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ORIGINAL ARTICLE

Comparison of patient-controlled epidural analgesia and epidural morphine for post-cesarean section analgesia: experience from a tertiary center in China

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Abstract

Purpose To compare patient-controlled epidural analgesia (PCEA) and epidural morphine (EM) for post-cesarean section analgesia in real-world experience from China.

Methods Parturients receiving one dose of EM (1–2 mg), PCEA, or both EM and PCEA from Peking Union Medical College Hospital were retrospectively recruited. Logistic models were used to identify risk factors.

Results Of 1079 parturients enrolled, 919 (85.2%) parturients received only EM, 105 (9.7%) parturients received PCEA, and 55 (5.1%) parturients received both EM and PCEA. Significantly more parturients from EM group requested supplementary analgesia than those from PCEA and PCEA + EM group (583, 63.4% vs 52, 49.5% vs 25, 45.5%, $P = 0.001$) with more times of supplementary analgesia (1, IQR: 0–2 vs 0, IQR: 0–1 vs 0, IQR: 0–1 times, $P < 0.001$) and larger amounts of nonsteroidal anti-inflammatory drugs (NSAIDs) (50, IQR: 0–100 mg vs 0, IQR: 0–50 mg vs 0, IQR: 0–50 mg, $P < 0.001$). In multivariable Logistic regression for the supplementary analgesia risk, the application of PCEA (OR: 0.557, 95%CI 0.396–0.783, $P = 0.001$) and the use of NSAIDs intraoperatively (OR: 2.996, 95%CI 1.811–4.957, $P < 0.001$) were identified as independent predictors. A total of 1040 (96.4%) patients received prophylactic antiemetic therapy during surgery. Only 13 (1.2%) and 7 (0.6%) patients in our cohort requested antiemetic and antipruritic drugs, respectively.

Conclusion The use of PCEA was an independent protective factor for supplementary analgesia during the post-cesarean section. Prophylactic antiemetic therapy may reduce the side effects of post-cesarean analgesia.

Keywords Cesarean section · Epidural morphine · Patient-controlled epidural analgesia · Supplementary analgesia

Introduction

Successful post-cesarean section analgesia is important as it could reduce surgery risks and help mothers provide optimal care for newborns [1]. Epidural morphine (EM) provides effective post-cesarean section analgesia and is a routine clinical practice in mainland China [2]. The side effects of EM, including pruritus, nausea, vomiting, and urinary retention, are annoying for many patients [3]. Patient-controlled epidural analgesia (PCEA) has been adopted as an alternative option for parturients as it provides satisfactory analgesic effects as well. However, PCEA inevitably limits the postoperative mobilization of patients and requires more patient care [4].

The analgesic effects of EM and PCEA remain controversial. Previous studies reported that PCEA was less effective than EM for postoperative analgesia following cesarean section [5, 6]. Yet, some studies reported an equivalent

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analgesic effect of PCEA and EM [7–9]. Patients adopting PCEA had higher satisfaction scores due to fewer side effects [7]. No data from a large cohort in the real world has been reported before. Therefore, this retrospective study aims to investigate the post-cesarean section analgesic effect of EM and PCEA in a real-world cohort.

Methods

Patients

Patients undergoing cesarean deliveries from departments of international medical services, Peking Union Medical College (PUMC) Hospital, between February 2017 and April 2020 were identified utilizing Anesthesia Information Managing System of PUMC Hospital. A total of 1090 patients received a single dose of epidural morphine (EM) and/or a combination of ropivacaine and sufentanil via patient-controlled epidural analgesia (PCEA) (Hospira, Lake Forest, U.S.A.). Eleven patients' medical records were not available or had significant data missing in the system and were consequently excluded. Therefore, a total of 1079 patients were finally enrolled. All patients underwent combined spinal-epidural anesthesia after establishing intravenous access.

The PCEA regimen includes a ropivacaine flow rate of 4 ml/h (IQR: 0–6 ml/h) with the concentration of 0.12 mg/100 ml (IQR: 0.10–0.13 mg/100 ml), sufentanil dosage of 50–100 mg, bolus dosage of 4–6 ml, lock time of 15–30 min, and a duration of administration lasting 1–2 days. The use of PCEA will be assessed by anesthesiologists daily. EM (1–2 mg) is administered during the surgery, specifically during the suturing of the peritoneum. Non-steroidal anti-inflammatory drugs (NSAIDs) were given to 109 (10.1%) patients during the surgery intravenous (EM group: 100/919 patients, PCEA group: 6/105 patients, EM + PCEA group: 3/55 patients). Intraoperatively NSAIDs may be given under two conditions: patients' request or as part of the anesthesiologist's decision for multimodal analgesia strategy in postoperative pain management. The normal hospital discharge is 3 days after delivery. The primary outcome was the requirement for supplementary analgesia. The secondary outcome was the need for antiemetic and antipruritic medication.

This retrospective study was approved by the Institutional Ethics Committee of PUMC Hospital (I-22PJ562). Since this study was based on retrospectively reviewing medical records, the requirement for written informed consent was waived.

Data collection

Demographic data, past medical history, detailed information about cesarean surgery, and medication records were collected. Times, methods, and doses of supplementary analgesia medications were retrieved. Inadequate analgesia was defined as patients requiring supplementary analgesia after receiving postoperative pain management. Times of supplementary analgesia was defined as frequencies of patients receiving analgesia medications after surgery including NSAIDs and opioids. Diclofenac and flurbiprofen axetil were the most commonly used NSAIDs for supplementary analgesia, administered at a dose of 50 mg or 100 mg. Oxycodone was the most commonly used opioids for supplementary analgesia, administered at a dose of 5 mg.

Statistical analysis

Categorical variables were presented as numbers and percentages (%) and continuous variables were presented as mean ± standard deviation (SD), or median (interquartile range, IQR) according to distribution. Comparisons were conducted using chi-square, Fisher's test, student's t-test, or Mann–Whitney U test according to distribution with the Bonferroni correction adopted for multiple comparisons. Univariate and multivariable Logistic models were used to identify the risk factors and their odds ratios (OR). Base-line variables, including age, weight, BMI, multiple pregnancy, past medical history, methods for analgesia, application of antiemetic and antipruritic medication, and additional analgesia during surgery, were evaluated in the Logistic regression model. A two-sided *P* value less than 0.05 was considered statistically significant. Analyses were performed with SPSS software version 25.0 (IBM SPSS Statistics, Boston, U.S.A).

Results

Demographic data

Of 1079 patients enrolled, 919 (85.2%) parturients received only EM, 105 (9.7%) patients received PCEA, and 55 (5.1%) patients received both EM and PCEA for post-cesarean section analgesia. The median age of parturients was 35 years (IQR: 32–34 years). The multiple pregnancy rate in our cohort was 1.8%. Three hundred and sixty-one parturients (33.5%) received cesarean section before (Table 1).

Supplementary analgesia requirement during the post-cesarean section

As shown in Table 2, a total of 660 (61.2%) patients required post-operative supplementary analgesia. A significantly

Table 1 Demographics of enrolled patients

	Total	EM	PCEA	EM + PCEA
Patient number	1079	919	105	55
Age, years (median, IQR)	35 (32–37)	35 (32–37)	34 (32–38)	36 (34–38)
Weight, kg (median, IQR)	70 (64–77)	70 (64–77)	70 (65–75)	70 (64–75)
Multiple pregnancy (n, %)	19, 1.8%	18, 2.0%	0, 0	1, 1.8%
Gestational diabetes mellitus (n, %)	276, 25.7%	226, 24.7%	36, 34.3%	14, 25.5%
Hypertensive disorders complicating pregnancy (n, %)	29, 2.7%	28, 3.1%	1, 1.0%	0, 0
Infections during pregnancy (n, %)	130, 12.0%	105, 11.4%	19, 18.1%	6, 10.9%
History of cesarean section (n, %)	361, 33.5%	302, 32.9%	31, 29.5%	28, 50.9%

higher percentage of parturients from EM group requested supplementary analgesia than those from PCEA and PCEA + EM group (583, 63.4% vs 52, 49.5% vs 25, 45.5%, $P = 0.001$) with more times of supplementary analgesia (1, IQR: 0–2 times vs 0, IQR: 0–1 time vs 0, IQR: 0–1 time, $P < 0.001$). The median consumption of NSAIDS was 50 mg (IQR: 0–100 mg) with significant difference observed among three groups (EM vs PCEA vs EM + PCEA: 50, IQR: 0–100 mg vs 0, IQR: 0–50 mg vs 0, IQR: 0–50 mg, $P < 0.001$). There was no difference in supplementary analgesia between patients receiving EM 1 mg (363, 62.1%) and those receiving more than 1 mg (220, 65.9%) (Supplementary Table S1).

Base-line variables were evaluated in the univariate Logistic regression model, and the identified significant ($p < 0.05$) and clinically significant prognostic factors are listed in Fig. 1. Univariate Logistic regression analysis showed the protective factors for supplementary analgesia are the application of PCEA only (OR: 0.591, 95%CI 0.394–0.885, $P = 0.011$) or EM plus PCEA (OR: 0.510, 95%CI 0.296–0.881, $P = 0.016$). The risk factors for supplementary analgesia include the application of EM only (OR: 1.870, 95%CI 1.334–2.622, $P < 0.001$) and the use of NSAIDs intraoperatively (OR: 3.110, 95%CI 1.883–5.135, $P < 0.001$).

In multivariable Logistic regression for the supplementary analgesia risk, the application of PCEA (OR: 0.557, 95%CI 0.396–0.783, $P = 0.001$) and the use of NSAIDs intraoperatively (OR: 2.996, 95%CI 1.811–4.957, $P < 0.001$) were identified as independent predictors (Table 3).

Table 2 Supplementary analgesia during the post-cesarean section

	Total	EM	PCEA	EM + PCEA	*P*
Patient number (n)	1079	919	105	55	
NSAIDs intraoperatively	109, 10.1%	100, 10.9%	6, 5.7%	3, 5.4%	0.126
Supplementary analgesia after surgery (n, %)	660, 61.2%	583, 63.4%	52, 49.5%	25, 45.5%	0.001*ζ†
NSAIDs	660, 61.2%	583, 63.4%	52, 49.5%	25, 45.5%	0.001*ζ†
Opioids	7, 0.6%	6, 0.7%	0, 0	1, 1.8%	0.415
Times of supplementary analgesia (median, IQR)	1 (0–2)	1 (0–2)	0 (0–1)	0 (0–1)	< 0.001*ζ†
< 24 h	1 (0–1)	1 (1–1)	0 (0–0)	0 (0–0)	< 0.001*ζ†
24–48 h	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0.130
> 48 h	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.957
NSAIDs consumption, mg (median, IQR)	50 (0–100)	50 (0–100)	0 (0–50)	0 (0–50)	< 0.001*ζ†
< 24 h	0 (0–50)	0 (0–50)	0 (0–0)	0 (0–0)	< 0.001*ζ†
24–48 h	0 (0–50)	0 (0–50)	0 (0–50)	0 (0–50)	0.169
> 48 h	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.152
Opioids consumption, mg (median, IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.393
< 24 h	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.258
24–48 h	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.169
> 48 h	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.917

*$P < 0.05$

ζadjusted $p < 0.05$ between EM and PCEA group after Bonferroni correction

†adjusted $p < 0.05$ between EM and EM + PCEA group after Bonferroni correction

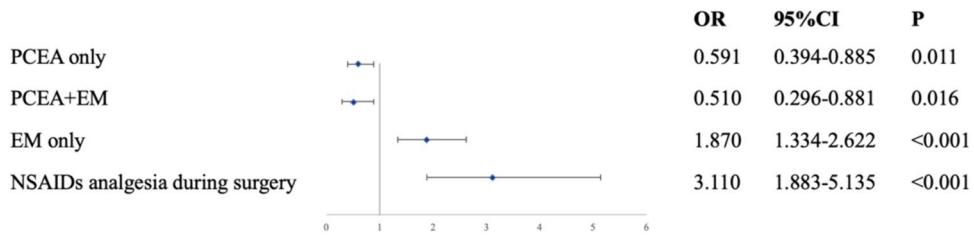

Fig. 1 Univariate Logistic regression for supplementary analgesia ($P < 0.05$)

Table 3 Multivariate Logistic regression for supplementary analgesia

	OR	95%CI	*P*	
PCEA	0.557	0.396–0.783	0.001	0.001
NSAIDs analgesia during surgery	2.996	1.811–4.957	< 0.001	

Antiemetic and antipruritic medication requirement during the post-cesarean section

As shown in Table 4, a total of 1040 (96.4%) patients received prophylactic antiemetic therapy during surgery, with no difference observed between groups. Thirteen (1.2%) patients required antiemetic drugs after surgery. Parturients from EM group requested significantly fewer antiemetic drugs than those from PCEA and PCEA + EM groups (7, 0.8% vs 3, 2.9% vs 3, 5.5%, $P = 0.006$). A total of 7 (0.6%) patients required antipruritic drugs during the post-cesarean section. A significantly lower percentage of parturients from EM group requested antipruritic drugs than those from PCEA and PCEA + EM groups (2, 0.2%vs 2, 1.9% vs 3, 5.5%, $P = 0.001$).

Discussion

To our knowledge, our study is the largest cohort to investigate supplementary analgesia requirements during post-cesarean section of patients receiving EM, PCEA, and EM + PCEA. Patients from EM group requested significantly more supplementary analgesia than those from PCEA and PCEA + EM groups. PCEA served as an independent prognostic factor for supplementary analgesia. And patients from EM group needed fewer antiemetic drugs than those from the other groups.

Effective and safe post-cesarean delivery pain relief is important as it can reduce thromboembolic disease risks and help mothers provide better care for their babies. Opioids are the most commonly used drugs for post-cesarean analgesia [10]. A single dose of EM can provide excellent post-cesarean analgesia effects [1]. The use of PCEA is more satisfactory to some mothers due to the lower frequency of side effects, but it may reduce mortality and require more professional care from healthcare workers, which leads to higher economic costs [7].

In our study, patients from PCEA group or PCEA + EM requested significantly less supplementary analgesia than patients from EM group, which demonstrated that the use of

Table 4 The use of antiemetic drugs and antipruritic drugs during post-cesarean section

	Total	EM	PCEA	EM + PCEA	*P*
Patient number (n)	1079	919	105	55	
Antiemetic drugs during surgery	1040, 96.4%	883, 96.1%	103, 98.1%	54, 98.2%	0.592
Ondansetron (n, %)	976, 90.5%	830, 90.3%	93, 88.6%	53, 96.4%	0.259
Granisetron (n, %)	29, 2.7%	23, 2.5%	5, 4.8%	1, 1.8%	0.340
Ondansetron & Granisetron (n, %)	35, 3.2%	30, 3.3%	5, 4.8%	0, 0	0.281
Antiemetic drugs after surgery (n, %)	13, 1.2%	7, 0.8%	3, 2.9%	3, 5.5%	0.006†
Ondansetron (n, %)	12, 1.1%	6, 0.7%	3, 2.9%	3, 5.5%	0.003†
Metoclopramide (n, %)	2, 0.2%	1, 0.1%	0, 0	1, 1.8%	0.109
Antipruritic drugs after surgery (n, %)	7, 0.6%	2, 0.2%	2, 1.9%	3, 5.5%	0.001ζ†
Diphenhydramine (n, %)	5, 0.5%	1, 0.1%	2, 1.9%	2, 3.6%	0.001ζ†
Cetirizine (n, %)	3, 0.3%	0, 0	1, 1%	2, 3.6%	0.001ζ†
Loratadine (n, %)	1, 0.1%	1, 0.1%	0, 0	0, 0	1.000

*P < 0.05

ζadjusted p < 0.05 between EM and PCEA group after Bonferroni correction

†adjusted p < 0.05 between EM and EM + PCEA group after Bonferroni correction

PCEA may be superior to a single dose of EM. In the meantime, an additional dose of EM to PCEA seemed to provide additional but not significant help for the effect of analgesia, which means an additional dose of EM may not be necessary. Previous studies have investigated the analgesic effects of EM and PCEA, and the outcome remains controversial. Our results are in accordance with one study demonstrating a superior effect of PCEA compared with EM [11]. Previous studies have reported an equivalent analgesia effect of PCEA and EM [7–9]. Experiential dosage of epidural morphine in our hospital (1–2 mg) was lower than those reported in other studies (2 mg, twice a day) [7, 12], which may lead to the differences in results. Of note, the supplementary analgesia did not show a significant difference between patients receiving 1 mg and more than 1 mg in our study. Some studies also reported an inferior effect of PCEA than EM for post-cesarean pain relief [5, 6].

Intraoperatively use of NSAIDs was identified as a risk factor for supplementary analgesia in our study. The possible reason may be that patients who required intraoperative administration of NSAIDs, regardless of the method of postoperative analgesia, may have had inadequate anesthesia at the time of surgery and may have had more immediate postoperative pain.

The widely reported adverse effects of post-cesarean analgesia include nausea, pruritus, and urinary retention. Previous studies have reported a higher frequency of side effects in patients receiving EM than in patients receiving PCEA [8, 9, 13]. Morphine-induced pruritis is very common and debilitating. The pruritis may be mediated by the opioid receptors via disinhibitions of neurons [14, 15]. Previous research from our hospital revealed that the use of serotonin receptor antagonists was a protective factor for morphine-induced pruritus [2]. Apart from the analgesia medication, the surgical operation and the use of oxytocin could also cause nausea after surgery. In our cohort, nearly all parturients received prophylactic antiemetic therapy (serotonin receptor antagonist) during surgery, and only a few of them required antiemetic drugs and antipruritic drugs after surgery. Our results showed that significantly less requirement for antiemetic and antipruritic drugs after surgery from EM group than the other two groups, which indicated that severe adverse effects were significantly less in EM group compared to patients adopting PCEA. And prophylactic use of antiemetic drugs may reduce the frequency of adverse effects.

Our study has several limitations. First, the clinical information may not be sufficiently detailed due to the retrospective design. Only patients using PCEA were followed by anesthesiologists with detailed complaints documented. Therefore, we retrieved medication records to reflect the severe pain and adverse effects objectively. Besides, data regarding postoperative mobilization and whether it is elective cesarean section were not available and were not included in this study. Second, patients in this study were from a single center in China, which may introduce bias. Third, the sample size of PCEA group, and PCEA + EM group was imbalanced among groups. Additionally, there was a considerable variability of PCEA regiments. The combination of these factors may lead to statistical bias. Fourth, the dosage of EM (1–2 mg) is experiential in our hospital. Although the dosage of 1 mg is different from what is mainly described in the literature, there was no difference in the supplementary analgesia amongst patients receiving 1 mg or a higher dose. In the future, prospective multicenter studies may be carried out to verify the findings from this study.

In conclusion, PCEA might provide better analgesia effects than EM and it served as an independent protective factor for supplementary analgesia during the post-cesarean section. Prophylactic antiemetic therapy may reduce the side effects of post-cesarean analgesia.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00540-024-03367-9.

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Data availability The original data of this study will not be uploaded to a public repository due to privacy and consent restrictions. De-identified data is available from the corresponding author on a reasonable request, subject to a data-sharing agreement.

Declarations

Conflict of interest The authors report no conflict of interest.

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