Review

Perioperative Buprenorphine Management and Post-Operative Pain Outcomes: A Retrospective Study with Literature Review and Recommendations

Amruta Desai , Shruti Parikh * , Sergio Bergese

Posted Date: 21 May 2024

doi: 10.20944/preprints202405.1346.v1

Keywords: buprenorphine; perioperative medicine; chronic pain; opioid use disorder

Review

Perioperative Buprenorphine Management and Post-Operative Pain Outcomes: A Retrospective Study with Literature Review and Recommendations

Amruta Desai, Shruti Parikh * and Sergio Bergese

Department of Anesthesiology, Stony Brook Medicine, 101 Nicolls Rd Stony Brook, NY 11794
* Correspondence: shruti.parikh@stonybrookmedicine.edu

Abstract: The prevalence of patients on buprenorphine therapy presenting for elective surgery has increased. Buprenorphine is a widely used medication for management of patients with chronic pain. It is also used for maintenance therapy for patients with a history of opioid use disorder (OUD). Due to lack of standardized protocol for managing patients on buprenorphine peri-operatively, we performed a retrospective analysis to compare pain score outcomes and post-operative opiate requirements between patients who continued versus discontinued buprenorphine. We identified 35 patients, 11 continued buprenorphine and 24 discontinued buprenorphine. The average Post-Anesthesia Care Unit (PACU) pain score was 7.54 for those who discontinued pre-operative buprenorphine and 5.59 for those who continued (P value 0.0339). The average post-operative Morphine Milligram Equivalent (MME) use was 86.13 for those who continued pre-operative buprenorphine and was 107.70 for those who discontinued buprenorphine (P value 0.6439). The results from our study correlate with several previous studies which showed lower PACU pain scores in patients who continued buprenorphine. There is a benefit of decreased pain post-operatively when pre-operative buprenorphine is continued and having a decrease in relapse in those with a history of OUD.

Keywords: buprenorphine; perioperative medicine; chronic pain; opioid use disorder

1. Introduction

Opioid use disorder (OUD), a chronic neurobehavioral syndrome that causes a desire to misuse opioids despite the associated physical, emotional, and social impairment has caused a significant rise in opioid-related deaths within the last two decades [1]. Many of these individuals concurrently suffer from chronic pain. Issues attributed to undertreatment of chronic pain has led to an increase in the use of opioids and subsequently deaths from overdose. In 2016, it was estimated that 50 million adults in the United States were diagnosed with chronic pain syndrome [2]. Patients recovering from OUD often require a combination of pharmacologic and non-pharmacologic therapies to remain in remission. Therefore, the prevalence of patients on buprenorphine therapy presenting for elective surgery has been steadily increasing [3]. There are a several options for pharmacologic agents that can be prescribed to prevent relapse. Of the available medication options, buprenorphine is commonly prescribed. Buprenorphine is a partial agonist of the mu opioid receptor with high receptor affinity [4]. Its partial agonism makes its safer than a full agonist in the event the patient abuses or overdoses on the medication. This is due to a ceiling effect on adverse side effects such, most importantly respiratory depression, in the event of an overdose. Additionally, its long duration of action makes it a suitable medication for treating OUD as it requires less frequent dosing and improves medication compliance. Buprenorphine is available in several formulations including tablets, sublingual films, transdermal patches and an extended-release, once-monthly subcutaneous injection allowing patients to choose an option that best fits their lifestyle. Sublingual film and tablets are the most widely used forms. Dosing starts at 2 to 4 mg per day and can be titrated up to 24 mg

 doi:10.20944/preprints202405.1346.v1

per day. Due to its long duration of action and relative safety profile, buprenorphine is also used for management of chronic pain in those who are not controlled with short acting opiates.

In the past, acute management of these medications, even in the acute setting, was often deferred to pain management subspecialists. Furthermore, chronic maintenance therapy is prescribed and monitored by pain management physicians. However, due to the increasing prevalence of OUD and patients on buprenorphine therapy presenting for surgery, all anesthesiologists should be prepared to manage these medications in the perioperative period. This includes preoperative buprenorphine dose management followed by intraoperative and postoperative pain control. When optimizing these patients preoperatively, there is currently no universal standard on how to adjust buprenorphine dosing in the days or weeks leading up to scheduled elective surgery. There are several approaches that are currently utilized amongst different institutions: buprenorphine can be continued at full dose leading up surgery, tapered to a lower dose over days leasing up surgery or discontinued prior to surgery [4]. Among these options, further investigation is needed to determine which one provides superior pain control post-operatively in this complex patient population. Discontinuing buprenorphine in the perioperative period increases the chance for relapse postoperatively in those with a history of OUD [5]. This risk of relapse should be seriously considered prior to discontinuing therapy for any patient who is in remission using buprenorphine. An additional consideration when discontinuing buprenorphine is that a short acting opiate will need to be prescribed to bridge between time of discontinuation to day of surgery. Inadequate dosing of this short-term medication can lead to potentially harmful consequences including opiate withdrawal symptoms or undertreatment of pain. Both of which can increase the chance of relapse and patients who are tapered from their maintenance dose require close monitoring during that time period.

In recent years at our institution, we have seen an increasing number of patients presenting for surgery while on buprenorphine therapy. There has not been a standardized plan for managing these patients peri-operatively. This led us to perform a retrospective analysis to compare pain score outcomes and post-operative opiate requirements between patients who continued buprenorphine versus patients who discontinued buprenorphine. We hypothesize that patients who continue buprenorphine perioperatively will have improved PACU pain scores and lower post operative MME use compared to patients who had therapy discontinued.

2. Materials and Methods

We received institutional review board approval to perform an electronic medical record analysis of patients on buprenorphine that were planned for elective surgery who presented to the institution's pre-operative services for optimization from April 2017 to June 2022. Those on buprenorphine transdermal patch were excluded due to the difference in dosing. We identified 35 patients from April 2017 to June 2022 who had elective surgery while on buprenorphine peri-operatively. Of these patients, 11 continued their full dose of buprenorphine and 24 discontinued buprenorphine. Even though these patients had surgery at our institution, many of them went to outside chronic pain physicians who managed their buprenorphine therapy. As a result, the decision to either continue or discontinue therapy was made by their outside physician and not by our pain or peri-operative physicians.

For each patient, the type of surgery was recorded. Surgeries were grouped into one of the following categories: Urology/Gynecology, General, Orthopedics (including spine), Neurosurgery or Thoracic. There were not any obstetric patients. The pre-operative dose of buprenorphine was recorded for each patient. The primary outcome measure was the variation in pain scores per patient via self-reported numerical pain rating scale of 0/10 to 10/10 pain, post-operatively. The pre-operative pain score was documented the day of the procedure and post-operative pain scores were collected every hour post-procedure by PACU nursing and were averaged. The secondary outcome measures included 48-hr post-operative MME non-buprenorphine opioid use. This was identified by calculating administered opioid medications charted in the EMR.

 doi:10.20944/preprints202405.1346.v1

The mean, standard deviation and standard error of the mean were performed for the average PACU pain score and 48-hour post operative MME use. Since there was a limited sample size, we used an unpaired t-test to evaluate if there was a significant difference between the two groups.

3. Results

3.1. Patient Demographics

There were 35 patients total that were evaluated for this retrospective observational study. Of the 35 patients, 11 patients continued their pre-operative buprenorphine at their prescribed dose and 24 patients discontinued their buprenorphine peri-operatively (Table 1). The average buprenorphine dose for those who discontinued buprenorphine pre-operatively was 9.75 and those who continued was 12.

Table 1. (A) Gender and Age distribution (B) Type of surgery.

A)					B)				
	Continued		Discontinued			Continued		Discontinued	
Male	6	54.50%	15	62.50%	Gen	3	27.30%	8	33.30%
Female	5	45.50%	9	37.50%	Ortho/Spine	4	36.40%	6	25.00%
					Uro/Gyn	4	36.40%	5	20.80%
20-39	3	27.30%	7	29.20%	Thoracic	0	0.00%	1	4.20%
40-59	6	54.50%	11	45.80%	Ophto	0	0.00%	1	4.20%
60+	2	18.20%	6	25.00%	ENT	0	0.00%	1	4.20%
					Neuro	0	0.00%	2	8.30%
OUD	8	72.70%	15	62.50%					
CP	3	27.30%	9	37.50%					

3.2. Average PACU Pain Score

The average PACU pain score was 7.54 for those who discontinued pre-operative buprenorphine and 5.59 for those who continued (Table 2). The P value for the unpaired t-test was 0.0339 and showed that there is a statistically significant difference between the two groups.

Table 2. Average PACU Pain Scores for Continued versus Discontinued Buprenorphine. P value =0.0339. 95% confidence interval of this difference: From -3.744 to -0.158.

Average PACU Pain Score		
	Continued Pre-operative Buprenorphine	**Discontinued Pre-operative Buprenorphine**
Mean	5.591	7.542
SD	2.709	2.284
SEM	0.817	0.466
N	11	24

3.3. Post-Operative MME Use

The average Post-operative MME use was 86.13 for those who continued pre-operative buprenorphine and was 107.70 for those who discontinued buprenorphine (Table 3). The P value for the unpaired T test was 0.6439 and did not show a statistical significance between both groups.

 doi:10.20944/preprints202405.1346.v1

Table 3. Post Operative MME Use for Continued versus Discontinued Buprenorphine. P value =0.6439. 95% confidence interval of this difference: From -115.638 to 72.495

	Post-Operative MME Use	
	Continued Pre-operative Buprenorphine	**Discontinued Pre-operative Buprenorphine**
Mean	86.136	107.708
SD	154.368	113.024
SEM	46.544	23.071
N	11	24

4. Discussion

The growing opioid epidemic and patients suffering from chronic pain has allowed for many individuals to be prescribed buprenorphine. From 2010-2016, annual prescriptions for buprenorphine have more than doubled [3]. Therefore, anesthesiologists are frequently encountering these patients peri-operatively and necessitate more guidance on their management.

Patients with OUD and/or chronic pain have high rates of hospitalization with long lengths of stay and escalating healthcare costs [3]. These patients also will present for surgery and their peri-operative management can be complex. This along with current national variability in the practice of peri-operative buprenorphine management sparked interest in this study and review of literature.

In evaluating available literature, a few studies have shown patients who continued their prescribed dose of buprenorphine pre-operatively had lower pain scores post-operatively compared to patients who discontinued [6–8]. One study showed no significant difference in post-operative pain scores between continued versus discontinued patients [4]. In patients on high dose buprenorphine, which was defined as greater than 16 mg per day, post-operative opiate requirements were not increased when buprenorphine was continued at full dose leading up to surgery [3]. This finding was attributed to the innate analgesic properties of buprenorphine. Furthermore, when buprenorphine was continued, inpatient post-operative opioid use and PCA use was lower compared to patients where buprenorphine was stopped [3]. Additionally, patients were discharged home with fewer opioid prescriptions when they continued buprenorphine [4,7,9,10]. Adjuvant pain medication use was also higher when buprenorphine was discontinued [8,11,13]. Additionally, in a case series of 8 parturients who were continued on buprenorphine leading up to delivery, all had adequate pain control following delivery with either a patient controlled epidural analgesia (PCEA) or patient-controlled analgesia (PCA) while continuing their buprenorphine postpartum [11].

Our retrospective data is comparable to those few studies that show a significant decrease in post-operative PACU pain scores in patients who continued their pre-operative dose of buprenorphine compared to those who discontinued. Additionally, there was a difference between average post-op MME use however, there was no statistically significant difference between both groups. The result from this retrospective analysis supports advising patients to continue their medication peri-operatively and highlights the analgesic property of buprenorphine.

Continuing buprenorphine peri-operatively may have additional benefits. Patients who discontinue buprenorphine for any reason have an increased risk for pain and withdrawal due to losing their baseline therapeutic dose. For those with a history of OUD, there is an increased risk of relapse with discontinuing buprenorphine. Therefore, a complete pre-operative evaluation as well as a discussion of peri-operative management with the patient, anesthesiologist, and pain management teams are crucial.

It is recommended that a thorough pre-operative evaluation occur for these patients that include obtaining a history, performing a physical exam, and discussing any medications where cessation could lead to withdrawal such as buprenorphine. Reviewing urine toxicology and prescription monitoring programs could be advantageous if there is a possibility of OUD as well.

 doi:10.20944/preprints202405.1346.v1

Patients are especially vulnerable during the peri-operative period if they discontinue their medication and now face increased pain after surgery which could result in drug cravings if buprenorphine is prescribed for OUD. Continuing buprenorphine and providing adequate postoperative analgesia for these patients could prevent undertreatment of pain. Improved pain control post-operatively also decreases unplanned admissions for inadequate pain control and improves patient satisfaction [12,13].

Many physicians during the peri-operative period have uncertainty regarding treatment with a full mu-opioid agonist being able to displace buprenorphine from the mu receptor to adequately treat these patients. Buprenorphine does have a high affinity for the mu-opioid receptor, has a long half-life (24-42 hours for sublingual or buccal administration; 26 hours for transdermal administration and 43-60 days for the slow-release subcutaneous injection), is highly lipophilic, and slowly dissociates from the receptor [3]. Oral buprenorphine takes 2–3 days to be eliminated from the body and it is metabolized completely by the liver to norbuprenorphine, an active metabolite with some weak analgesic activity [3]. These findings allowed the previous recommendations of discontinuing buprenorphine prior to anticipated surgery. This influenced the mainstream practice of discontinuing buprenorphine prior to surgery. However, this was the result of case reports depicting the undertreatment of pain in this patient population and may suggest the difficulty in managing opioid-tolerant or dependent patients than the effects of buprenorphine itself [3]. It has been documented that even though buprenorphine has high affinity at the mu receptor, some receptors remain unoccupied and can continue to bind full mu agonists needed to treat pain in the perioperative period [3].

This retrospective analysis and review of current literature, the perioperative management of buprenorphine appears to be changing from holding buprenorphine to allow for mu receptors to free up, to the consensus of continuing buprenorphine with or without naloxone.

Additionally, it could be beneficial to further investigate these outcomes in future studies specifically tracking unplanned admissions, satisfaction with pain control, as well as time to discharge between the two groups.

Despite available literature with retrospective data, prospective data is still scarce on pre-operative management of buprenorphine. Randomized controlled trials are necessary to further assess the effects of continuing buprenorphine in this specific population of patients. In doing so, a standardized time frame should be used to discontinue, or potentially taper, buprenorphine prior to scheduled surgery which would eliminate the variability among subjects we had with our retrospective data to compare with those patients who continue the medication. A balanced study cohort of patients on buprenorphine for OUD and chronic pain would further help identify differences in pain outcomes in the two groups that could affect buprenorphine perioperatively as dosing can vary between OUD and chronic pain patients.

Additionally, there were limitations to our retrospective study. For patients who discontinued their pre-operative buprenorphine dose, there was no standard protocol that was followed. The process of tapering buprenorphine was discovered to be varied in terms of duration and dosing since this was performed by various outpatient chronic pain physicians. Patients in this group stopped their medication anywhere from one to seven days prior to their scheduled surgery. Of these patients, some were instructed by their medical providers to discontinue their medication while others self-discontinued their medication contributing to the variability of timing of discontinuation. Regional anesthetics were not accounted for when considering post-operative pain management and pain outcomes. Non-opiate adjuncts including ketamine were also not included. Both latter options can affect post-operative pain scores and post-operative opioid use. Of the 35 patients, three patients received a PCEA post-operatively and nine received a PCA. Due to the way these medications are recorded in our electronic medical record (EMR), the opioid doses administered were unable to be added in the post-operative MME totals which affected our post-operative total MME use values and statistics. Patients on PCEA had improved pain scores however the sample size was low, and these results did not reach significance. Post-discharge MME prescriptions are available via New York State Pre-scription Monitoring Program and would have been valuable data to consider. Unfortunately,

 doi:10.20944/preprints202405.1346.v1

these records are available for one year prior and therefore were not available for patients who had surgery over one year ago since our study period spanned several years. Lastly, this study had a small sample size, and it would be beneficial to evaluate outcomes in a larger group.

There is clearly a benefit of decreased pain post-operatively when pre-operative buprenorphine is continued as well as having a decrease in relapse in those who use the medication for a history of substance use disorder. However, further investigation is needed to create standardized guidelines in treating this growing population of patients when they present for elective surgery.

5. Conclusions

This retrospective study provides additional evidence for patients to continue buprenorphine at their prescribed dose in the peri-operative period to improve pain control post-operatively, with significantly lower PACU pain scores.

Author Contributions: Conceptualization, A.D., S.P. and S.B.; methodology, A.D.; formal analysis, A.D. and S.P.; data curation, S.P.; writing—original draft preparation, A.D. and S.P.; writing—review and editing, A.D., S.P. and S.B. All authors have read and agreed to the published version of the manuscript.

- **Funding:** This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Stony Brook Research (protocol code IRB2022-00478 approved on 10/05/2022).

Informed Consent Statement: Informed Consent Statement: Informed consent was waived due to the retrospective nature of this study.

Data Availability Statement: The data presented in this study are available on request from the.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Quaye, Aurora MD; Mardmomen, Niayesh BS; Mogren, Grace BS; Ibrahim, Yussr MD; Richard, Janelle BA, CCRP; Zhang, Yi MD. Current State of Perioperative Buprenorphine Management—A National Provider Survey. Journal of Addiction Medicine 17(6):p 640-645, 11/12 2023. | DOI: 10.1097/ADM.0000000000001191
2. Sritapan Y, Clifford S, Bautista A. Perioperative Management of Patients on Buprenorphine and Methadone: A Narrative Review. Balkan Med J. 2020 Aug 11;37(5):247-252. doi: 10.4274/balkanmedj.galenos.2020.2020.5.2. Epub 2020 May 14. PMID: 32407063; PMCID: PMC7424191.
3. Kohan L, Potru S, Barreveld AM, Sprintz M, Lane O, Aryal A, Emerick T, Dopp A, Chhay S, Viscusi E. Buprenorphine management in the perioperative period: educational review and recommendations from a multisociety expert panel. Reg Anesth Pain Med. 2021 Oct;46(10):840-859. doi: 10.1136/rapm-2021-103007. Epub 2021 Aug 12. PMID: 34385292.
4. Li, Alice H. BA; Schmiesing, Cliff MD; Aggarwal, Anuj K. MD. Evidence for Continuing Buprenorphine in the Perioperative Period. The Clinical Journal of Pain 36(10):p 764-774, October 2020. | DOI: 10.1097/AJP.0000000000000858
5. Shulman M, Wai JM, Nunes EV. Buprenorphine Treatment for Opioid Use Disorder: An Overview. CNS Drugs. 2019 Jun;33(6):567-580. doi: 10.1007/s40263-019-00637-z. PMID: 31062259; PMCID: PMC6585403.
6. 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.
7. Komatsu R, Nash M, Peperzak KA, Wu J, Dinges EM, Bollag LA. Postoperative Pain and Opioid Dose Requirements in Patients on Sublingual Buprenorphine: A Retrospective Cohort Study for Comparison Between Postoperative Continuation and Discontinuation of Buprenorphine. Clin J Pain. 2021 Nov 1;38(2):108-113. doi: 10.1097/AJP.0000000000000996. PMID: 34723862.
8. Goel A, Azargive S, Lamba W, Bordman J, Englesakis M, Srikandarajah S, Ladha K, Di Renna T, Shanthanna H, Duggan S, Peng P, Hanlon J, Clarke H. The perioperative patient on buprenorphine: a

 doi:10.20944/preprints202405.1346.v1

systematic review of perioperative management strategies and patient outcomes. Can J Anaesth. 2019 Feb;66(2):201-217. English. doi: 10.1007/s12630-018-1255-3. Epub 2018 Nov 27. PMID: 30484167.

9. Mehta D, Thomas V, Johnson J, Scott B, Cortina S, Berger L. Continuation of Buprenorphine to Facilitate Postoperative Pain Management for Patients on Buprenorphine Opioid Agonist Therapy. Pain Physician. 2020 Mar;23(2):E163-E174. PMID: 32214293.
10. 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 Sep 1;21(9):1955-1960. doi: 10.1093/pm/pnaa020. PMID: 32167541.
11. Tith S, Bining G, Bollag L. Management of eight labor and delivery patients dependent on buprenorphine (Subutex™): A retrospective chart review. F1000Res. 2018 Jan 3;7:7. doi: 10.12688/f1000research.13350.2. PMID: 29527296; PMCID: PMC5820592.
12. Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, Ferri M, Pastor-Barriuso R. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ. 2017 Apr 26;357:j1550. doi: 10.1136/bmj.j1550. PMID: 28446428; PMCID: PMC5421454.
13. Quaye AN, Zhang Y. Perioperative Management of Buprenorphine: Solving the Conundrum. Pain Med. 2019 Jul 1;20(7):1395-1408. doi: 10.1093/pm/pny217. PMID: 30500943; PMCID: PMC7963209.