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Original Article

Patient -controlled epidural ropivacaine as a post-Cesarean analgesia: A comparison with epidural morphine

Li-Kuei Chen [a], Pei-Lin Lin [a], Chen-Jung Lin [a], Chi-Hsiang Huang [a], Wan-Chi Liu [b], Shou-Zen Fan [a], Mao-Hsien Wang [b,*]

[a] *Department of Anesthesiology, National Taiwan University Hospital, Taipei, Taiwan*
[b] *Department of Anesthesiology, En-Chu-Kon Hospital, Taipei, Taiwan*

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Abstract

Objective: Conventional, intermittent, epidural morphine is widely applied as a post-Cesarean delivery analgesia. We compared the analgesic efficacy, motor weakness, and side effects of administering a patient-controlled epidural analgesia (PCEA) of pure ropivacaine versus the intermittent administration of epidural morphine after Cesarean delivery.

Materials and Methods: This randomized, double-blind study included 120 full-term parturients who underwent elective Cesarean delivery and received either PCEA with pure ropivacaine or an intermittent bolus epidural of 2 mg/10 mL morphine in normal saline twice per day. The efficacy of pain relief, post-Cesarean side effects, motor blockades, time to first ambulation, and global satisfaction scores were evaluated.

Results: Pain scores were recorded at the four evaluation times (2, 12, 24, and 48 hours post-Cesarean delivery), and the time to first ambulation did not statistically differ between the two groups. Patients in the ropivacaine group experienced more motor weakness at 2 and 12 hours, fewer side effects, and higher global satisfaction scores than those in the morphine group ($p < 0.05$).

Conclusion: The analgesic efficacy after cesarean delivery was almost equivalent between two groups. PCEA with pure ropivacaine induced significant motor blockade during the first 12 hours, but without delaying the time to first ambulation. Patients in the ropivacaine group reported higher patient satisfaction scores due to the significant reduction of annoying side effects, such as pruritus, nausea, vomiting, and urinary retention.

Keywords: PCEA; Ropivacaine; Morphine

Introduction

Many studies have shown that the use of opioids or local anesthetics as an epidural analgesia, either alone or in combination, provides superior pain control compared with intravenous opioids after abdominal and thoracic surgical procedures [1–3]. The use of morphine (2–3 mg, twice per day) as an epidural analgesia after cesarean delivery is superior to other techniques, such as the intramuscular or intravenous administration of opioids, because it provides better and longer-lasting analgesic effects with fewer sensory, motor, or sympathetic side effects [4,5]. Considering the high incidence of annoying side effects that are induced by epidural morphine, such as nausea, vomiting, pruritus, and urinary retention, some patients are dissatisfied with epidural morphine after cesarean delivery [6,7]. In the past few years, some prophylactic methods have been developed to reduce or prevent the incidence of side the effects induced by morphine [8,9]. Furthermore, some reports have advocated using a modified regimen, such as different combinations of local anesthetics with opioids, to decrease opioid dosage and, thus, reduce the incidence of annoying side effects. However, the incidence of these side effects, such as pruritus, nausea, vomiting, and urinary retention, may or may not be related to

* Corresponding author. Mao-Hsien Wang, MD, Department of Anesthesiology, En-Chu-Kon Hospital, Taipei, Taiwan.
E-mail address: clk0619@ntu.edu.tw (M.-H. Wang).

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the amount of opioids that are administered [6,10,11]. Regimens that contain even small doses of opioids still cause those side effects, which are clinically bothersome to many patients.

While patient-controlled epidural analgesia (PCEA) with local anesthetics alone provides good analgesic effects, it causes motor weakness that inevitably limits postoperative mobilization [12]. Ropivacaine produces less effects to the central nervous system, cardiac toxicity, and motor blockades and provides equivalent onset time, duration, and quality of analgesia compared with bupivacaine [13–15]. Buggy et al compared PCEA with ropivacaine alone and ropivacaine in combination with fentanyl for post-Cesarean-delivery pain relief and found a higher incidence of motor weakness after 8 hours [16]. However, their observation period was restricted to the initial 24-hour postoperative period. Thus, the data collected about analgesic efficacy, motor weakness, side effects, and global satisfaction were incomplete due to the limited observation period. Hypothesizing that these two regimens should show equivalent analgesic efficacy post-Cesarean delivery, we performed a prospective, randomized, and double-blind study to compare the analgesic efficacy, motor weakness, and side effects of PCEA with ropivacaine versus intermittent bolus of epidural morphine for post-Cesarean delivery analgesia.

Methods

After institutional review board approval and written informed consent was obtained from each patient, the 120 patients (American Society of Anesthesiology [ASA] physical status classification I or II; age range: 20–40 years), who were scheduled to undergo elective Cesarean deliveries with regional anesthesia, were randomized to receive either epidural morphine analgesia or PCEA with ropivacaine during the postoperative 48-hour period. Randomization was accomplished by randomly selecting sealed envelopes that each contained one piece of paper with either "epidural morphine" or "epidural ropivacaine" written on it. Patients with a history of chronic pain, chronic opioid use, drug and/or alcohol abuse, chronic headaches, backaches, or peripheral neuropathy, and those who could not understand the use of PCEA or the visual analogue scale (VAS) were excluded. Baseline assessments of vital signs, including respiration rate, pain score on a 10-cm VAS, motor functions based on a modified Bromage scale, nausea, vomiting, and pruritus, were recorded for every patient. After intravenous access had been established and an infusion of crystalloid (0.9% sodium chloride) had been administered, all patients underwent combined spinal-epidural (CSE) anesthesia. Dural puncture was performed using the needle-through-needle technique with a Whitacre 26G needle. A local anesthetic (0.5% heavy bupivacaine) was intrathecally injected before the epidural catheter was inserted, and then the epidural catheter was placed in the L4-5 or L3-4 interspace of each patient. A 3-mL injection of 2% lidocaine was administrated through the epidural catheter to test for intrathecal versus intravascular placement. Spinal anesthesia was induced using 10–12 mg bupivacaine. No additional intravenous or epidural opioids or epidural local anesthetics were administered during surgery.

Postoperative analgesic techniques and assessment

Before cesarean delivery, each patient drew a sealed envelope and were then randomized into one of two groups after delivery based on their selected envelope. The R group ($n = 60$) received 0.1% ropivacaine alone via PCEA (Provider 5500, Pancretec, ABBOTT Lab, USA) (5 mg bolus, 15 minute lockout, with 3 mg/hour background infusion and a maximum dose of 60 mg/4 hours) for 3 days [16]. The M group ($n = 60$) received 2 mg morphine in 10 mL normal saline epidurally administered twice per day (8 AM and 8 PM) for 3 days. All patients started their postoperative analgesic program immediately after Cesarean delivery in the operating room. All of the epidural catheters were attached to infusion pumps for both therapeutic groups so that the observers (i.e., the nursing staff) were blinded to the treatment groups. Inadequate analgesia was defined as patients still feeling pain (VAS score >40 mm) after receiving postoperative pain management. Inadequate analgesia was managed by an intermittent, intramuscular injection of 25 mg meperidine. Nausea and vomiting were managed by 0.5 mg droperidol that was intravenously delivered. Hypotension was prevented by challenge with 500 mL of normal saline before spinal anesthesia, and was treated with intermittent intravenous ephedrine. If a motor blockade impaired ambulation, PCEA was withheld for 1 hour and the bolus dose was reduced to half of the previous dose. If drowsiness or respiratory depression occurred, epidural morphine was also reduced by half. The analgesic regimen was prepared by the anesthesiologist managing the patient, who was not involved in data collection, and was administered in the recovery room while the spinal block was still effective. Patients and nursing staff were blinded to the group randomization during data collection.

All patients were assessed using the 100-mm VAS while at rest and when moving by nursing staff who were not involved in the bedside patient care; side effects of the postoperative analgesia were also assessed at four different evaluation times (2, 12, 24, and 48 hours after the first bolus of ropivacaine or morphine). The VAS pain scales consisted of 100-mm horizontal lines drawn on a sheet of paper without any markings, anchored with "no pain" at the left and "worst pain possible" at the right. Nausea, vomiting, and pruritus were rated four times in terms of incidence and severity over the postoperative 48-hr period using the following scoring system: 0, side effect not experienced; 1, side effects experienced, no treatment needed; 2, side effect experienced, treatment effective; 3, side effect experienced, treatment ineffective [17]. Vomiting was defined as an integrated reflex that results in forceful expulsion of the stomach contents, including a nonproductive expulsion. Nausea was defined as the sensation of wishing to vomit or retch [18]. Pruritus was defined as the central type of itching induced by epidural opioids, where the itching sensation occurs only on the face or central part of the trunk, excluding itching of the arms or legs.

Proper equipment functions and stable vital signs (i.e., respiratory rate, pulse rate, and noninvasive blood pressure measurements) were measured and all of these data were recorded every 6 hours on the first day and then every 12 hours on the following day. The appearance of respiratory depression (respiratory rate <8 breaths/minute) and hypotension (systolic blood pressure [SBP] <90 mmHg or 20% below baseline SBP) were also recorded. Sedation was assessed using a four-point scale: 0, fully alert; 1, drowsy, eyes closed occasionally; 2, asleep but easily roused by speaking to the patient; 3, profoundly sedated, roused by physical stimulation. The occurrence of a motor block was evaluated using the modified Bromage scale (0, no motor blockade; 1, able to flex hip and knee but unable to perform a straight leg raise; 2, able to move ankle only; 3, unable to move the lower limbs). Demonstrable motor weakness was defined as Bromage grade 1 or higher and was recorded by the nursing staff.

The time of first ambulation was recorded for each patient. The criteria used to declare a patient capable of her first ambulation were the following: stable vital signs for at least 1 hour; no sign of respiratory depression or airway obstruction; patient aware of time, place, and person; patient able to walk and dress unaided; patient having bearable or little pain during ambulation (VAS <30 mm).

The number of patients in each group who requested supplementary analgesia (intermittent intramuscular injection of 25 mg meperidine) due to inadequate analgesia (VAS > 40 mm) was recorded during the 48-hour evaluation period. All patients reported their global satisfaction with the quality of their post-Cesarean analgesia using a 5-point verbal rating scale (1, very satisfied; 2, satisfied; 3, indifferent; 4, dissatisfied; 5, very dissatisfied) on the day before hospital discharge [19]. The normal hospital discharge is 5 days after delivery.

Statistical analysis

In this study, we recorded and compared the analgesic efficacy as the primary outcome and side effects (e.g., nausea, vomiting, pruritus, and drowsiness), motor blockade, time to first ambulation, and global satisfaction scores were regarded as secondary outcomes. We hypothesized that the analgesic efficacies of the two pain management treatments would be equivalent. A power analysis showed that 51 patients per group would provide 80% of the power to detect a relative difference of 20% in terms of the secondary outcomes between the two groups.

Continuous variables (e.g., patient characteristics such as maternal age, height, weight, etc.) were analyzed using Student's unpaired *t*-tests. Categorical data for each of the two study groups (including incidence of side effects and the number of patients requesting extra analgesia) were reported as numbers and percentages and were analyzed using the chi-square test. Nonparametric data (such as VAS pain scores at rest and while moving at different evaluation times, global satisfaction scores, and time of first ambulation) were reported as the means ± SDs and were analyzed using the Kruskal-Wallis test. A value of $p < 0.05$ was considered statistically significant.

Table 1
Patient demographic and clinical characteristics.

	Ropivacaine group ($n = 60$)	Morphine group ($n = 60$)
Age (y)	29.3 ± 5.8	28.8 ± 6.3
Height (cm)	161.8 ± 6.1	162.7 ± 5.5
Weight (kg)	69.5 ± 7.9	71.7 ± 8.6
Parity: nulliparous/ multiparous (n)	24/36	26/34
Time of first ambulation after delivery (h)	23.45 ± 5.72	22.28 ± 5.38
Patients who requested supplementary aanalgesia	0	2

Values are the means ± SD or number (n).
No differences were found between the two groups.

Results

There were no demographic differences between the ropivacaine PCEA and epidural morphine groups (Table 1).

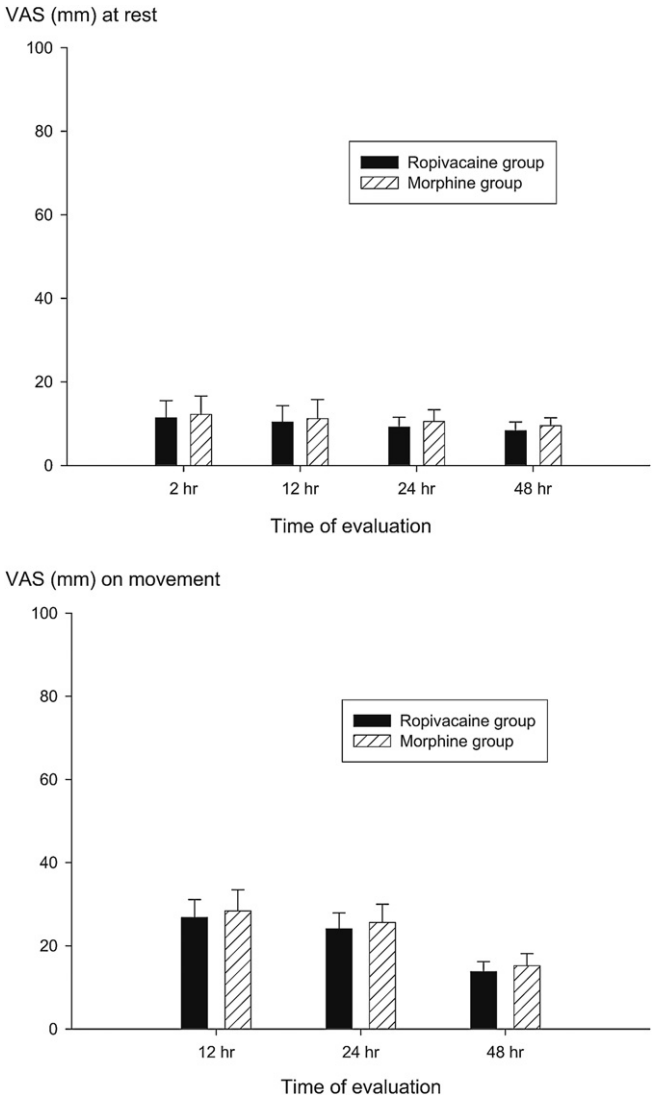

Fig. 1. Comparisons of visual analog scale scores for pain that occurred at rest or while moving for ropivacaine and morphine. Bars denote the means ± SDs. Scores did not differ significantly between the two groups.

Overall VAS pain scores and the time of first ambulation did not differ significantly between the two groups (Fig. 1). In the morphine group, one patient was sleepy but was able to respond to verbal commands. One patient in the ropivacaine group became hypotensive. No respiratory depression or tachyphylaxis occurred. Zero patients in the ropivacaine group, but two patients in the morphine group, complained of inadequate analgesia and requested supplementary pain relief; however, the difference between the two groups was not statistically significant (Table 1). The overall global satisfaction of the ropivacaine group was greater than that of the morphine group at each of the four evaluation times ($p < 0.05$) (Fig. 2).

The incidence, mean severity score, and distribution of motor weakness and side effects (e.g., nausea, vomiting, and pruritus) are shown in Table 2. The incidence of side effects (nausea, vomiting, and pruritus) were significantly higher in the morphine group compared with the ropivacaine group at 2, 12, 24, and 48 hours after the first bolus was administered ($p < 0.05$) (Table 2). The incidence of demonstrable motor weakness (Bromage grade 1 or higher) was significantly higher in the ropivacaine group than in the morphine group at 2 and 12 hours post-Cesarean delivery ($p < 0.05$), but not at 24 or 48 hours postdelivery (Table 2).

The mean severity scores of the side effects (e.g., nausea, vomiting, and pruritus) were significantly higher in the morphine group at 2, 12, 24, and 48 hours after bolus administration ($p < 0.05$) (Table 2). The mean Bromage motor weakness score was insignificantly higher in the ropivacaine group compared with the morphine group at 2 and 12 hours post-Cesarean delivery ($p < 0.05$), but not at 24 or 48 hours postdelivery (Table 2). For patients in the ropivacaine group, the total ropivacaine consumption was 189 ± 26 mg in 24 hours and 77 ± 31 mg in 48 hours.

Discussion

Intravenous or epidural morphine following post-Cesarean delivery has been used clinically in recent decades with excellent analgesic effects, but it has bothersome side effects, such as pruritus, nausea, and vomiting, which are difficult to prevent [8,9,20]. Recently, patients have become dissatisfied

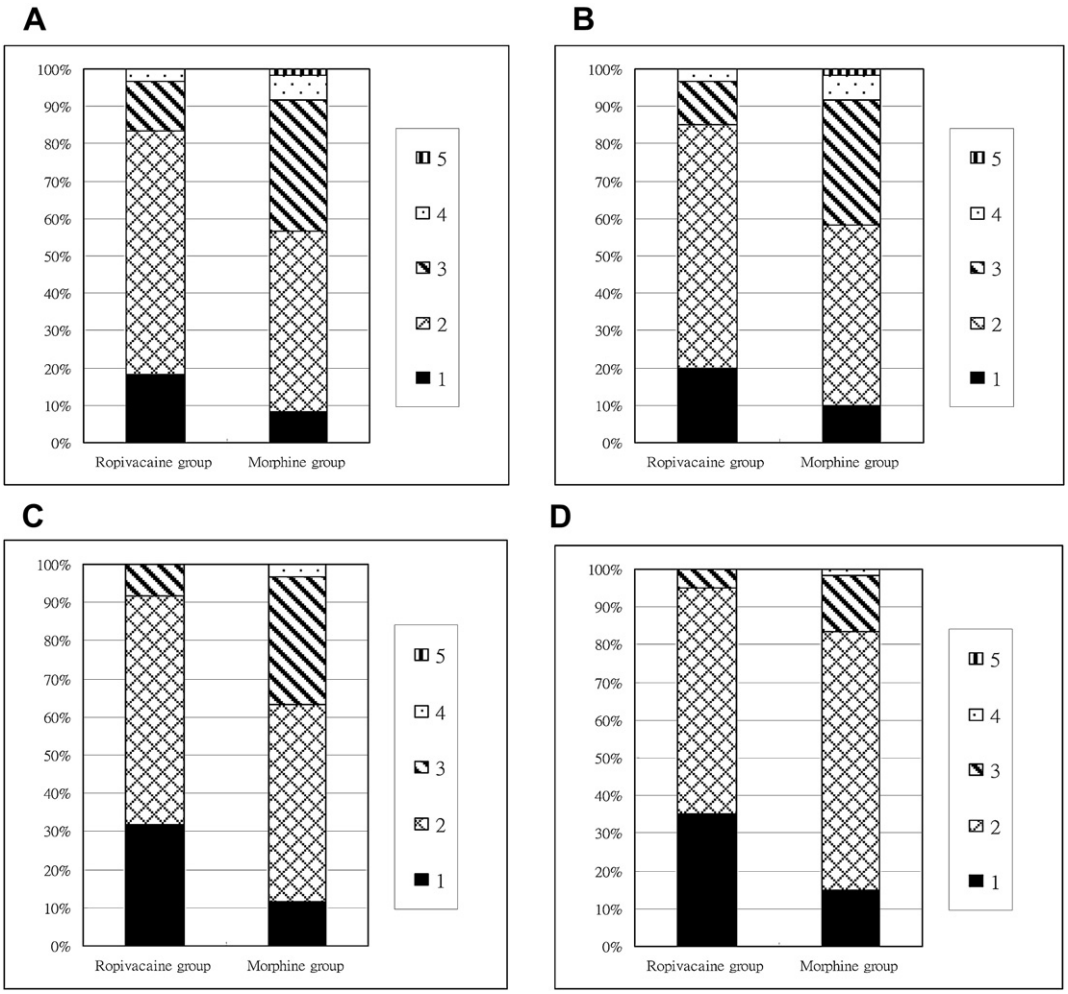

Fig. 2. Comparisons of global satisfaction scores at (A) 2 hours, (B) 12 hours, (C) 24 hours, and (D) 48 hours post-Cesarean delivery between the ropivacaine and morphine groups. Results are based on the satisfaction scale rating, where 1 is the most and 5 is the least satisfied.

Table 2
Incidence, severity score (mean), and distribution of reported motor weakness and side effects in the ropivacaine and morphine groups.

	Score (Mean)	Ropivacaine ($n = 60$)				Score (Mean)	Morphine ($n = 60$)			
		Degree of severity					Degree of severity			
		0	1	2	3		0	1	2	3
Nausea score (n)										
2 h	0.57*	29#	28	3	0	1.23*	13#	20	27	1
12 h	0.51*	32#	25	3	0	1.18*	17#	16	26	1
24 h	0.38*	44#	9	7	0	0.75*	25#	16	18	1
48 h	0.18*	51#	7	2	0	0.41*	41#	13	6	0
Pruritus score (n)										
2 h	0.08*	57#	2	1	0	1.47*	9#	15	35	1
12 h	0.05*	58#	1	1	0	1.43*	11#	13	35	1
24 h	0.03*	59#	0	1	0	0.78*	26#	22	11	1
48 h	0*	60#	0	0	0	0.6*	31#	22	7	0
Bromage grade (n)										
2 h	0.91*	28#	16	9	7	0.3*	50#	4	4	2
12 h	0.47*	42#	10	6	2	0.1*	55#	4	1	0
24 h	0.05	57	3	0	0	0.02	59	1	0	0
48 h	0.02	59	1	0	0	0	60	0	0	0

*$p < 0.05$ for mean severity scores compared between the ropivacaine and morphine groups.
#$p < 0.05$ for the incidence of motor weakness and side effects compared between the ropivacaine and morphine groups.

with using epidural morphine for post-Cesarean delivery pain control [6,7]. The increasing use of combined spinal-epidural anesthesia increases the possibility of the epidural administration of a local anesthetic, such as bupivacaine, after spinal anesthesia. Ropivacaine has motor-sparing effects and less central nervous system and cardiac toxicity [15]; thus, PCEA with ropivacaine has been suggested as superior to bupivacaine for postoperative pain control.

In 2000, Buggy et al showed that the incidence of demonstrable motor weakness (Bromage grade 1 or higher) was significantly higher in patients receiving PCEA ropivacaine at 8-hours postadministration, but not at 12 hours; nevertheless, they did not evaluate the time of first ambulation or global satisfaction [16]. Based on the methods used in their assessment, could they conclude that the higher incidence of motor weakness at 8 hours interfered with the time of first ambulation and the quality of ambulation? Therefore, we designed this prospective, randomized, and double-blind study to evaluate the efficacy of pain relief, side effects (nausea, vomiting, and pruritus), motor blockade, time of first ambulation, and global satisfaction of PCEA with ropivacaine and epidural morphine and, therefore, obtain useful clinical information on post-Cesarean pain control. Among all of the patients examined, no episode of significant vital sign instability was detected throughout the 48-hour, post-Cesarean delivery period, except for one episode of sedation in the morphine group (score > 1) and one episode of hypotension in the ropivacaine group; however, both of these episodes were transient. PCEA with a pure local anesthetic without the addition of an opioid could result in tachyphylaxis, resulting in the prolonged use of the local anesthetic, as has been reported in previous studies [12,15]. In our study, no episode of tachyphylaxis was detected in any patient throughout the 48-hour, post-Cesarean delivery period.

The PCEA settings for the ropivacaine group (0.1% ropivacaine, 5 mg bolus, 15 minute lockout with a 3 mg/hour background infusion and a maximum dose of 60 mg/4 hours) was the same as that used in the study by Buggy et al in 2000 because we believed that this setting provided an acceptable balance between adequate analgesia and minimal occurrence of motor blocking. Furthermore, Liu et al compared three solutions of ropivacaine and fentanyl (1 μg/mL 0.05% ropivacaine/fentanyl , 2 μg/mL 0.1% ropivacaine/fentanyl, and 4 μg/mL 0.2% ropivacaine/fentanyl) as a postoperative patient-controlled analgesia after lower abdominal surgery. They found that higher concentrations of ropivacaine (0.2%) induced a 30% incidence of motor block, but not in those receiving lower concentrations of ropivacaine (0.05% or 0.1%) [21]. Chaplan et al also demonstrated that the relative analgesic potency of ropivacaine compared with bupivacaine was about 0.6 and the EC_{50} for the minimum concentration of ropivacaine administered during labor was approximately 0.16% [20]. Thus, 0.1% ropivacaine might not aggravate motor weakness and be less likely to produce motor block than 0.1% bupivacaine.

From this prospective, randomized, and double-blind study, our results demonstrate that PCEA with 0.1% ropivacaine alone provides equivalent analgesic effects as epidural morphine (2 mg administered twice per day) without delaying the time to first ambulation, although the percentage of demonstrable motor weakness was still significantly higher in the ropivacaine group at 2 and 12 hours post-Cesarean delivery. The reason why the time of first ambulation was not delayed and motor blockade was insignificant after 12 hours between the two patient groups could be attributed to the use of low-concentration ropivacaine (0.1%) in the PCEA formula and because the duration of spinal anesthesia for all patients was about 8–12 hours. Within the first 12 postoperative hours, there could have been a synergistic effect between spinal anesthesia and epidural analgesia in the ropivacaine group. By significantly reducing the annoying side effects (nausea, vomiting, and pruritus) and limiting the influence on ambulation, patients reported higher global satisfaction scores with PCEA than with ropivacaine. We conclude that PCEA with 0.1 % ropivacaine alone provides a better quality of pain relief than epidural morphine; thus, it is a more efficient and acceptable analgesia for controlling pain after a Cesarean delivery.

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