

The Effects of the Use of Diluted Bupivacaine in Sequential Combined Spinal and Epidural Anesthesia for Cesarean Delivery on Maternal Hypotension and Motor Block after Surgery: A Retrospective Observational Study

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Background: Maternal hypotension is a common hemodynamic consequence of spinal anesthesia during cesarean delivery, but low-dose spinal anesthesia (<9 mg bupivacaine) ensures stable hemodynamics and reduces motor block. The purpose of this retrospective observational study was to examine the effects of baricity of intrathecal administration of diluted bupivacaine in combined spinal-epidural anesthesia (CSEA) for cesarean delivery on maternal hypotension and motor block after surgery.

Methods: The anesthesia and nursing records of 35 patients who had given birth by cesarean delivery under CSEA with intrathecal administration of plain or hyperbaric bupivacaine diluted in cerebrospinal fluid were reviewed. All patients were assigned to who received hyperbaric bupivacaine(hyperbaric group) or plain bupivacaine(plain group). Definition of feasibility of cesarean delivery by diluted low dose bupivacaine was set as no requirement of epidural administration of levobupivacaine during surgery. The incidences of hypotension (nadir blood pressure less than 80% of preanesthetic value) and motor block were reviewed.

Results: In 24 of the patients (68%), no additional epidural anesthesia was needed during surgery. One patient(3%) required additional epidural anesthesia before delivery. Feasibility of cesarean delivery was not different between hyperbaric group and plain group($p>0.99$). Eighteen of the patients (51%) did not require vasopressors, while 17 (49%) developed hypotension. There was no difference in incidence of maternal hypotension between hyperbaric and plain group. Only 6 patients (17%) required more than 3 times of administration of vasopressors among all patients. Modified Bromage scale scores were recorded in 28 of the patients (80%); scores of 0 (no motor block) were recorded in seven of them, and 1 in eight of them.

Conclusion: Low-dose either plain or hyperbaric bupivacaine diluted in cerebrospinal fluid to approximately twice the volume may provide sufficient analgesia, fast motor recovery. Incidence of maternal hypotension was similar in hyperbaric and plain group. (J Nippon Med Sch 2022; 89: 533–539)

Key words: cesarean delivery, spinal anesthesia, dilution technique, hypotension

Introduction

Hypotension is a common hemodynamic consequence of spinal anesthesia during cesarean delivery, and severe hypotension leads to low neonatal Apgar scores and umbilical acidosis. Various measures are used to prevent hy-

potension, such as co-infusion of large volumes of colloids during anesthesia and wrapping the legs with bandages¹. Also, low-dose spinal anesthesia (bupivacaine, <9 mg) during cesarean delivery is known to provide more stable hemodynamics and lead to less motor block than

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normal doses of bupivacaine^{2,3}. Because low-dose spinal anesthesia sometimes provides inadequate analgesia, however, Dyer and Joubert recommend the use of optimal-dose spinal anesthesia for cesarean sections⁴. The effective dose 50% (ED50) and dose 95% (ED95) of intrathecal administration of hyperbaric bupivacaine combined with opioids to accomplish cesarean delivery are reported to be 7.6 mg and 11.2 mg, respectively⁵. Dilution of a local anesthetic in cerebrospinal fluid (CSF) was reported by Pitkänen et al.⁶ We have been using low-dose bupivacaine diluted in CSF during combined spinal and epidural anesthesia (CSEA) for cesarean delivery since December 2018, intrathecally administering hyperbaric or plain bupivacaine (5.0-7.5 mg [1-1.5 mL]) diluted in up to 2.5 mL CSF. It is not known the effect of baricity on the feasibility to achieve sufficient analgesia and incidence of hypotension during cesarean delivery using diluted bupivacaine.

The purposes of this retrospective observational study were to examine the feasibility of intrathecal administration of diluted plain or hyperbaric bupivacaine in CSF for cesarean delivery, and the effects of baricity of diluted bupivacaine on maternal hypotension and the development of motor block after surgery.

Materials and Methods

This study was approved by the Ethics Committee of Yatsu Health Hospital (#56), and informed consent was obtained via an opt-out method involving the hospital's website. The anesthesia and nursing records of 35 patients who had given birth by cesarean delivery (elective or emergency) under combined spinal-epidural anesthesia (CSEA) with diluted bupivacaine at Yatsu Health Hospital in Chiba, Japan between December 2018 and September 2020 were reviewed. The following information was obtained: patient's stature, gestational age of fetus at delivery (weeks), indication for cesarean section, baricity (hyperbaric or plain) and dose (mg) of 0.5% bupivacaine, volume of cerebrospinal fluid (mL) for dilution, nadir blood pressure before and after intrathecal administration of bupivacaine, intervention to treat hypotension (administration of colloids or vasopressors), dermatomal level of sensory block as assessed with an alcohol swab, and modified Bromage score (0 - 3, with 0 indicating no motor block) as obtained when feasible after surgery. The total volume of bupivacaine (mL) was calculated as the sum of the volume of 0.5% bupivacaine and the volume of CSF that had been aspirated for dilution.

The routine anesthetic procedure for patients undergoing cesarean section at our hospital is as follows. 1) Before entering the operating room, the patient receives an intravenous infusion of approximately 200 mL of 5% glucose for 3 hours in the obstetrical ward. 2) In the operating room, the CSEA procedure is performed with the patient in the right decubitus position. An epidural catheter is placed at the Th12/L1 interspace, and a 25-gauge Quincke needle is inserted at the L2/3 interspace. 3) After it has been confirmed that CSF can be drained, a 2.5-mL syringe containing 1.0 mL - 1.5 mL of 0.5% bupivacaine is attached to the needle. 4) CSF (1.0 mL - 1.3 mL) is gently drawn into the syringe. If aspiration does not proceed smoothly, the syringe is detached, the needle is repositioned, and the process is repeated. 5) A mixture of bupivacaine and CSF is administered over a 3-second period. 6) The patient lies back in the supine position, blood pressure is measured, and the left-hand side of the operating table is lowered approximately 10 degrees for left uterine displacement. The dermatomal level of sensory block is checked with an alcohol swab approximately 5 minutes after intrathecal administration.

We do not co-infuse large amounts of colloids or crystalloids at our hospital. Blood pressure is measured every 2.5 minutes after spinal administration of bupivacaine. Additional epidural administration of 0.75% levobupivacaine (5 mL - 6 mL) is performed if the dermatomal level of sensory block is below Th8, or if the patient complains of pain during the surgery. After delivery, intravenous administration of midazolam (10 mg) and epidural administration of fentanyl (100 µg) are performed. Continuous epidural administration of 0.24% bupivacaine at 4 mL/hr combined with fentanyl (9.2 µg/hr) is performed after the surgery to manage postoperative pain.

Definition

Feasibility of cesarean delivery by dilute bupivacaine was defined as no additional need of epidural administration of levobupivacaine until the end of surgery. Hypotension was diagnosed when nadir blood pressure after administration of the local anesthetic was less than 80% of that before intrathecal administration. Neonatal Apgar scores at 1 and 5 minutes after delivery and the pH value of blood in the umbilical artery were also obtained.

Statistical Analysis

We assigned all patients to hyperbaric group (n=20) and plain group (n=15). Patients' height and weight, total volume, concentration, dose of bupivacaine, nadir blood pressure was compared between plain and hyperbaric

Table 1 Patient characteristics (n=35)

	Hyperbaric (n=20)	Plain (n=15)	Pvalue
Age (y) ^a	34 (23-41)	33 (22-41)	0.6
Height (cm) ^a	156 (148-172)	158 (150-174)	0.42
Weight (kg) ^a	62.5 (52-87)	62 (50-107)	0.75
Gestation (week) ^a	38 (36-41)	38 (37-40)	0.86
Urgent case	3	2	>0.99
Indication (previous CS, breech presentation, CPD, prolonged labor, others) ^b	(11, 1, 4, 3, 1)	(4, 4, 3, 2, 2)	0.22
Nadir systolic blood pressure before anesthesia ^c	110.3 ± 13.15	118.6 ± 10.0	0.050

a Median (range)

b Number of patients

c Mean ± standard deviation

CPD: cephalopelvic disproportion, CS: cesarean section, CSF: cerebrospinal fluid

group using student-t test. Feasibility of cesarean delivery by diluted bupivacaine, and incidence of maternal hypotension as well as requirement of vasopressors before delivery was compared between hyperbaric and plain group using Chi-squared test. Dermatome level of sensory block, distribution of Bromage Scale, Apgar score 1 minutes and 5 minutes after delivery and were compared between groups using Mann-Whitney U-test.

Results

All 35 of the study participants had given birth by cesarean delivery under CSEA, and there was no record of conversion to general anesthesia during surgery. Twenty of the patients received hyperbaric bupivacaine (hyperbaric group, n=20), and the other 15 were given plain bupivacaine (plain group n=15). There was no difference in number of urgent cases between hyperbaric group and plain group (3 and 2, p>0.99). Patients' characteristics are summarized in **Table 1**.

Feasibility of Intrathecal Administration of Diluted Bupivacaine

Twenty four(68%) patients underwent cesarean delivery without additional epidural administration of levobupivacaine during surgery. Ten patients(28%) received additional epidural administration after delivery and only one patient one (3%) was given epidural anesthesia because she complained of pain despite a dermatome level of sensory block of Th6. There were no difference in feasibility of cesarean delivery by diluted bupivacaine between hyperbaric and plain group(p>0.99). In plain group, higher dose of bupivacaine had been administered compared with hyperbaric group(p=0.006). Dermatome level of sensory block was not different between the group(p=0.64). Patient's outcome is presented in **Table 2**.

Effects of Diluted Bupivacaine on Maternal Hemodynamics

Seventeen patients (48%) required vasopressors before delivery (11 in hyperbaric and 6 in plain group, p=0.5). In **Figure 1**, distribution of number of patients who required various number of administration of vasopressors is demonstrated. Only 6 patients (17%) required more than 3 times of administration of vasopressors among all patients. There was no difference in incidence of hypotension as well as nadir blood pressure after administration of bupivacaine between hyperbaric and plain group (p=0.73 and p=0.096, respectively).

Effects of Diluted Bupivacaine on Motor Block after Surgery

Modified Bromage scores at the end of surgery were recorded in 28 patients: seven had a score of 0 (no motor block), eight had a score of 1, three had a score of 2, and 10 had a score of 3 (complete motor block) (**Table 3**).

In plain group, there were no correlation between dose as well as total volume and modified Bromage scale after surgery (p=0.39 and 0.45, p=0.39 and 0.14, dose and volume respectively), whereas in hyperbaric group, there was significant relationship between dose and modified Bromage scale after the surgery (p=0.58, p=0.01) but between total volume and modified Bromage scale after the surgery (p=0.2, p=0.44) (**Figure 2a, 2b**).

There was no difference in neonatal outcome such as apgar score 1 minutes and 5 minutes after delivery nor umbilical pH.

Discussion

In this retrospective study, we demonstrated the feasibility of using intrathecal administration of diluted bupivacaine without opioids as anesthesia for cesarean section. Ninety-seven percent of the study participants required

Table 2 Patient's outcome

	Hyperbaric (n=20)	Plain (n=15)	Pvalue
Total dose of bupivacaine (mg) ^c	5.5 ± 0.43	6.0 ± 0.48	0.006
Total volume of bupivacaine (mL) ^c	2.35 ± 0.13	2.4 ± 0.07	0.189
Dermatomal level of sensory block	T4 (T6-T3)	T4 (T4-T3)	0.64
Requirement of additional epidural administration ^b	14	10	>0.99
Incidence of hypotension ^b	10	9	0.73
Nadir systolic blood pressure after spinal anesthesia ^c	80.75 ± 21.7	93.6 ± 22.4	0.096
Requirement of vasopressors before delivery ^b	11	6	0.5
Modified Bromage score at the end of surgery (0, 1, 2, 3, NA) ^b	(4, 7, 0, 5, 4)	(3, 1, 3, 5, 3)	0.13
Total colloid infusion (mL) ^a	100 ± 194	70 ± 155	0.62
Total crystalloid infusion (mL) ^c	930 ± 270	946 ± 184	0.83
Total blood loss (mg) ^c	400 (400-1,780)	560 (300-1,850)	0.04
Time from incision to delivery (min) ^a	10 (6-19)	9 (3-22)	0.09

a Median (range), b Number of patients, c Mean ± standard deviation

NA: not applicable.

Modified Bromage scores were not assessed at the end of surgery in patients who were sedated.

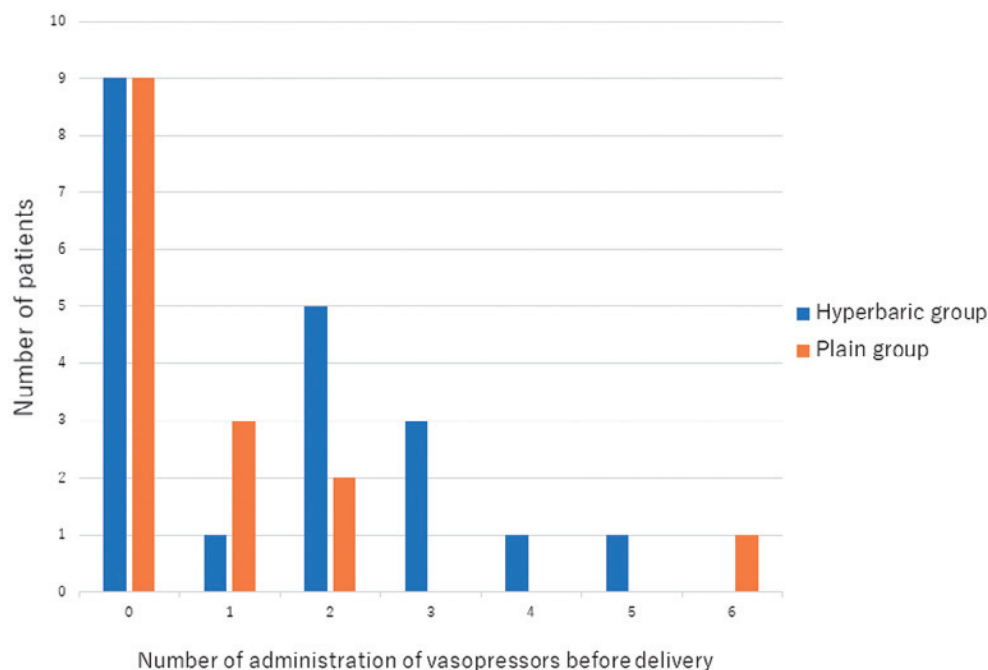


Fig. 1 The number of administrations of vasopressors before delivery

no additional epidural administration before delivery, and approximately 70% of them had no need of additional epidural local anesthetics during surgery.

There was no significant difference in feasibility and the dermatomal level of sensory block between hyperbaric and plain group. Thanks to pregnancy-induced hormonal changes and increased abdominal pressure in pregnant women at term, the requirement for local anesthetics in women undergoing cesarean delivery is low^{7,8}. Danelli et al.⁹ demonstrated that the dose of hyperbaric bupivacaine providing effective anesthesia for cesarean section is 0.06 mg/cm of the patient's height. In present

study, average dose in hyperbaric group was approximately 0.035 mg/cm and that in plain group was 0.037 mg/cm, which is less than previously reported^{2,3,9}. Dilution in CSF may change the density, viscosity, and acid-base status of local anesthetics, but it has been reported that the injected volume does not affect the spread of sensory block when the dose of plain bupivacaine is 17.5 mg¹⁰. In another study, no expansion in the level of sensory block was observed when 22.5 mg glucose-free bupivacaine was given as either 3.0 mL of 0.75% solution or 4.5 mL of 0.5% solution¹¹. Three mL of 0.5% bupivacaine diluted in 1 mL or 2 mL of CSF for a total volume of 4 or

Table 3 Neonatal outcome

	Hyperbaric (n=20)	Plain (n=15)	Pvalue
Apgar score at 1 min after birth ^a	8 (8-9)	9 (8-9)	0.64
Apgar score at 5 min after birth ^a	9.5 (9-10)	9 (9-10)	0.86
Umbilical pH ^b	7.32 ± 0.06	7.28 ± 0.04	0.018

a Median (range).

b Mean ± standard deviation

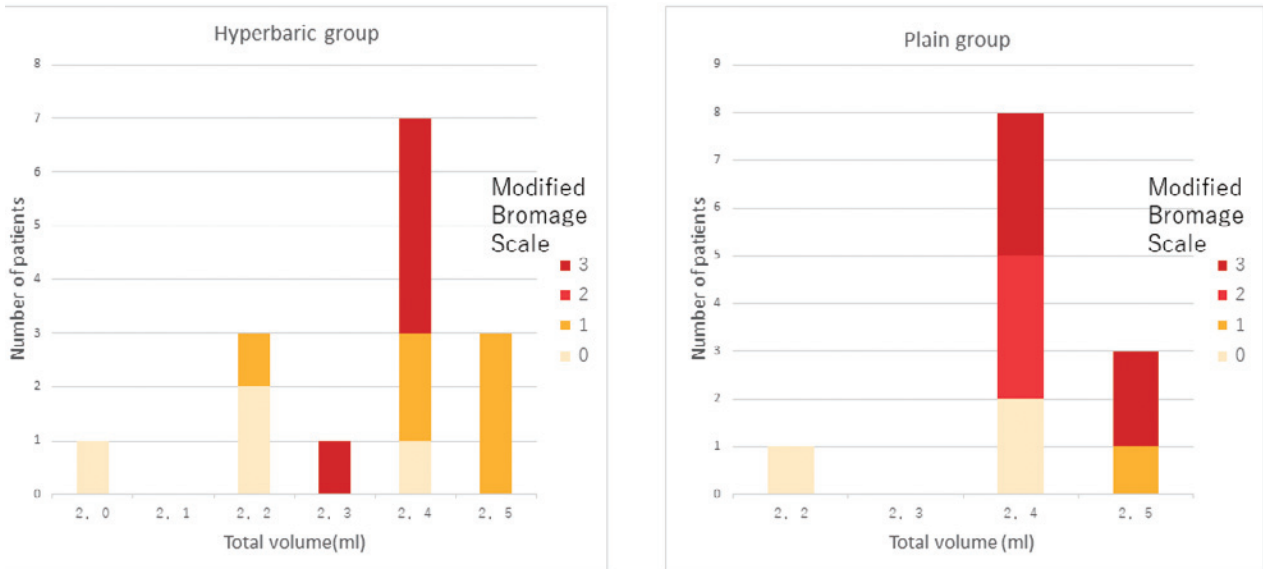


Fig. 2a Distribution of patients in relation to modified Bromage scales at the end of surgery and the total volume of bupivacaine in hyperbaric group (left) and plain group (right). (Scores were recorded in 28 patients.)

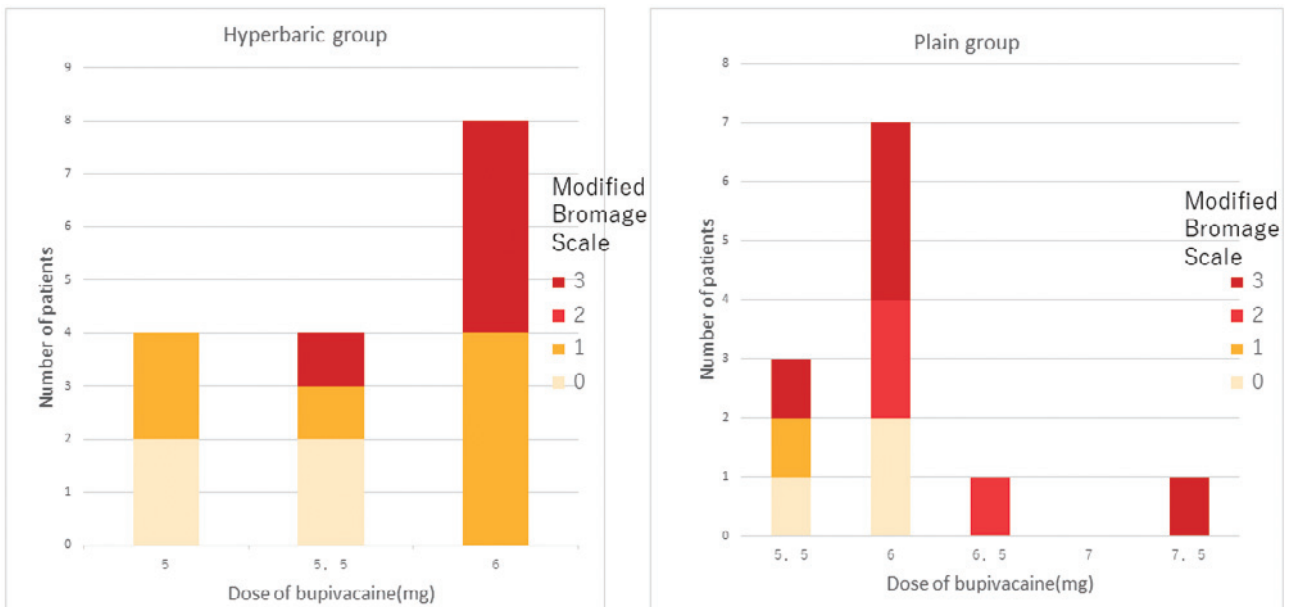


Fig. 2b Distribution of patients in relation to modified Bromage scores at the end of surgery and the dose of bupivacaine in hyperbaric group (left) and plain group (right). (Scores were recorded in 28 patients.)

5 mL did not provide additional spread compared with undiluted bupivacaine (3 mL)¹². Dilution in a relatively large volume of CSF may not have any additional effect if the dose of bupivacaine is high. However, Schmidt et al. found that when the amount of plain bupivacaine was decreased to 15 mg, there was a significantly wider spread of sensory block when it was administered in a 3 mL solution (0.5%) than in a 2 mL solution (0.75%)¹³. In present study, dose of administered bupivacaine was less than 7.5 mg. Thus, small dose of bupivacaine was administered, dilution in CSF may contribute to the provision of a sufficient level of analgesia, and the volume of bupivacaine may be a determining factor in the spread of the dermatomal level of sensory block.

In the present study, although 48% of the patients developed hypotension, more than 80% of patients with maternal hypotension could be treated by two times of administrations of vasopressors. Incidence of hypotension had been similar between hyperbaric and plain group. This may be because similar density of injected solution and similar dermatomal spread of sensory block. A low dose of bupivacaine, 6.5 mg in spinal anesthesia for cesarean delivery has been reported to provide more stable hemodynamics than the conventional dose such as 9.5 mg¹⁴. Leo et al, demonstrated the incidence of maternal hypotension were 30%, 55%, and 90% in the patients who received 7 mg, 8 mg, and 9 mg respectively². In the study, demonstrated by Van de Velde et al., incidence of maternal hypotension after spinal anesthesia using 6.5 mg hyperbaric bupivacaine was 15%. Incidence of maternal hypotension in present study was higher compared with that in the study using undiluted low-dose bupivacaine. This may be because volume of bupivacaine was large, results in higher level of sensory compared with undiluted low-dose bupivacaine¹³. Effect of diluted bupivacaine on maternal hemodynamic should be studied further.

In our hospital, infusions of fluids before the administration of anesthesia are carried out by obstetricians, and the patients in our study received only 200 mL of 5% glucose before anesthesia. They may, therefore, have been dehydrated. Furthermore, they were not co-administered with large amounts of crystalloids or colloids during the anesthesia procedure. Even though co-administration of colloids prevents the development of spinal anesthesia-induced hypotension, a study of the effects of co-loading with 1,000 mL of colloids showed that almost 80% of patients developed hypotension after administration of 8 mg - 10 mg of hyperbaric bupivacaine¹⁵. Again, in present

study, the patients who developed hypotension were less than 50%. Neonatal acidosis has also been shown to be associated with sustained maternal hypotension^{16,17}. Generally, it could be said that effect of diluted bupivacaine on maternal hemodynamic had been mild in present study.

In the present study, motor function was preserved (as indicated by a modified Bromage score of ≤ 1) in about 50% of the patients whose motor function was evaluated at the end of surgery. The importance of recovery of motor function after cesarean section has been highlighted¹⁸, because residual motor block after regional anesthesia is the main reason for delayed discharge after cesarean section. In the present study, we found that the degree of motor block was related to the dose of bupivacaine in hyperbaric group. Leo et al.² also demonstrated that recovery of motor function was associated with the dose of bupivacaine, and that the Bromage score regressed to 2 at approximately 100 minutes after administration of bupivacaine. Vercauteren et al.¹⁷ demonstrated that more than 90% of patients who received plain or hyperbaric bupivacaine (6.6 mg) were able to flex their knees on arrival in the recovery room. In our study, the patients who received additional epidural administration had higher Bromage scores than those who did not. We also found that the need for additional epidural administration was not associated with the baricity, dose, or volume of bupivacaine. The co-relation between dose of bupivacaine and degree of motor block indicates that an increased dose of bupivacaine induces a higher incidence of non-preserved motor function. However, increasing the dose of bupivacaine does not necessarily increase the probability that surgery can be performed without additional epidural administration. Thus, it makes sense to try lower doses of bupivacaine in sequential CSEA.

Limitations of This Study

One limitation of study is that because the anesthesiologist knew the baricity of solution, and patients in plain group received higher dose of bupivacaine. This may indicate the possibility that the anesthesiologist had tend to obtain greater level of sensory block, in case of plain group (i.e, rapid injection). However, it does not match clinical situation to blind the anesthesiologist to the baricity of bupivacaine. We believe that unblinding procedure may be better to investigate the effect of baricity in this procedure. In present study, the majority of the study participants underwent cesarean section without additional epidural administration of anesthetics, and the hemodynamic consequences were mild.

Conclusion

Low-dose either plain or hyperbaric bupivacaine diluted in CSF to approximately twice the volume appears to provide sufficient analgesia for patients undergoing cesarean section, along with relatively fast motor recovery. It should, therefore, be considered in the setting of sequential CSEA.

Conflict of Interest: The authors have no conflict of interest to declare in relation to this article.

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