Things We Do for No Reason™: Discontinuing Buprenorphine When Treating Acute Pain

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR™) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR™ series do not represent "black and white" conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CLINICAL SCENARIO

A 40-year-old woman with a history of opioid use disorder (OUD) on buprenorphine-naloxone treatment is admitted to medicine following incision and drainage of a large forearm abscess with surrounding cellulitis. The patient reports severe pain following the procedure, which is not relieved by ibuprofen. The admitting hospitalist orders a pain regimen for the patient, which includes oral and intravenous hydromorphone and discontinues the patient's buprenorphine-naloxone so that the short-acting opioids can take effect.

BACKGROUND

Medications to treat OUD include methadone, buprenorphine, and extended-release naltrexone. Buprenorphine is a Schedule III medication under the United States Food and Drug Administration that reduces opioid cravings, subsequently decreasing drug use[1] and opioid-related overdose deaths.[2] It has a favorable safety profile and can be prescribed for OUD in an office-based, outpatient setting since the Drug Addiction Treatment Act of 2000 (DATA 2000). Due to extensive first-pass metabolism, buprenorphine for OUD is typically administered sublingually, either alone or in a fixed combination with naloxone.

WHY YOU MIGHT THINK YOU SHOULD HOLD BUPRENORPHINE WHEN TREATING ACUTE PAIN

Buprenorphine is a partial opioid agonist with a long half-life and high affinity for the mu opioid receptor. Given these properties, prior recommendations assumed that buprenorphine blocked the effectiveness of additional opioid agonists.[3,4] In 2004, guidelines by the Department of Health and Human Service Center for Substance Abuse Treatment recommended discontinuing buprenorphine in patients taking opioid pain medications.[5] These suggestions were based on limited case reports describing difficulty controlling pain in patients with OUD with a high opioid tolerance who were receiving buprenorphine.[6]

Providers may hold buprenorphine when treating acute pain out of concern it could precipitate withdrawal by displacing full opioid agonists from the mu receptor. Providers may also believe that the naloxone component in the most commonly prescribed formulation, buprenorphine-naloxone, blocks the effects of opioid analgesics. Evolving understanding of buprenorphine pharmacology and the absence of high-quality evidence has resulted in providers holding buprenorphine in the setting of acute pain.

Finally, providers without dedicated training may feel they lack the necessary qualifications to prescribe buprenorphine in the inpatient setting. DATA 2000 requires mandatory X waiver training for physicians, nurse practitioners, and physician assistants to prescribe outpatient buprenorphine for OUD treatment outside of specialized opioid treatment programs.

WHY DISCONTINUING BUPRENORPHINE WHEN TREATING ACUTE PAIN IS NOT NECESSARY

Despite buprenorphine's high affinity at the mu receptor, additional receptors remain available for full opioid agonists to bind and activate,[6] providing effective pain relief even in patients using buprenorphine. In contrast to the 2004 Department of Health and Human Service guidelines, subsequent clinical studies have demonstrated that concurrent use of opioid analgesics is effective for patients maintained on buprenorphine, similar to patients on other forms of OUD treatment such as methadone.[7,8]

Precipitated withdrawal only occurs when buprenorphine is newly introduced to patients with already circulating opioids. Patients receiving buprenorphine-naloxone can also be exposed to opioids without precipitated withdrawal from the naloxone component, as naloxone is not absorbed via sublingual or buccal administration, but only present in the formulation to dissuade intravenous administration of the medication.

Even in the perioperative period, there is insufficient evidence to support the discontinuation of buprenorphine.[9] Stud-

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ies in this patient population have found that patients receiving buprenorphine may require higher doses of short-acting opioids to achieve adequate analgesia, but they experience similar pain control, lengths of stay, and functional outcomes to controls.[10] Despite variable perioperative management of buprenorphine,[11] protocols at major medical centers now recommend continuing or dose adjusting buprenorphine in the perioperative period rather than discontinuing.[12-14]

Patients physically dependent on opioid agonists, including buprenorphine, must be maintained on a daily equivalent opioid dose to avoid experiencing withdrawal. This maintenance requirement must be met before any analgesic effect for acute pain is obtained with additional opioids. Temporarily discontinuing buprenorphine introduces unnecessary complexity to a hospitalization, places the patient at risk of exacerbation of pain, opioid withdrawal, and predisposes the patient to return to use and overdose if not resumed before hospital discharge.[5]

Finally, clinicians do not require additional training or an X waiver to administer buprenorphine to hospitalized patients. These requirements are limited to providers managing buprenorphine in the outpatient setting or those prescribing buprenorphine to patients to take postdischarge. Hospitalists frequently prescribe opioid medications in the inpatient setting with similar or greater safety risk profiles to buprenorphine.

WHEN YOU SHOULD CONSIDER HOLDING BUPRENORPHINE

Providers may consider holding buprenorphine if a patient with OUD has not been taking buprenorphine before hospitalization and has severe acute pain needs. This history can be confirmed with the patient and the state's online prescription drug monitoring program. If further clarification is needed, this can be accomplished with a pharmacist and urine testing or by verifying with the patient's opioid treatment program, as some programs provide directly administered buprenorphine.

In cases where a patient may have stopped buprenorphine before admission but wants to restart it in the hospital, it is essential to ascertain when the patient last used an opioid. The buprenorphine reinduction should be timed to a sufficient number of hours since last opioid use and/or to when the patient shows signs of active withdrawal. The re-induction can take place before, during, or after an acute pain episode, depending on the individual circumstances.

Patient preference is extremely important in the management of both pain and OUD. After shared decision-making, some patients may ultimately opt to hold buprenorphine in certain situations or switch to an alternative treatment, such as methadone, during their hospitalization. Such adjustments should be made in conjunction with the patient, primary care provider, and pain or addiction medicine specialty consultation.

WHAT YOU SHOULD DO INSTEAD

For patients on buprenorphine admitted to the hospital with anticipated or unanticipated acute pain needs, hospitalists should continue buprenorphine. Continuation of buprenorphine meets a patient's baseline opioid requirement while still allowing the use of additional short-acting opioid agonists as needed for pain.[15]

As with all pain, multimodal pain management should be provided with adjunctive medications such as acetaminophen, nonsteroidal anti-inflammatory drugs, neuropathic agents, topical analgesics, and regional anesthesia.[8]

Acute pain can be addressed by taking advantage of buprenorphine's analgesic effects and adding additional short-acting opioids if needed.[15] Several options are available, including:

1. Continuing daily buprenorphine and prescribing short-acting opioid agonists, preferably those with high intrinsic activity at the mu receptor (such as morphine, fentanyl, or hydromorphone). Full opioid agonist doses to achieve analgesia for patients on buprenorphine will be higher than in opioid naïve patients due to tolerance.[16]
2. Dividing the total daily buprenorphine dose into three or four times per day dosing, since buprenorphine provides an analgesic effect lasting six to eight hours. Short-acting opioid agonists can still be prescribed on an as-needed basis for additional pain needs.
3. Temporarily increasing the total daily buprenorphine dose and dividing into three or four times per day dosing, as above. Short-acting opioid agonists can still be prescribed on an as-needed basis for additional pain needs.

It is essential to make a clear plan with the patient for initiation and discontinuation of short-acting opioid agonists or buprenorphine changes. Patients on buprenorphine should be managed collaboratively with the primary care provider or addiction specialist to coordinate prescribing and follow-up after discharge.

RECOMMENDATIONS

- Continue outpatient buprenorphine treatment for patients admitted with acute pain.
- Use adjunctive nonopioid pain medications and nonpharmacologic modalities to address acute pain.
- Adjust buprenorphine to address acute pain by dividing the total daily amount into three or four times a day dosing, and/or up-titrate the buprenorphine dose (federal prescribing regulations recommend a maximum of 24 mg daily, but state regulations may vary).
- Add short-acting opioid agonists on an as-needed basis in conjunction with a defined plan to discontinue short-acting opioid agonists to avoid a return to use.
- Make plans collaboratively with the patient and outpatient provider, and communicate medication changes and plan at discharge.

CONCLUSION

Concerning our case, the hospitalist can continue the patient's buprenorphine-naloxone, even with her acute pain needs. The patient has a baseline opioid requirement, fulfilled by continuing buprenorphine. Additional short-acting opioid agonists, such as hydromorphone, will provide analgesia for the patient, though the clinician should be aware that higher doses might

be required. The practice of holding buprenorphine during episodes of acute pain is not supported by current evidence and may predispose to inadequate analgesia, opioid withdrawal, and risk of return to use and death.[2]

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason™"? Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason™" topics by emailing TWDFNR@hospitalmedicine.org.

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References

1. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev*. 2014;(3):CD002207. https://doi.org/10.1002/14651858.CD002207.
2. Sordo L, Barrio G, Bravo M, et al. Morality risk during and after opioid substitution treatment: systemic review and meta-analysis of cohort studies. *BMJ*. 2017;357:1550. https://doi.org/10.1136/bmj.j1550.
3. Johnson RE, Fudula PJ, Payne R. Buprenorphine: considerations for pain management. *J Pain Symptom Manage*. 2005;29(3):297-326. https://doi.org/10.1016/j.jpainsymman.2004.07.005.
4. Marcelina JS, Rubinstein A. Continuous perioperative sublingual buprenorphine. *J Pain Palliat Care Pharmacother*. 2016;30(4):289-293. https://doi.org/10.1080/15360288.2016.1231734.
5. Greenwald MK, Johanson CE, Moody DE, et al. Effects of buprenorphine maintenance dose on mu-opioid receptor binding potential, plasma concentration and antagonist blockade in heroin-dependent volunteers. *Neuropsychopharmacology*. 2003;28(11):2000-2009. https://doi.org/10.1038/sj.npp.1300251.
6. 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. https://doi.org/10.1093/pm/pny019.
7. Kornfeld H, Manfredi L. Effectiveness of full agonist opioids in patients stabilized on buprenorphine undergoing major surgery: A case series. *Am J Ther*. 2010;17(5):523-528. https://doi.org/10.1097/MJT.0b013e3181be0804.
8. Harrison TK, Kornfeld H, Aggarwal AK, Lembke A. Perioperative considerations for the patient with opioid use disorder on buprenorphine, methadone, or naltrexone maintenance therapy. *Anesthesiol Clin*. 2018;36(3):345-359. https://doi.org/10.1016/j.anclin.2018.04.002.
9. Goel A, Azargive S, Lamba W, et al. The perioperative patient on buprenorphine: a systematic review of perioperative management strategies and patient outcomes. *Can J Anesth*. 2019; 66(2):201-217. https://doi.org/10.1007/s12630-018-1255-3.
10. Hansen LE, Stone GL, Matson CA, Tybor DJ, Pevear ME, Smith EL. Total joint arthroplasty in patients taking methadone or buprenorphine/naloxone preoperatively for prior heroin addiction: a prospective matched cohort study. *J Arthroplasty*. 2016;31(8):1698-1701. https://doi.org/10.1016/j.arth.2016.01.032.
11. Jonan AB, Kaye AD, Urman RD. Buprenorphine formulations: clinical best practice strategies recommendations for perioperative management of patients undergoing surgical or interventional pain procedures. *Pain Physician*. 2018;21(1):E1-12.
12. Quaye AN, Zhang Y. Perioperative management of buprenorphine: solving the conundrum. *Pain Med*. 2018. https://doi.org/10.1093/pm/pny217.
13. Silva MJ, Rubinstein A. Continuous perioperative sublingual buprenorphine. *J Pain Palliative Care Pharmacother*. 2016;30(4):289-293. https://doi.org/10.1080/15360288.2016.1231734.
14. Kampman K, Jarvis M. ASAM National practice guidelines for the use of medications in the treatment of addiction involving opioid use. *J Addict Med*. 2015;9(5):358-367. https://doi.org/10.1097/ADM.0000000000000166.
15. Childers JW, Arnold RM. Treatment of pain in patients taking buprenorphine for opioid addiction. *J Palliat Med*. 2012;15(5):613-614. https://doi.org/10.1089/jpm.2012.9591.
16. Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med*. 2006;144(2):127-134. https://doi.org/10.7326/0003-4819-144-2-200601170-00010