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ORIGINAL ARTICLE

Neuraxial clonidine is not associated with lower post-cesarean opioid consumption or pain scores in parturients on chronic buprenorphine therapy: a retrospective cohort study

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Abstract

Purpose Adequate post-cesarean delivery analgesia can be difficult to achieve for women diagnosed with opioid use disorder receiving buprenorphine. We sought to determine if neuraxial clonidine administration is associated with decreased opioid consumption and pain scores following cesarean delivery in women receiving chronic buprenorphine therapy.

Methods This was a retrospective cohort study at a tertiary care teaching hospital of women undergoing cesarean delivery with or without neuraxial clonidine administration while receiving chronic buprenorphine. The primary outcome was opioid consumption (in morphine milligram equivalents) 0–6 h following cesarean delivery. Secondary outcomes included opioid consumption 0–24 h post-cesarean, median postoperative pain scores 0–24 h, and rates of intraoperative anesthetic supplementation. Multivariable analysis evaluating the adjusted effects of neuraxial clonidine on outcomes was conducted using linear regression, proportional odds model, and logistic regression separately.

Results 196 women met inclusion criteria, of which 145 (74%) received neuraxial clonidine while 51 (26%) did not. In univariate analysis, there was no significant difference in opioid consumption 0–6 h post-cesarean delivery between the clonidine (8 [IQR 0, 15]) and control (1 [IQR 0, 8]) groups ($P=0.14$). After adjusting for potential confounders, there remained no significant association with neuraxial clonidine administration 0–6 h (Difference in means 2.77, 95% CI [− 0.89 to 6.44], $P=0.14$) or 0–24 h (Difference in means 8.56, 95% CI [− 16.99 to 34.11], $P=0.51$).

Conclusion In parturients receiving chronic buprenorphine therapy at the time of cesarean delivery, neuraxial clonidine administration was not associated with decreased postoperative opioid consumption, median pain scores, or the need for intraoperative supplementation.

Keywords Chronic buprenorphine therapy · Neuraxial clonidine · Opioid use disorder · Post-cesarean analgesia

Introduction

Rates of opioid use disorder in pregnancy continue to rise in the United States, with nearly 1 in 100 women hospitalized for delivery diagnosed with opioid use or dependence [1]. Data shows that from 2010 to 2017 the number of parturients presenting with opioid-related diagnoses increased a remarkable 131% [1]. This concerning rise with important maternal and fetal implications parallels the prevalence of prescription opioid overdose deaths among women [2] as well as the incidence of neonatal abstinence syndrome [3]. Despite opioid use disorder during pregnancy being associated with increased maternal and neonatal morbidity and mortality [4], medication-assisted treatment with opioid agonists is recommended over medically supervised withdrawal due to

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overall improved maternal and fetal outcomes [5]. Buprenorphine is a partial μ-opioid receptor agonist with multiple advantages over methadone for this indication, including fewer adverse drug interactions; lower incidence of neonatal abstinence syndrome; and reduced risk of preterm birth, respiratory depression, sedation, abuse, and overdose [5–8]. Pharmacologic characteristics including long half-life and high receptor binding affinity, however, lead to challenges in providing adequate post-cesarean delivery pain control in women receiving chronic buprenorphine.

Retrospective studies have shown that women maintained on buprenorphine during pregnancy experience significantly higher post-cesarean delivery pain scores and opioid requirements [9, 10]. This finding is worrisome given that inadequate peripartum pain control interferes with maternal-newborn bonding and breastfeeding and is associated with the development of persistent post-cesarean delivery pain and postpartum depression [11–13].

Neuraxial clonidine is an α_2-adrenergic receptor agonist that has shown analgesic efficacy as a pharmacologic adjuvant to local anesthetics for cesarean anesthesia in patients without opioid use disorder or buprenorphine treatment [14, 15]. Given that neuraxial opioids commonly used for this indication may be less effective in patients on chronic buprenorphine, neuraxial clonidine may be especially helpful in this population; however, its use has not been well described in these patients.

We hypothesized that neuraxial clonidine would be associated with decreased opioid consumption 0–6 h post-cesarean delivery in women receiving chronic buprenorphine therapy (primary outcome) and would also decrease opioid consumption and median pain scores 0–24 h postoperatively as well as need for intraoperative anesthetic supplementation.

Materials and methods

Study approval was granted by the Vanderbilt University Medical Center Institutional Review Board on November 30, 2020 (Nashville, Tennessee; IRB Number 202318). As this was a retrospective observational chart review, informed written consent was waived.

By query of the electronic medical record database, we identified parturients receiving chronic buprenorphine treatment who underwent cesarean delivery at our institution between January 1, 2010 and December 31, 2020. Chronic buprenorphine use was defined as any patient who was prescribed and filled at least one outpatient prescription for buprenorphine prior to admission for delivery. Per the American College of Obstetricians and Gynecologists' guidelines, buprenorphine was continued preoperatively and throughout the perioperative period [5].

Study data was extracted via manual chart review by a study investigator or research assistant and entered into a secure study spreadsheet. Subjects were excluded if they required general anesthesia, cesarean-hysterectomy, or postoperative intensive care unit admission or if they received neuraxial clonidine during labor and within 6 h prior to cesarean but did not receive neuraxial clonidine intraoperatively. Those who received neuraxial clonidine during cesarean delivery were assigned to the clonidine group, while those who did not were assigned to the control group. All patients who received a combined spinal-epidural were administered intrathecal clonidine.

The primary outcome was opioid consumption (in morphine milligram equivalents, MME) during the first 6 h following cesarean delivery (0–6 h). Secondary outcomes included MME during the first 24 h post-cesarean (0–24 h), median postoperative pain scores (on numeric rating scale, NRS) 0–24 h, and rates of intraoperative anesthetic supplementation. Intravenous intraoperative anesthetic supplementation was defined as administration of propofol, ketamine, opioids, or benzodiazepines. Pain scores were collected by nursing staff during routine vital sign checks. As this was a retrospective study, intraoperative and postoperative management of all subjects was at the discretion of the treating physician and adherence to a standardized anesthetic protocol was not required. Standard postoperative orders included ibuprofen and acetaminophen administered as needed in an alternating pattern, and opioids were given for higher pain scores and patient request per nursing protocol. Neuraxial doses of clonidine as well as other adjuvants administered were consistent with those previously studied in the literature [16].

Univariate comparisons between the clonidine and control group were performed using the Pearson chi-square test, Fisher exact test, T-test, and Wilcoxon rank-sum test as appropriate. Variables were summarized using mean (standard deviation [SD]) and median (25–75th interquartile range [IQR]) for quantitative variables and counts (percentages) for qualitative variables. A multivariable analysis evaluating the adjusted effects of neuraxial clonidine on MME, median NRS pain scores, and rates of intraoperative anesthetic supplementation was conducted using linear regression, proportional odds model, and logistic regression separately, and accounting for the following potential confounding variables: age, parity, body mass index, number of prior cesarean deliveries, psychiatric comorbidities (yes/no), preadmission daily buprenorphine dose, buprenorphine dose 0–24 h postoperatively, surgery scheduling status, operative time, incision type, neuraxial type, truncal blocks, and other medication administrations (neuraxial morphine, neuraxial fentanyl, ketorolac, ibuprofen, acetaminophen, gabapentin). Operative time, age, and body mass index were modeled to allow the possibility of a nonlinear association with each

outcome. The neuraxial clonidine effect was summarized using an estimate (difference in means or odds ratios) with corresponding 95% confidence intervals and *P* values. In the sensitivity analysis, we implemented a propensity score weighting method to account for the potential confounding of the association between neuraxial clonidine and MME consumption. Multivariable logistic regression was used to estimate the propensity score for each patient, adjusting for the same confounding variables used in the primary analysis (age, parity, body mass index, number of prior cesarean deliveries, psychiatric comorbidities, pre-admission daily buprenorphine dose, buprenorphine dose 0–24 h postoperatively, surgery scheduling status, operative time, incision type, neuraxial type, truncal blocks, and other medication administrations). The propensity score matching weights were used to weight the contribution of each patient in the subsequent analysis. Balance checking was done using the standardized mean difference between groups; a successful weighting was demonstrated if the imbalance was improved in patient factors and the standardized mean difference was < 0.1. The adjusted effects of neuraxial clonidine on MME were examined using a propensity score weighted linear regression model. The neuraxial clonidine effect was summarized using the difference in means and 95% confidence interval.

All analyses were performed using the R Programming Language 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria). A *P* value of < 0.05 was considered a statistically significant difference.

Results

From 2010 to 2020, 196 parturients met inclusion criteria (Fig. 1), of which 145 (74%) received neuraxial clonidine during cesarean delivery while 51 (26%) did not. At the time of this study, our institution had not yet formulated a post-cesarean delivery protocol for women receiving chronic buprenorphine therapy, and the decision to include neuraxial clonidine was made by the attending anesthesiologist. Of those receiving neuraxial clonidine, median doses were 50 µg [IQR 50, 100] epidural and 30 µg [IQR 25, 30] intrathecal. Compared to control subjects, those who received neuraxial clonidine more commonly underwent repeat and scheduled cesarean delivery and more frequently received spinal anesthesia than epidural or combined spinal epidural. Baseline characteristics and clinical variables were otherwise similar between the two groups (Table 1).

Opioid consumption

In univariate analysis, there was no difference in MME consumption 0–6 h in cases with neuraxial clonidine versus not (8 mg [15] vs. 1 mg [8], $P = 0.14$) (Table 2). After adjusting for potential confounders, administration of neuraxial clonidine was not significantly associated with MME consumption 0–6 h (Difference in means 2.77, 95% CI [− 0.89 to 6.44], $P = 0.14$) or 0–24 h (Difference in means 8.56, 95% CI [− 17.00 to 34.11], $P = 0.51$) (Table 3, Supplementary Material Table 1).

Pre-admission daily buprenorphine dose was associated with increased opioid consumption 0–6 h (1.74 additional MME were administered on average for patients whose pre-admission buprenorphine dose was 20 mg [75th percentile] versus 16 mg [25th percentile], 95% CI [0.29 to

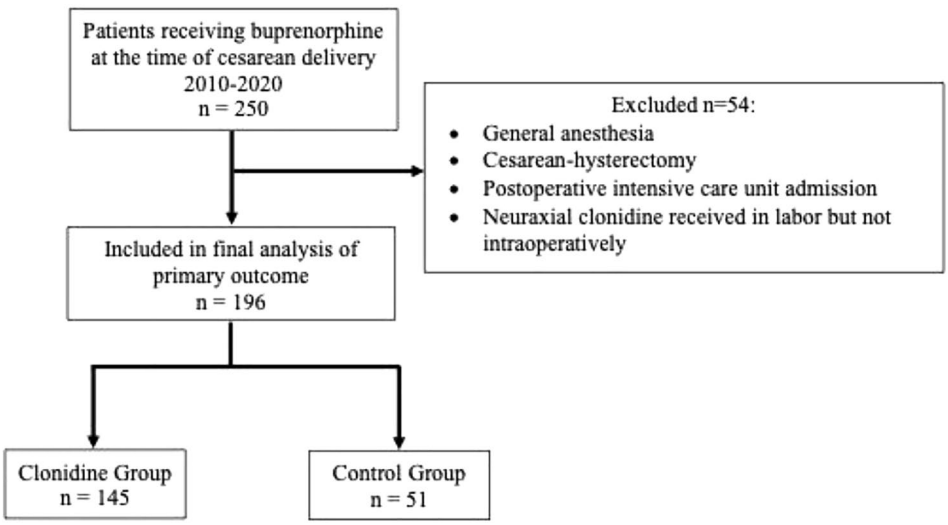

Fig. 1 Flow diagram for inclusion and exclusion of parturients

Table 1 Baseline characteristics and clinical variables of neuraxial clonidine versus control subjects

	Neuraxial Clonidine (n = 145)	No Neuraxial Clonidine (n = 51)	*SMD*	*P*-value[a]
Baseline Characteristics				
Age (years)	29 ± 5	29 ± 5	0.07	0.68
Gravidity	3 [2, 5]	3 [2, 4]	0.29	0.07
Parity	1 [1, 2]	1 [0, 2]	0.21	0.03
Body mass index (kg/m^2)	31 ± 7	30 ± 6	0.17	0.31
Prior cesarean deliveries				
0	42 (29%)	29 (57%)	0.59	< 0.01
1	57 (39%)	11 (22%)		
≥ 2	46 (32%)	11 (22%)		
Smoking status				
Current	123 (85%)	43 (84%)	0.04	0.94
Former	10 (7%)	4 (8%)		
Never	11 (8%)	4 (8%)		
Psychiatric comorbidity[b]				
Yes	92 (63%)	31 (61%)	0.06	0.87
No	53 (37%)	20 (39%)		
Pre-admission daily buprenorphine dose (mg)	16 [16, 20]	16 [12, 20]	0.19	0.20
Clinical variables				
Scheduling status				
Scheduled	104 (72%)	18 (35%)	0.79	< 0.001
Unscheduled	41 (28%)	33 (65%)		
Operative time (min)	53 [42, 61]	47 [42, 61]	0.19	0.23
Incision type				
Transverse	143 (99%)	51 (100%)	0.17	1.00
Vertical	2 (1%)	0 (0%)		
Neuraxial type				
Spinal	103 (71%)	16 (31)	1.17	< 0.001
Epidural	12 (8%)	27 (53%)		
CSE	30 (21%)	8 (16%)		
Neuraxial morphine				
Yes	135 (93%)	47 (92%)	0.04	0.76
No	10 (7%)	4 (8%)		
Neuraxial fentanyl				
Yes	28 (19%)	15 (29%)	0.24	0.19
No	117 (81%)	36 (71%)		
Truncal block				
Yes	5 (3%)	2 (4%)	0.03	1.00
No	140 (97%)	49 (96%)		
Buprenorphine total dose 0–24 h (mg)	16 [16, 24]	16 [8, 19]	0.19	0.13
Ketorolac total dose 0–24 h (mg)	90 [60, 120]	90 [60, 90]	0.00	0.95
Ibuprofen total dose 0–24 h (mg)	600 [0, 1200]	600 [0, 1200]	0.08	0.44
Acetaminophen total dose 0–24 h (mg)	1000 [650, 1950]	975 [650, 1625]	0.13	0.57

SMD standardized mean differences, *CSE* combined spinal-epidural

All values are reported as mean ± standard deviation, median [interquartile range], or n (%)

[a]*P*-values computed using the Pearson chi-square test or Fisher's exact test as appropriate for categorical variables and the Wilcoxon rank sum test or t test for quantitative variables

[b]Other than opioid use disorder

Table 2 Univariate analysis of primary and secondary outcomes comparing neuraxial clonidine with control subjects

	Neuraxial Clonidine (n = 145)	No Neuraxial Clonidine (n = 51)	*P*-value[a]
MME 0–6 h	8 [0, 15]	1 [0, 8]	0.14
MME 0–24 h	55 [30, 75]	38 [23, 60]	0.02
NRS 0–24 h	7 [6, 8]	6 [5, 7]	0.02
Intraoperative anesthetic supplementation	72 (49.7%)	28 (54.9%)	0.63
Propofol (mg)	23.3 ± 46.7	23.7 ± 55.6	0.96
Ketamine (mg)	3.1 ± 12.7	6.8 ± 16.8	0.10
Fentanyl (μg)	3.9 ± 17.7	12.6 ± 32.2	0.02
Hydromorphone (mg)	0.0 ± 0.0	0.0 ± 0.1	0.09
Morphine (mg)	0.1 ± 0.6	0.2 ± 1.0	0.34
Remifentanil (μg)	10.9 ± 34.0	3.9 ± 19.6	0.17
Midazolam (mg)	0.3 ± 0.8	0.3 ± 0.8	0.72

All values are reported as mean ± standard deviation, median [interquartile range], or n (%)

[a]Unadjusted *P*-values, computed using the Pearson chi-square test for categorical variables and the Wilcoxon rank sum test or t test for quantitative variables

3.18], $P = 0.02$) and 0–24 h (13.10 additional MME were administered on average for patients whose pre-admission buprenorphine dose was 20 mg [75th percentile] versus 16 mg [25th percentile], 95% CI [3.01 to 23.19], $P = 0.01$).

After propensity score weighted matching, the standardized mean differences for propensity score adjusted covariates were all < 0.1, indicating balance between the neuraxial and control groups (Supplementary Material Table 2). In the adjusted analysis, neuraxial clonidine was associated with a higher average MME consumption during 0–6 h (Difference in means 3.17, 95% CI [0.42 to 5.92], $P = 0.02$). There was no significant effect of neuraxial clonidine on average MME consumption during 0–24 h (Difference in means 11.20, 95% CI [− 1.11 to 23.51], $P = 0.07$).

Pain scores

In univariate analysis, the administration of neuraxial clonidine was associated with *increased* median NRS pain scores 0–24 h (7 [6, 8] vs. 6 [5, 7], $P = 0.02$) (Table 2). In the adjusted analysis, this association was still present. There was a significant effect of neuraxial clonidine on the odds of reporting a *higher* median pain score (Odds ratio 2.52,

Table 3 Results of regression analysis for opioid consumption 0–6 h postoperatively

Variable	Effect[a]	95% Confidence Interval	25th Percentile	75th Percentile	*P*-value[b]
Neuraxial clonidine, Yes:No	2.77	− 0.89 to 6.44	NA	NA	0.14
Age (years)	− 0.55	− 4.57 to 3.46	26	32	0.94
Parity	− 0.42	− 1.70 to 0.86	1	2	0.52
Body mass index (kg/m^2)	0.20	− 3.66 to 4.07	26	33	0.87
Prior cesarean delivery, 1:0	1.69	− 2.37 to 5.75	NA	NA	0.32
Prior cesarean delivery, ≥ 2:0	3.54	− 1.10 to 8.17	NA	NA	
Psychiatric comorbidity, Yes:No	0.35	-2.54 to 3.23	NA	NA	0.81
Pre-admission daily buprenorphine dose (mg)	1.74	0.29 to 3.18	16	20	0.02
Scheduling status, Unscheduled:Scheduled	− 0.66	− 4.34 to 3.02	NA	NA	0.72
Operative time (min)[c]	1.77	− 2.18 to 5.73	42	61	0.63
Incision type, Vertical:Transverse	7.35	− 6.64 to 21.35	NA	NA	0.30
Neuraxial type, CSE:SAB	− 5.04	− 9.24 to − 0.84	NA	NA	0.07
Neuraxial type, EPID:SAB	2.43	-2.89 to 7.75	NA	NA	
Neuraxial morphine, Yes:No	− 3.39	-8.94 to 2.16	NA	NA	0.23
Neuraxial fentanyl, Yes:No	− 1.40	-5.04 to 2.23	NA	NA	0.45
Truncal block, Yes:No	− 4.45	− 12.54 to 3.64	NA	NA	0.28
Buprenorphine total dose 0–24 h (mg)	− 1.43	− 4.52 to 1.66	12	24	0.36
Ketorolac total dose 0–24 h (mg)	2.47	0.25 to 4.68	60	120	0.03
Ibuprofen total dose 0–24 h (mg)	1.60	− 1.60 to 4.80	0	1200	0.32
Acetaminophen total dose 0–24 h (mg)	2.57	0.59 to 4.56	650	1950	0.01
Gabapentin total dose 0–24 h (mg)	0.19	0.34 to − 0.49	0	200	0.58

NA not applicable, *CSE* combined spinal-epidural, *SAB* subarachnoid block, *EPID* epidural

[a]The effect represents the 75th versus 25th percentile for quantitative variables

[b]*P*-values calculated using Wald test

[c]Operative time demonstrates nonlinear effect on opioid consumption

95% CI [1.24 to 5.11], $P=0.01$) (Supplementary Material Table 3). Pre-admission daily buprenorphine dose was also significantly associated with increasing odds of a higher median NRS pain score (Odds ratio 1.59, 95% CI [1.20 to 2.10], $P<0.01$).

Intraoperative supplementation

In the unadjusted analysis, rates of intraoperative anesthetic supplementation were similarly high in both the clonidine and control groups (49.7% vs. 54.9%, $P=0.63$) (Table 2). In logistic regression analysis, the need for intraoperative supplementation was not significantly associated with neuraxial clonidine administration (Odds ratio 0.89, 95% CI [0.37 to 2.12], $P=0.79$) (Supplementary Material Table 4). Operative time (Odds ratio 2.90, 95% CI [1.09 to 7.74], $P=0.01$) was associated with an increased rate of intraoperative anesthetic supplementation.

Discussion

In our study of 196 parturients receiving chronic buprenorphine at the time of cesarean delivery, no significant differences in opioid consumption or postoperative pain scores were observed in women who received neuraxial clonidine. Additionally, half of the subjects in both the clonidine and control groups received intraoperative anesthetic supplementation.

Prior studies in patients without opioid use disorder or chronic buprenorphine use demonstrate significant analgesic benefit of neuraxial clonidine for cesarean delivery. Intrathecal clonidine has been shown to prolong the duration of post-cesarean analgesia, defined as the time to first supplemental analgesic request [14, 15]. A double-blind placebo-controlled study by Filos and colleagues demonstrated that intrathecal clonidine as the sole analgesic provided four to six hours of pain relief following elective cesarean delivery performed under general anesthesia [17]. Finally, two recent meta-analyses evaluating the effects of intrathecal bupivacaine with clonidine for cesarean delivery concluded that the addition of clonidine prolongs sensory block duration, reduces 24-h post-cesarean delivery morphine consumption, and prolongs the time to first supplemental analgesic request [16, 18]. Benefits of neuraxial clonidine have also been demonstrated for labor analgesia, where epidural clonidine potentiates both the quality and duration of analgesia as well as provides a 30 to 40% local anesthetic dose-sparing effect [19, 20].

Studies evaluating neuraxial clonidine in parturients with opioid use disorder are more limited. A small series of seven women on chronic buprenorphine described maintenance epidural infusions with bupivacaine and clonidine for 24 h following cesarean delivery [21]. Six of seven women achieved median pain scores < 5/10, and three of seven women did not require supplemental opioids during the first 24 h postoperatively [21]. A recent article by Cook et al. retrospectively examined the analgesic effects of intrathecal clonidine for cesarean delivery in women diagnosed with opioid use disorder [22]. The study included 160 parturients (22 receiving intrathecal clonidine and 138 controls); however, only 15 patients in the clonidine group were receiving medication-assisted treatment with buprenorphine or methadone at the time of delivery. The authors observed reduced 24-h opioid consumption and a longer time to first analgesic request after surgery in patients receiving intrathecal clonidine [22].

Unlike the study by Cook et al., we were unable to demonstrate a benefit of neuraxial clonidine on pain scores or opioid consumption after cesarean delivery. The discrepancy between these results may be due to the study of different populations (opioid use disorder with or without chronic buprenorphine treatment), the variable dosing and route of clonidine administration in our study, or other unknown confounders. The lack of benefit with neuraxial clonidine in our study could thus indicate a true lack of clinical effect or possible type II error. Additionally, while the possibility of an unrecognized type II error remains, our results demonstrate that neuraxial clonidine may decrease 0–6 h opioid consumption by no more than 0.89 MME and 0–24 h opioid consumption by no more than 17.00 MME. These values correspond to less than one and approximately two oxycodone 5 mg tablets, respectively, during each of those time periods.

In the non-obstetric patient population, intrathecal clonidine has been shown to reduce capsaicin or heat-induced hyperalgesia [23], chronic cancer pain not relieved by oral opioids [24], and neuropathic pain following spinal cord injury [25]. Epidural clonidine administration has been found to improve chronic low back and surgical scar pain [26], refractory reflex sympathetic dystrophy [27], and intractable neuropathic cancer pain [28]. The absence of these aforementioned chronic pain conditions in our patient population may help further explain the lack of beneficial effect of neuraxial clonidine observed in our present study.

Interestingly, we found that neuraxial clonidine administration was associated with *higher* 0–24 h pain scores, even after adjusting for multiple confounders. While it is unlikely that neuraxial clonidine directly caused higher pain scores, this finding may be due to patient selection bias or residual confounding unaccounted for in our analysis. Given that providers used clinical judgement in deciding whether to administer neuraxial clonidine, they likely used patient and surgical characteristics associated with perceived greater risk of severe pain. While we attempted to control for the available variables which might influence this

decision (number of prior cesarean deliveries, pre-admission buprenorphine dose, etc.), there are other unmeasured factors which could have impacted this decision in real time and are not accounted for in our analysis (patient report of pain with prior cesareans, patient catastrophizing, etc.). Alternatively, given that the duration of action of neuraxial clonidine has been reported to be 3–9 h and may not provide a long-lasting benefit, it is also possible that patients experienced a subjective increase in pain scores once the effects of neuraxial clonidine receded [14, 17].

Finally, our study also demonstrated that increasing doses of pre-admission buprenorphine are significantly associated with post-cesarean opioid consumption and pain scores. These findings are supported by prior studies showing that a patient's maintenance buprenorphine dose is inversely proportional to μ-opioid receptor availability in opioid-dependent individuals [29].

One strength of our retrospective cohort study includes a large sample size of parturients undergoing cesarean delivery while receiving buprenorphine. Given the United States Food and Drug Administration "black box" warning for potential hemodynamic effects of neuraxial clonidine, definitive evidence of benefit is needed to justify routine use, and this study contributes to the body of evidence required [30, 31]. Nevertheless, the results of this study must be interpreted in the context of several limitations. First, we included varying doses and routes of administration of neuraxial clonidine, which make interpretation and generalization of our results more difficult. However, the neuraxial doses of clonidine administered in our study (median doses 50 µg [IQR 50, 100] epidural and 30 µg [IQR 25, 30] intrathecal) are consistent with acceptable clinical doses previously studied and published in the literature [16, 18, 32]. Second, our study was performed between 2010 and 2020 as the knowledge and best practice guidelines for parturients diagnosed with opioid use disorder were rapidly evolving. During this ten-year period, our institution had not yet established a post-cesarean delivery analgesia protocol for women receiving chronic buprenorphine therapy during the peripartum period. As a result of the variability in clinical management, there may have been residual confounding effects on our primary and secondary outcomes. Finally, and most importantly, given the limited number of parturients undergoing cesarean delivery while on chronic buprenorphine, our study included a convenience sample without an a priori power calculation to determine sample size. Thus, the possibility of an unrecognized type II error cannot be excluded. However, by examining the confidence intervals of our primary and secondary outcomes, we have excluded the possibility of a large, clinically significant effect of neuraxial clonidine in this patient population.

In conclusion, no significant differences in postoperative opioid consumption, median pain scores, or need for intraoperative supplementation were observed in our cohort of 196 parturients on chronic buprenorphine therapy who received intraoperative administration of neuraxial clonidine for cesarean delivery. Given the current opioid epidemic and increasing prevalence of opioid use disorder in pregnant women, future studies investigating post-cesarean delivery analgesia in parturients receiving buprenorphine are needed.

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Declarations

Conflict of Interest The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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