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Perioperative Buprenorphine Management and Postoperative Pain Outcomes: A Retrospective Study with Evidence-Based Recommendations

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Abstract: The prevalence of patients on buprenorphine therapy presenting for elective surgery has increased. Buprenorphine is a widely used medication for the management of patients with chronic pain. It is also used as maintenance therapy for patients with a history of opioid use disorder (OUD). Due to the lack of a standardized protocol for managing patients on buprenorphine perioperatively, we performed a retrospective analysis to compare pain score outcomes and postoperative opiate requirements between patients who continued buprenorphine versus patients who discontinued buprenorphine. We identified 35 patients: 11 continued buprenorphine and 24 discontinued buprenorphine. The average Post-Anesthesia Care Unit (PACU) pain score was 5.59 for those who continued buprenorphine and 7.54 for those who discontinued preoperative buprenorphine (p value 0.0339). The average postoperative morphine milligram equivalent (MME) use was 86.13 for those who continued preoperative buprenorphine and 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 postoperative pain when preoperative buprenorphine is continued, and a decreased possibility for relapse in those with a history of OUD.

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

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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 individuals with OUD concurrently suffer from chronic pain. Issues attributed to undertreatment of chronic pain have led to an increase in the use of opioids, and subsequently to 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 several 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 (Figure 1) [4]. Its partial agonism makes it 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, 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 per day. Due to its long duration of action and relative safety profile, buprenorphine is also used for the management of chronic pain in those whose pain is not controlled with short-acting opiates.

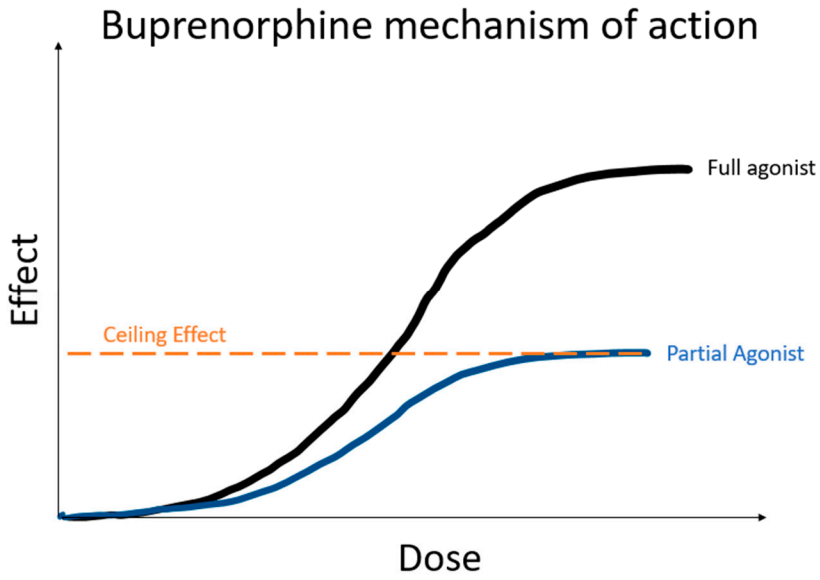

Figure 1. Partial agonist mechanism of action of buprenorphine compared to full agonist.

In the past, acute management of these medications, even in acute settings, 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 in different institutions: buprenorphine can be continued at the full dose leading up surgery, tapered to a lower dose over the days leading up surgery or discontinued prior to surgery [4]. Among these options, further investigation is needed to determine which one provides superior postoperative pain control in this complex patient population. Discontinuing buprenorphine in the perioperative period increases the chance for postoperative relapse 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 needs to be prescribed to bridge the period between the time of discontinuation and the day of surgery [3–5]. Inadequate dosing of this short-term medication can lead to potentially harmful consequences, including opiate withdrawal symptoms or undertreatment of pain. Both can increase the chance of relapse, and patients who are tapered from their maintenance dose require close monitoring during this 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 perioperatively. This led us to perform a retrospective analysis to compare pain score outcomes and postoperative opiate requirements between patients who continued buprenorphine versus patients who discontinued buprenorphine. We hypothesized that patients who continued buprenorphine perioperatively would have

improved PACU pain scores and lower postoperative MME use compared to patients whose therapy was discontinued.

2. Materials and Methods

We received institutional review board approval to perform an electronic medical record analysis of patients on buprenorphine who had planned elective surgery and presented to the institution's preoperative services for optimization from April 2017 to June 2022. Patients on a buprenorphine transdermal patch were excluded due to the difference in dosing attributed to the different route of delivery. We identified 35 patients from April 2017 to June 2022 who had elective surgery while perioperatively on buprenorphine. 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 perioperative physicians.

For each patient, the type of surgery was recorded. Each surgery was grouped into one of the following categories: urology/gynecology, general, orthopedic (including spine), neurosurgery or thoracic surgery, to account for differences in pain with different types of surgery. There were no obstetric patients. The preoperative dose of buprenorphine was recorded for each patient. The primary outcome measure was the variation in pain scores per patient via a self-reported numerical VAS pain rating scale of 0/10 to 10/10 pain, postoperatively. Preoperative pain scores were documented on the day of the procedure, and postoperative pain scores were collected every hour post-procedure by PACU nursing staff, and were averaged. Secondary outcome measures included 48 h postoperative MME non-buprenorphine opioid use. This was identified by calculating amounts of administered opioid medications charted in the EMR.

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

3. Results

3.1. Patient Demographics

In total, 35 patients were evaluated in this retrospective observational study. Of these 35 patients, 11 patients continued preoperative buprenorphine at their prescribed dose and 24 patients perioperatively discontinued their buprenorphine (Table 1). The average buprenorphine dose for those who continued buprenorphine was 12 mg, and for those who discontinued buprenorphine it was 9.75 mg.

Table 1. (**A**) Gender, age distribution and (**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 5.59 for those who continued preoperative buprenorphine and 7.54 for those who discontinued it (Table 2). The *p* value for the unpaired t-test was 0.0339, which showed that there was a statistically significant difference between the two groups.

Table 2. Average PACU VAS pain scores for continued versus discontinued buprenorphine groups gro. *p* value = 0.0339. 95% confidence interval of this difference: from −3.744 to −0.158.

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

3.3. Postoperative MME Use

The average postoperative MME use was 86.13 for those who continued preoperative buprenorphine and 107.70 for those who discontinued buprenorphine (Table 3). The *p* value for the unpaired t test was 0.6439, which did not show a statistical significance between the groups.

Table 3. Postoperative MME use for continued versus discontinued buprenorphine. *p* value = 0.6439. 95% confidence interval of this difference: from −115.638 to 72.495.

Postoperative MME Use		
	Continued Preoperative Buprenorphine	**Discontinued Preoperative 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 have lead to many individuals being prescribed buprenorphine. From 2010 to 2016, annual prescriptions for buprenorphine more than doubled [3]. Therefore, anesthesiologists frequently encounter these patients perioperatively, which necessitates more guidance in 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 present for surgery, and their perioperative management can be complex.

In evaluating the available literature, a few studies have that shown patients who continued their prescribed dose of buprenorphine preoperatively had lower postoperative pain scores compared to patients who discontinued buprenorphine [6–8]. One study showed no significant difference in postoperative pain scores between patients who continued buprenorphine versus those who discontinued it [4]. For patients on a high dose of buprenorphine, which was defined as greater than 16 mg per day, postoperative opiate requirements were not increased when buprenorphine was continued at the full dose leading up to surgery [3]. This finding was attributed to the innate analgesic properties of buprenorphine. Furthermore, when buprenorphine was continued, inpatient postoperative opioid use and PCA use were lower compared to patients whose 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 [8,11,12]. Also, in a case series of eight patients 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 [13]. Lastly, in a study of 2176 patients who underwent a surgical procedure while on continuous preoperative buprenorphine therapy, 176 (8.1%) who did not continue buprenorphine in the 14 days after discharge were more likely to have palliative status, higher Charlson comorbidity scores and less stable buprenorphine treatment over the past year post discharge [14]. Thus, perioperative buprenorphine maintenance has not been shown to result in poorer clinical outcomes after surgery [15].

Our retrospective data are comparable to those few studies that showed a significant decrease in postoperative PACU pain scores in patients who continued their preoperative dose of buprenorphine compared to those who discontinued it [6–8]. Additionally, there was a difference between average post-op MME use; however, there was no statistically significant difference between these groups. The result from this retrospective analysis supports advising patients to continue their medication perioperatively, and highlights the analgesic property of buprenorphine. The significant decrease in postoperative pain scores with continuation of buprenorphine indicates overall improved pain control in this population that often poses challenges for achieving adequate pain control.

Continuing buprenorphine perioperatively may have additional benefits. Patients who discontinue buprenorphine for any reason have an increased risk of pain and withdrawal due to losing their baseline therapeutic dose. For those with a history of OUD, there is an increased risk of relapse when discontinuing buprenorphine [3,4]. Therefore, a complete preoperative evaluation, as well as a discussion of perioperative management with the patient, anesthesiologist and pain management teams, are crucial. At our institution, the perioperative pathway for all patients on buprenorphine now includes continuing buprenorphine at the prescribed dose (Figure 2).

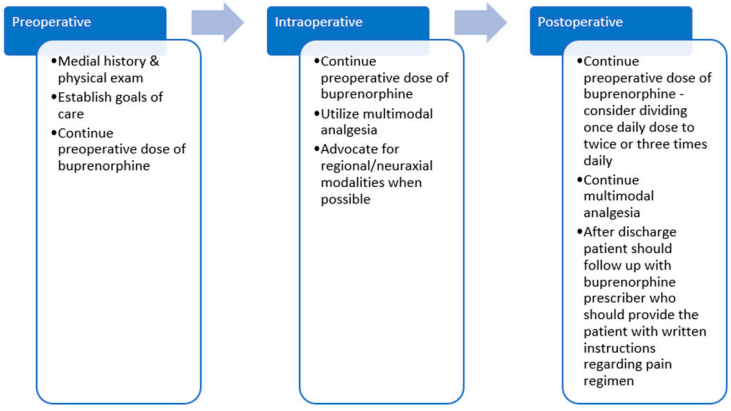

Figure 2. Perioperative recommendations for patients on buprenorphine.

Additionally, a multimodal pain management approach considering dexmedetomidine, acetaminophen, NSAIDs, gabapentinoids, muscle relaxants and ketamine has shown success in providing adequate perioperative pain control among patients taking buprenorphine for OUD [2]. Regional or neuraxial techniques are preferred in this population, as they can allow for targeted isolation of painful/noxious stimuli, which decreases systemic pain medication requirements and mitigating side effects [16]. Consideration should also be made for indwelling peripheral nerve catheters for continuous infusion of local anesthetic to provide longer-lasting relief.

Patients are especially vulnerable during the perioperative period if they discontinue their medication and 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

postoperative pain control also decreases unplanned admissions for inadequate pain control and improves patient satisfaction [12,13].

Buprenorphine does have a high affinity for the mu-opioid receptor and a long half-life (24–42 h for sublingual or buccal administration, 26 h for transdermal administration, and 43–60 days for slow-release subcutaneous injection). It 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 by the liver into 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 might have suggested the difficulty in managing opioid-tolerant or opioid-dependent patients rather 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 the full mu agonists needed to treat pain in the perioperative period [3].

The perioperative management of buprenorphine appears to be changing from the previous practice of holding buprenorphine with the intent of freeing up mu receptors. However, the consensus is now shifting towards continuing buprenorphine based on reviews of the current literature and retrospective analysis. 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. This would allow for a better understanding of gaps in current care and assess the benefits of new interventions.

Despite the available literature with retrospective data, prospective data is still scarce on preoperative management of buprenorphine. Randomized controlled trials are necessary to further assess the effects of continuing buprenorphine in this specific population of patients. Due to the nature of retrospective studies, there is inherent variability amongst groups that cannot be controlled for. With a randomized, prospective trial, 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 in 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, which could affect buprenorphine use perioperatively, as dosing can vary between OUD and chronic pain patients.

Additionally, there were limitations to our retrospective study. For patients who discontinued their preoperative buprenorphine dose, there was no standard protocol followed. The process of tapering buprenorphine was discovered to be varied in terms of duration and dosing, as 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 postoperative pain management and pain outcomes. Non-opiate adjuncts, including ketamine, were also not included. Both latter options can affect postoperative pain scores and postoperative opioid use. Of the 35 patients, 3 patients received a PCEA postoperatively and 9 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 to the postoperative MME totals, which affected our postoperative 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 the New York State Prescription Monitoring Program and would have been valuable data to consider. Unfortunately, these records are available for only one year prior, and therefore were not available for patients who had surgery over one

year ago, as 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 decreased postoperative pain when preoperative buprenorphine is continued. Improved pain control is important in this population to prevent relapse in those who use the medication for a history of substance use disorder. Buprenorphine administration needs a patient-centered multidisciplinary strategy that incorporates the risks and benefits of the many available perioperative therapy options in order to be successful [14]. However, further investigation is needed to create standardized guidelines for treating this growing population of patients when they present for elective surgery.

5. Conclusions

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

This limited retrospective study provides additional evidence for patients to continue buprenorphine at their prescribed dose in the perioperative period to improve postoperative pain control, with significantly lower PACU pain scores.

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

Data Availability Statement: Data presented in this study are available on request from the corresponding author.

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

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