Providers Clinical Support System

PCSS Guidance

Topic: Treatment of Acute Pain in Patients Receiving Buprenorphine/Naloxone

Original Author: David Fiellin, M.D.

Last Updated: 03/24/22 (A. Benjamin Srivastava, M.D.)

Guideline Coverage:
This topic is also addressed in:

(1) SAMHSA Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction (TIP 40), page 75-76. http://www.ncbi.nlm.nih.gov/books/NBK64245/pdf/TOC.pdf
(2) Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. HHS Publication No. (SMA) 12-4214. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2005. Available online at: http://www.ncbi.nlm.nih.gov/books/NBK64164/pdf/TOC.pdf

Clinical Question:
How do I manage acute pain in a patient receiving buprenorphine/naloxone (bup/nx; Suboxone, Zubsolv) for the treatment of opioid dependence?

Background:
Sublingual buprenorphine/naloxone (Bup/nx), a partial agonist at the mu opioid receptor, is approved for addiction treatment and may be a useful strategy for pain management, particularly for opioid-treated chronic pain patients with non-adherence behaviors. In Europe, transdermal buprenorphine is commonly used for the management of non-cancer, moderate-to-severe chronic pain (Gatti et al., 2010, Likar et al., 2006). For sublingual buprenorphine, the duration of analgesic effect is limited to 6-8 hours; thus, pain management with buprenorphine would require dosing on a TID or QID schedule. As a mu agonist, buprenorphine effectively blocks, or significantly attenuates, the analgesic properties of other opioids that could be use to treat acute pain. In addition, providing buprenorphine can result in precipitated withdrawal in a patient who has recently taken a full agonist opioid medication to treat acute pain.

Emerging Evidence for Management of Acute Pain in Buprenorphine-maintained Individuals:
As the use of buprenorphine or buprenorphine/naloxone agonist treatment for opioid dependence has increased in the past decade, managing acute and sub-acute post-operative pain in such patients has become a recognized clinical challenge. The high-affinity mu-receptor binding of buprenorphine renders other opioids ineffective or reduces their efficacy. Yet it is important to continue opioid substitution therapy for patients undergoing surgery. Conventionally, most algorithms have recommended discontinuation of buprenorphine prior to surgery; however recent evidence suggests that a buprenorphine dose reduction coupled with full mu opioid receptor agonist treatment may be a tenable solution for maintaining adequate analgesia without increasing risks associated with discontinuation (OUD relapse, difficulties with buprenorphine re-initiation post-surgery). (Warner et al 2020, Lembke 2019) A dose of 8-12mg of buprenorphine may represent the ideal dose that allows for full agonist analgesia without necessitating buprenorphine discontinuation (Greenwald 2003). In patients taking buprenorphine (Suboxone, Subutex, Zubsolv) who require oral surgery, it is important to be certain that procedural sedation and analgesia is sufficient, and to be aware of the risk of significant interactions between buprenorphine and other opioids, in order to avoid perioperative complications (Wasson et al., 2013).

If buprenorphine is discontinued, re-starting it while there is a full opioid agonist present can precipitate acute opioid withdrawal. Thus, resuming buprenorphine maintenance should be deferred until the opioid being administered for acute pain is withdrawn. The general principles of buprenorphine induction will then be applicable (see PCSS-MAT Clinical Guidance on this topic; Lee at al., 2009). In general, it is necessary to wait 12-18 hours after administration of a short opioid, and 24-36 hours after administration of a long-acting opioid. Buprenorphine should be resumed by starting with a small test dose

of 1-2 mg and observing for signs and symptoms of opioid withdrawal. If the patient tolerates the dose well (relief of withdrawal, either temporary or sustained), then a second dose of 2-4 mg can be given, and the dose quickly titrated up over the next 1-2 days to achieve the previous maintenance dose.

It is important to distinguish the management of acute pain in patients taking buprenorphine from the use of buprenorphine in patients with chronic pain. In treatment settings for opioid dependence such as methadone programs or residential treatment, rates of current pain are as high as 80% (Rosenblum et al. 2003). Buprenorphine is FDA approved for chronic pain, whereas buprenorphine/naloxone is often used off label for the treatment of chronic pain (Rosen et al, 2014). Recommendations from the United States Department of Health and Human Services indicate that buprenorphine is appropriate for patients with co-morbid OUD and chronic pain (US Department of Health and Human Services, 2019). A recent meta-analysis showed a small effect size on reduction in pain in patients with chronic pain and OUD and moderate to large effect sizes in reducing pain in patients with chronic pain without OUD, suggesting that more investigation in the treatment of co-occurring OUD and chronic pain with buprenorphine is warranted (Lazaridou et al 2020).

General Principles:
Inform patient of your awareness of his or her addiction and provide reassurance that a history of opioid addiction will not be an obstacle to acute pain management. Include the patient in the decision-making process to allay anxiety about relapse. Offer addiction counseling as needed. Patients who are opioid dependent should not be denied pain treatment with opioids when medically indicated. Maintenance opioids should not be expected to adequately treat new onset acute pain, and discontinuation of buprenorphine/naloxone in patients experiencing acute pain will increase the patient's requirement for acute analgesic relief. Patient-controlled anesthesia (PCA) can be used in opioid-dependent patients with acute pain. To avoid precipitated withdrawal, resuming buprenorphine maintenance should be deferred until the opioid being administered for acute pain is withdrawn.

Recommendations:
Level of evidence: **Low – moderate: expert opinion/clinical experience, non-controlled trials, and small controlled trials**

For patients receiving bup/nx who develop or are anticipated to have acute and limited (e.g. 2 hours to 2 weeks) pain that will not be adequately treated with non-opioid analgesia, the following steps are recommended:

1. Anticipated pain (e.g. elective surgery, tooth extraction)
    - Reduce buprenorphine/naloxone to 8-12mg 24-36 hours prior to anticipated need for analgesia
    - Provide adequate opioid analgesia, titrate to effect. Given risks of opioid relapse with discontinuation of buprenorphine and difficulty of re-initiation after surgery, bup/nx discontinuation is not recommended. It is good practice to know the usual dosesneeded for patients undergoing the planned procedure. Discuss with your colleagues and remember that patients who are opioid dependent and who are currently bup/nx will likely need higher-than-usual doses of opioid analgesics due to their physical tolerance and/or narcotic blockade from bup/nx.
    - Discontinue opioid analgesia once pain has remitted or can be managed with non-opioid analgesia.
    - If bup/nx was discontinued, allow patient to experience mild to moderate opioid withdrawal and re-induce patient onto bup/nx as per usual induction protocol.

2. Unanticipated pain (e.g. major trauma, renal colic, acute fracture)
    - Determine when the last dose of bup/nx was given.
    - For acute trauma, options to consider: regional anesthesia, increased dose of buprenorphine, high potency opioidsuch as fentanyl, providing alternate opioid agonist treatment such as methadone during period

of pain management.

- If opioid analgesia is needed, Reduce bup/nx to 8-12mg 24-36 hours prior to anticipated need for analgesia. Provide adequate opioid analgesia, titrate to effect. It is good practice to know the usual dosesneeded for patients who experience this event. Discuss with your colleagues and remember that patients who are opioid dependent and who are taking bup/nx will likely need higher than usual doses of opioid analgesics due to their physical tolerance and/or narcotic blockade from recent doses of bup/nx.
- Monitor/caution patients regarding the potential for over-sedation during treatment with both bup/nx and opioid analgesics. While some effect of a full agonist may be blocked by buprenorphine, the full agonist effect may become clinically evident.
- If buprenorphine is discontinued, discontinue opioid analgesia once pain has remitted or can be managed with non-opioidanalgesia. Then Allow patient to experience mild-to-moderate opioid withdrawal for safe re-initiation of bup/nx, and re-induce patient onto bup/nx as per usual induction procedure.

References:

Center for Substance Abuse Treatment. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. Treatment Improvement Protocol (TIP) Series 40. DHHS Publication No. (SMA) 04-3939. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2004. Available online at http://www.ncbi.nlm.nih.gov/books/NBK64245/pdf/TOC.pdf

Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. HHS Publication No. (SMA) 12-4214. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2005. Available online at http://www.ncbi.nlm.nih.gov/books/NBK64164/pdf/TOC.pdf

Daitch J, Frey ME, Silver D, Mitnik C, Daitch D, Pergolizzi J Jr. Conversion of chronic pain patients from full-opioid agonists to sublingual buprenorphine. Pain Physician 2013; 15(3 Suppl):ES59-66.

Gatti A, Dauri M, Leonardis F, Longo G, Marinangeli F, Mammucari M, Sabat AF. Transdermal buprenorphine in non-oncological moderate-to-severe chronic pain. Clinical Drug Investigation 2010; 30 Suppl 2:31-38.

Greenwald MK, Johanson CE, Moody DE, Woods JH, Kilbourn MR, Koeppe RA, Schuster CR, Zubieta JK. Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. Neuropsychopharmacology. 2003 Nov;28(11):2000-9. doi: 10.1038/sj.npp.1300251. PMID: 12902992.

Lazaridou A, Paschali M, Edwards RR, Gilligan C. Is Buprenorphine Effective for Chronic Pain? A Systematic Review and Meta-analysis. Pain Med. 2020 Dec 25;21(12):3691-3699. doi: 10.1093/pm/pnaa089. PMID: 32330264.

Lee JD, Grossman E, DiRocco D, Gourevitch MN. Home buprenorphine/naloxone induction in primary care. Journal of General Internal Medicine 2009; 24(2): 226-232.

Lembke A, Ottestad E, Schmiesing C. Patients Maintained on Buprenorphine for Opioid Use Disorder Should Continue Buprenorphine Through the Perioperative Period. Pain Med. 2019 Mar 1;20(3):425-428. doi: 10.1093/pm/pny019. PMID: 29452378; PMCID: PMC6387981.

Likar R, Kayser H, Sittl R. Long-term management of chronic pain with transdermal buprenorphine: a multi-center, open-label, follow-up study in patients from three short-term clinical trials. Clinical Therapeutics 2006; 28(6):943-952.

Macintyre PE, Russell RA, Usher KA, Gaughwin M, Huxtable CA. Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. Anaesthesia and Intensive Care 2013; 41(2):222-230.

Neumann AM, Blondell RD, Jaanimagi U, Giambrone AK, Homish GG, Lozano JR, Kowalik U, Azardfard M. A preliminary study comparing methadone and buprenorphine in patients with chronic pain and coexist opioid addiction. Journal of Addictive Disorders 2013; 32(1):68-78.

Rosen K, Gutierrez A, Haller D, Potter JS. Sublingual buprenorphine for chronic pain: a survey of clinician prescribing practices. Clinical Journal of Pain 2014; 30(4): 295-300.

Rosenblum A, Cruciani RA, Strain EC, Cleland CM, Joseph H, Magura S, Marsch LA, McNicholas LF, Savage SR Sundaram A, Portenoy RK. Sublingual buprenorphine/naloxone for chronic pain in at-risk patients: development and pilot test of a clinical protocol. Journal of Opioid Management 2012; 8(6):369-382.

Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RL. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA 2003; 289: 2370-2378.

Roux P, Sullivan MA, Cohen J, Fugon L, Jones JD, Vosburg SK, Cooper ZD, Manubay JM, Mogali S,

Comer SD. Buprenorphine/naloxone as a promising therapeutic option for opioid abusing patients with chronic pain: Reduction of pain, opioid withdrawal symptoms, and abuse liability of oral oxycodone. Pain 2013; 154(8):1442-1448.
US Department of Health and Human Services. Pain Management Best Practices Inter-Agency Task Force report: updates, gaps, inconsistencies, and recommendations. 2019. https://www.hhs.gov/sites/default/files/pmtf-final-report-2019-05-23.pdf (accessed Dec 20, 2019).
Warner NS, Warner MA, Cunningham JL, Gazelka HM, Hooten WM, Kolla BP, Warner DO. A Practical Approach for the Management of the Mixed Opioid Agonist-Antagonist Buprenorphine During Acute Pain and Surgery. Mayo Clin Proc. 2020 Jun;95(6):1253-1267. doi: 10.1016/j.mayocp.2019.10.007. Epub 2020 Feb 13. PMID: 32061413.
Wasson M, Beirne OR. Buprenorphine therapy: an increasing challenge in oral and maxillofacial surgery. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology 2013; 116(2):142-146.

PCSS Guidance's use the following levels of evidence*:
High = Further research is very unlikely to change our confidence in the estimate of effect
Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low = Any estimate of effect is very uncertain.

Type of evidence:
Randomized trial = **high**
Observational study = **low**
Any other evidence = **very low**

* Grading quality of evidence and strength of recommendations
British Medical Journal. 2004:328:1490-