposed to untreated pain or opioids. For the healthcare providers, concerns may include: a distrust of patients with OUD; over-treating pain; diversion of opioids prescribed at discharge; embellished pain scores to receive more opioids; and fear of patients leaving against medical advice without receiving full, crucial medical care.[9] It is crucial to continually address these concerns with patients and healthcare providers to provide the best care for the patients.[9]

In the inpatient setting, one challenge for healthcare providers is managing acute pain in patients with OUD who are using buprenorphine. Buprenorphine is widely used for the treatment of OUD and has complex pharmacology. It is a partial mu receptor agonist, a weak kappa receptor antagonist, and a delta receptor agonist. Due to its partial mu agonist property, when compared to full opioid agonists, buprenorphine's maximum analgesic effect is lessened. At higher doses, its analgesic effects plateau and can become antagonistic. With sublingual buprenorphine, a 16 mg dose occupies between 79% and 95% of the mu-opioid receptors. With sublingual doses greater than 24 mg, up to 95% of the mu-opioid receptors are occupied. Compared to other opioids, buprenorphine also has a higher mu receptor binding affinity and it displaces other opioids from the receptor site.[11,12] There are several FDA-approved buprenorphine formulations for the treatment of OUD (Table 2). Many of those oral formulations of buprenorphine contain naloxone, an opioid antagonist, to decrease the likelihood of intravenous or intranasal misuse of buprenorphine.[13] The oral bioavailability of naloxone is ≤2% and will not have an effect when given orally. However, if the medication is taken intravenously or intranasally, the naloxone will have an antagonistic effect on the buprenorphine. Due to the potency and complicated pharmacology of buprenorphine, the management of acute pain is challenging to navigate.[14] There are also several FDA-approved buprenorphine products for chronic pain management. However, in cases of acute pain management for patients being treated with buprenorphine for OUD, the utility of converting the patient to a buprenorphine formulation approved for pain management is limited due to the dosing of those formulations.

TABLE 1. Terms to Use and Avoid When Talking about Addiction[8,10]

Avoid	*Use Instead*
Addict, abuser	Person with an opioid use disorder
Abuse, misuse	Substance use Use other than prescribed
Clean	Being in remission or recovery Abstinent from drugs Not currently or actively using drugs
Dirty	Person who uses drugs
Relapse	Resumed substance use Recurrence of substance use
Medication-assisted treatment (MAT)	Opioid agonist therapy Pharmacotherapy Addiction medication Medication for a substance use disorder Medication for opioid use disorder (MOUD)

TABLE 2. Buprenorphine Products FDA-Approved for the Treatment of Opioid Use Disorder[15]

Generic Name	*Brand Name*	*Available Strengths*
Buprenorphine sublingual tablets	Subutex®	2 mg 8 mg
Buprenorphine/naloxone sublingual films	Suboxone®	2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg 12 mg/3 mg
Buprenorphine/naloxone sublingual tablets	Zubsolv®	0.7 mg/0.18 mg 1.4 mg/0.36 mg 2.9 mg/0.71 mg 5.7 mg/1.4 mg 8.6 mg/2.1 mg 11.4 mg/2.9 mg
Buprenorphine/naloxone buccal film	Bunavail®	2.1 mg/0.3 mg 4.2 mg/0.7 mg 6.3 mg/1 mg
Buprenorphine/naloxone implants	Probuphine®	74.2 mg
Buprenorphine extended-release injection	Sublocade®	100 mg/0.5 mL 300 mg/1/5 mL

Evidence-Based Answer

Given the misconceptions related to managing acute pain in this patient population, there is a risk of undertreating the pain. While there is a lack of consensus on the management of acute pain in patients treated with buprenorphine for OUD, there are several proposed strategies for acute pain management to consider in

this patient population.

The 2020 Focused Update to the American Society of Addiction Medicine National Practice Guideline for the Treatment of Opioid Use Disorder addresses the management of individuals with pain, and there is a specific section on buprenorphine and pain management.[16] Regarding perioperative pain management, prior to surgery, the discontinuation of buprenorphine is not required. In general, if pharmacologic therapy is needed for acute pain control, non-opioid analgesics should be considered first. However, the use of opioid analgesics should not be precluded by the presence or history of OUD. When needed, higher-potency full agonist opioids, such as hydromorphone or fentanyl, can be used for acute pain management. If possible, there should be coordination with the patient's OUD treatment provider to optimize acute pain control and to reduce the potential for relapse. For patients on buprenorphine maintenance therapy, there are several recommended strategies that can be considered:

1. Temporarily increase the total daily maintenance buprenorphine dose and/or divide the dose into three to four doses daily. The guidelines specifically mention that acute pain can often be adequately addressed by increasing the daily buprenorphine dose by 20% to 25% and splitting it into three to four doses.
2. For patients whose acute pain is refractory to other treatments and who require additional opioid-based analgesia, the addition of as-needed doses of buprenorphine may be considered. The addition of short-acting opioid analgesics to buprenorphine maintenance therapy may also provide benefit to controlling acute pain.
3. If buprenorphine maintenance therapy is discontinued during the treatment of severe acute pain, patients may need high doses of full opioid agonists to control pain. As the partial opioid agonist effects of buprenorphine dissipates, the effects of the full opioid agonists can lead to increased sedation and respiratory depression. Patients should be monitored closely.[16]

The Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Improvement Protocol (TIP) 63 addresses medications for OUD, with a section highlighting the medical management of patients taking OUD medications in hospital settings.[17] In general, for patients with acute pain, buprenorphine can be continued during hospitalization. For patients with mild-to-moderate pain, it is recommended to divide the patient's usual total daily maintenance buprenorphine dose into three doses to provide better pain control. For some patients, it may also be reasonable to increase the total daily buprenorphine dose to maintain adequate pain control. In patients with moderate-to-severe pain, the approach is more complicated, because additional analgesia, beyond an increase in the buprenorphine dose, is typically required. It is important to recognize that higher doses of opioids may be required to attain adequate pain control. There are two approaches to consider for these patients:

1. Use full agonist opioids for additional pain relief in addition to continuing the maintenance buprenorphine dose. Once the pain has improved, but the patient is still experiencing mild-to-moderate pain, the total daily maintenance buprenorphine dose can be divided into three doses.
2. Discontinue buprenorphine. To treat the acute pain and prevent withdrawal, use full opioid agonists. This strategy may be useful if the first approach does not attain adequate pain control.[17]

While the discontinuation of buprenorphine during a period of acute pain is a strategy that could be considered, in general, it is not necessary. There is a lack of evidence that continuation of buprenorphine therapy during acute pain management leads to poorer outcomes. One study showed that the continuation of buprenorphine during a perioperative period is associated with decreased outpatient opioid prescribing and decreased postoperative pain.[18] The discontinuation of buprenorphine while treating acute pain should only be considered as a last-line option due to the risks associated with it. The buprenorphine discontinuation increases the complexity of acute pain management and causes an increased burden on the patient, including the re-induction of buprenorphine. If the patient was treated with full opioid agonists for acute pain, the re-induction of buprenorphine will likely be physically painful and destabilizing for the patient due to the forced opioid withdrawal. There is also an increased risk for relapse because the patient will be in an opioid deficit while also being exposed to full agonist opioids.[19] By continuing buprenorphine, the patient's baseline opioid requirements are met, and it also allows for the use of short-acting full opioid agonists to manage acute pain.[20] Once the acute pain resolves, a plan to taper short-acting opioid agonists can be considered. However, it is important to consider the length of recovery from the procedure and the patient's recovery status when developing a taper plan.[21]

Conclusion

As with many aspects of medicine, there is not a single strategy for treating acute pain in patients taking buprenorphine. While multiple strategies can be considered when managing acute pain in patients who take buprenorphine for OUD, the most important factors to consider are what is best for the patient and keeping open communication with them about the pain management plan. As the opioid epidemic continues to ravish the country, there will continue to be a need for the use of pharmacotherapy in treating opioid use disorder. Buprenorphine remains a common treatment option, and there will be a continued need to understand how to manage acute pain in patients treated with buprenorphine. Open communication between the patient and providers is key when developing a plan to properly manage acute pain. By understanding the different options for managing acute pain in patients taking buprenorphine, pharmacists can play a key role in ensuring a smooth transition of care and assisting other healthcare providers in navigating this complicated situation.

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References

1. U.S. Department of Health and Human Services. What is the U.S. opioid epidemic? Published October 27, 2021. Updated October 27, 2021. Accessed January 10, 2022. https://www.hhs.gov/opioids/about-the-epidemic/index.html
2. Centers for Disease Control and Prevention. Understanding the epidemic. Published June 28, 2021. Updated June 1, 2022. Accessed June 4, 2022. https://www.cdc.gov/opioids/basics/epidemic.html
3. U.S. Department of Health and Human Services. HHS Acting Secretary declares public health emergency to address national opioid crisis. Published October 26, 2017. Accessed January 10, 2022. https://public3.pagefreezer.com/browse/HHS.gov/31-12-2020T08:51/https://www.hhs.gov/about/news/2017/10/26/hhs-acting-secretary-declares-public-health-emergency-address-national-opioid-crisis.html
4. Dydyk AM, Jain NK, Gupta M. Opioid use disorder. In: StatPearls. NCBI Bookshelf version. StatPearls Publishing: July 12, 2021. Updated June 21, 2022. Accessed January 10, 2022. https://www.ncbi.nlm.nih.gov/books/NBK553166/#:~:text=Opioid%20use%20disorder%20consists%20of,severe%20form%20of%20the%20disorder
5. Hedegaard H, Miniño AM, Spencer MR, Warner M. Drug overdose deaths in the United States, 1999–2020. *NCHS Data Brief*. 2021;428:1-8. doi: 10.15620/cdc:112340
6. Goodsitt E, Miller J. New report shows COVID-19 pandemic impact on opioid overdoses; McKinsey & Company settlement funds aid response to opioid epidemic. Wisconsin Department of Health Services. Published August 10, 2021. Accessed January 12, 2022. https://www.dhs.wisconsin.gov/news/releases/081021.htm
7. Wisconsin Department of Health Services. Dose of reality: opioid data summary dashboard. Published August 6, 2019. Updated February 15, 2022. Accessed March 7, 2022. https://www.dhs.wisconsin.gov/opioids/dashboards.htm
8. National Institute on Drug Abuse. Words matter – terms to use and avoid when talking about addiction. Published November 29, 2021. Accessed March 7, 2022. https://www.drugabuse.gov/nidamed-medical-health-professionals/health-professions-education/words-matter-terms-to-use-avoid-when-talking-about-addiction
9. Quinlan J, Cox F. Acute pain management in patients with drug dependence syndrome. *Pain Rep.* 2017;2(4):e611. doi:10.1097/PR9.0000000000000611
10. Recovery Research Institute. *Addictionary*. Published January 1, 2017. Accessed March 7, 2022. https://www.recoveryanswers.org/addiction-ary/
11. Buresh M, Ratner J, Zgierska A, Gordin V, Alvanzo A. Treating perioperative and acute pain in patients on buprenorphine: narrative literature review and practice recommendations. *J Gen Intern Med*. 2020;35(12):3635-3643. doi:10.1007/s11606-020-06115-3
12. Kumar R, Viswanath O, Saadabadi A. Buprenorphine. In: StatPearls. *NCBI Bookshelf version.* StatPearls Publishing: May 2, 2022. Accessed June 15, 2022.
13. Velander JR. Suboxone: rationale, science, misconceptions. *Ochsner J.* 2018;18(1):23-29. doi:10.1043/TOJ-17-0095
14. Naloxone. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed June 15, 2022. http://online.lexi.com
15. Substance Abuse and Mental Health Services Administration. *Buprenorphine.* Published August 20, 2020. Updated April 21, 2022. Accessed June 15, 2022. https://www.samhsa.gov/medication-assisted-treatment/medications-counseling-related-conditions/buprenorphine
16. American Society of Addiction Medication (ASAM). The ASAM national practice guideline for the treatment of opioid use disorder: 2020 Focused Update. *J Addict Med.* 2020;14(2S)(suppl 1):1-91. doi:10.1097/ADM.0000000000000633
17. Substance Abuse and Mental Health Services Administration. Medications for opioid use disorder for healthcare and addiction professionals, policymakers, patients, and families – treatment improvement protocol 63. Published August 3, 2021. Accessed January 10, 2022. https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-002.pdf
18. Quaye A, Potter K, Roth S, Acampora G, Mao J, Zhang Y. Perioperative continuation of buprenorphine at low-moderate doses was associated with lower postoperative pain scores and decreased outpatient opioid dispensing compared with buprenorphine discontinuation. *Pain Med.* 2020;21(9):1955-1960. doi:10.1093/pm/pnaa020
19. Lembke A, Ottestad E, Schmiesing C. Patients maintained on buprenorphine for opioid use disorder should continue buprenorphine through the perioperative period. *Pain Med.* 2019;20(3):425-428. doi:10.1093/pm/pny019
20. Haber LA, DeFries T, Martin M. Things we do for no reason™: discontinuing buprenorphine when treating acute pain. *J Hosp Med.* 2019;14(10):633-635. doi:10.12788/jhm.3265
21. Kohan L, Potru S, Barreveld AM, et al. Buprenorphine management in the perioperative period: educational review and recommendations from a multisociety expert panel. *Reg Anesth Pain Med.* 2021;46(10):840-859. doi:10.1136/rapm-2021-103007