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Relationship Between Body Mass Index and Spread of Spinal Anesthesia in Pregnant Women: A Randomized Controlled Trial

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

BDEF 1 Huai-Zhen Wang*
DEF 2 Han-Wen Chen*
ABCD 1 Yan-Ting Fan
BCD 1 Yu-Ling Jing
AEF 1 Xing-Rong Song
ABCDEF 1 Ying-Jun She

1 Department of Anesthesiology, Guangzhou Women and Children Medical Center, Guangzhou Medical University, Guangzhou, Guangdong, P.R. China
2 Department of Anesthesiology, Shunde Hospital, Southern Medical University, Foshan, Guangdong, P.R. China

* Both authors contributed equally to this work and should be considered co-first authors

Corresponding Author: Ying-Jun She, e-mail: yjsheh@yeah.net

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Background: The effect of body mass index (BMI) on the spread of spinal anesthesia is not completely clear. The aim of this study was to determine the dose requirements of ropivacaine and the incidence of hypotension in pregnant women with different BMIs during cesarean delivery.





Material/Methods: In this double-blind study, 405 women undergoing elective cesarean delivery were allocated to group S (BMI <25), group M (25 ≤ BMI <30), or group L (BMI ≥30). Women in each group were further assigned to receive 7, 8, 9, 10, 11, 12, 13, 14, or 15 mg of spinal ropivacaine.

Results: The ED₅₀ and ED₉₅ values of ropivacaine were 9.487 mg and 13.239 mg in Group S, 9.984 mg and 13.737 mg in Group M, and 9.067 mg and 12.819 mg in Group L. There were no significant differences among the 3 groups (p=0.915). Group L had a higher incidence of hypotension and a greater change in MAP after spinal anesthesia compared to the other 2 groups, and also required more doses of ephedrine than the other 2 groups when a dose of 15 mg ropivacaine was used. The incidence of hypotension had a positive correlation with the dose of ropivacaine (OR=1.453, p<0.001) and gestational age (OR=1.894, p<0.001).

Conclusions: Spinal ropivacaine dose requirements were similar in the normal BMI range. However, higher doses of spinal ropivacaine were associated with an increased incidence and severity of hypotension in obese patients compared with that in non-obese patients.

MeSH Keywords: **Anesthesia, Spinal • Body Mass Index • Cesarean Section**

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Background

Spinal anesthesia is the primary mode of anesthesia for cesarean sections but the reported doses of local anesthetics used in obese women vary widely [1–3]. Several studies have explored the relationship between body mass index (BMI) and the spread of spinal local anesthetics [4–6]. Some have recommended a reduced spinal dose in morbidly obese women, presumably due to the lower cerebrospinal fluid volume [4]. Other studies, however, have found no correlation between BMI and the spread of bupivacaine during cesarean delivery [5,6].

Hypotension induced by spinal anesthesia remains an important adverse effect, with a reported incidence between 20% and 100% [7,8]. Morbidly obese women have significant risk for anesthesia complications during cesarean delivery, and some studies found that a BMI ≥ 40 Kg/m² was an independent factor for spinal hypotension [9,10]. Also, usage of high doses of local anesthetics is a risk factors associated with hypotension during spinal anesthesia [11].

Optimal doses of spinal ropivacaine in women with varying BMIs, which provide sufficient analgesia and lower incidence of hypotension, have not been well established. Here, we aim to determine the effect of BMI on the dose requirements of spinal ropivacaine and incidence of hypotension in pregnant women for cesarean delivery.

Material and Methods

The trial protocol was approved by the Medical Ethics Committee of Guangzhou Women's and Children's Medical Center and was registered at www.chictr.org.cn (ChiCTR-OCH-13003109). Written informed consent was obtained from all enrolled participants. Enrolled women were divided into 3 groups based on their BMI, according to the World Health Organization criteria (overweight patients with BMI ≥ 25 Kg/m², obesity ≥ 30 Kg/m²) as follows: low BMI group (group S, BMI < 25 Kg/m²), medium BMI group (group M, $25 \text{ Kg/m}^2 \leq \text{BMI} < 30 \text{ Kg/m}^2$), and high BMI group (group L, BMI $\geq 30 \text{ Kg/m}^2$).

Healthy term women, aged 18 to 40 years, scheduled to undergo elective cesarean delivery for benign conditions, requiring American Society of Anesthesiologists physical status class I or II, singleton pregnancy, less than 2 previous cesarean deliveries, and gestational age of more than 37 completed weeks, were screened for eligibility. Patients were excluded from the study if 1 or more of the following criteria were met: labor, ruptured membranes, significant medical or obstetric morbidity, placenta previa, cardiorespiratory, renal or hepatic dysfunction, receiving medications known to affect anesthetic requirements, or allergy.

Women in each group were then randomly assigned to receive 1 of 9 doses of spinal ropivacaine by computer generated labels contained in opaque envelopes (n=15 per subgroup). An independent anesthesiologist performed the neuraxial procedure and spinal injection, and the anesthesiologist managing the case during the operation was blinded with regards to the dosage of spinal ropivacaine. All women were pre-hydrated with 1000 mL of lactated Ringer's solution. A combined spinal epidural block was performed, and the epidural space was located at the L3–4 interspace by using a 16-gauge Tuohy needle and loss of resistance to saline technique with the patient in the left lateral position. Spinal puncture was then performed by using a 27 G pencil-point needle. All spinal solutions were prepared in identical syringes by mixing ropivacaine 10 mg/ml (Naropin, AstraZeneca, Sweden) and normal saline to a total volume 2.5 ml (9 doses: 7, 8, 9, 10, 11, 12, 13, 14, or 15 mg). This isobaric mixture had a density of 1.0093 at 37°C based on our lab testing. An epidural catheter was threaded to 4 cm into the epidural space, but no drug was administered into the epidural catheter at this time except for a 3-ml 1% lidocaine epidural test.

The primary outcome of this study was the success or failure of the intrathecal block. A failure was recorded when a T6 sensory block was not achieved within 15 min after intrathecal drug administration, or when supplemental epidural analgesia was required to complete surgery because of either patient's request for additional analgesia or a visual analogue pain scale (VAPS) score > 40 mm. If a failure occurred, 5-mL bolus injections of 2% lidocaine were administered through the epidural catheter and repeated as needed. Patients received a repeat 10-mg IV bolus dose of ketamine in case of complaint of intraoperative pain with moderate to severe discomfort after an epidural top-up.

The maternal demographic variables were collected on enrollment in the study, including age, height, weight, parity, BMI, and gestational age. Neonatal weight and Apgar scores were recorded after delivery. Maternal mean arterial pressure (MAP) was determined by noninvasive blood pressure measurements made at baseline (averaged over 3 measurements), at 2-min intervals after completion of the spinal injection for the first 15 min, and at 5-min intervals thereafter. Hypotension, defined by a decrease in MAP to less than 60 mmHg or less than 80% from baseline, was treated with intravenous boluses of 6 mg ephedrine or repeated as required. The lowest MAP, the change in MAP after spinal anesthesia, the incidence of hypotension, and the total dose of ephedrine administered were all recorded.

The sensory level was determined bilaterally by pinprick every 2 min for the first 15 min after spinal injection. It was then assessed every 5 min for another 15 min and every 15 min thereafter. Results of the pinprick test were determined bilaterally

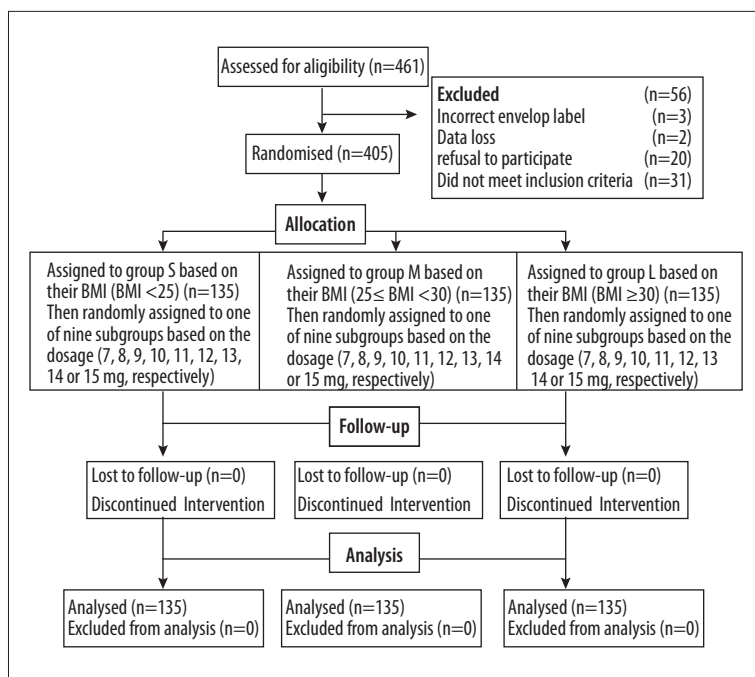


Figure 1. Consort flow diagram.

at midclavicular level by using a short-beveled 27-gauge needle, and time to reach a bilateral T6 sensory level was recorded. Subjective pain scores were rated at 10 min intervals during the surgery with the use of a VAPS, from 0 (no pain) to 100 (worst pain imaginable). The incidence of nausea and vomiting was recorded at 15-min intervals from intrathecal drug administration until the end of surgery.

Statistical analysis

Demographic data are presented as mean \pm standard deviation or median and range as appropriate. Data were assessed for normal distribution of variance. A total sample size of 405 subjects, with a minimum requirement of 15 patients in each subgroup, would give 80% power to detect a linear trend with a significance level at 0.05. Means were analyzed using one-way analysis of variance followed by Tukey multiple comparison test. Medians and non-normally distributed means were assessed by Kruskal-Wallis test. Incidence data were analyzed by Fisher exact test. The dose-response relation for spinal ropivacaine was determined using Probit regression with the SPSS version 13.0 (Chicago, IL). Data for successful responses for each dosage category were used to draw a sigmoid dose-response curve and interpolation was used to obtain the ED₅₀ and ED₉₅ values. Incidence of hypotension with each BMI group was calculated using the trend chi-square test in all 3 groups. Correlations were assessed with use of binary logistic regression or linear regression. Statistical significance was defined as $P < 0.05$.

Results

A total of 461 women were screened for the study and 405 were included in final analysis, with 15 women in each of the 9 dose subgroups under each of the 3 BMI groups (Figure 1). Apgar scores were similar and all babies had 1- and 5-min Apgar scores ≥ 9 . The demographics and obstetric characteristics were summarized in Table 1. The number of successful blocks, epidural blocks, and the use of ketamine in 3 groups were summarized in Table 2. The heights of the block in 3 groups are summarized in Table 3.

The ED₅₀ and ED₉₅ values (ED: effective dose) of ropivacaine obtained from Probit analysis were 9.487 mg (95% CI: 8.853–10.085) and 13.239 mg (95% CI: 12.497–14.189) in Group S, 9.984 mg (95% CI: 9.364–10.582) and 13.737 mg (95% CI: 12.979–14.715) in Group M, and 9.067 mg (95% CI: 8.395–9.696), and 12.819 mg (95% CI: 12.066–13.772) in Group L (Figure 2). There were no significant differences among the 3 groups ($p=0.915$). Larger doses of ropivacaine were associated with a higher rate of success of anesthesia (OR=2.112, 95% CI: 1.828–2.440, $p < 0.001$).

The mean time to T6 sensory block onset to pinprick was 8.65 min (95% CI: 8.20–9.10) in group S, 8.73 min (95% CI: 8.26–9.19) in group M, and 8.20 min (95% CI: 7.75–8.65) in group L ($p=0.220$). Times to T6 sensory block onset in the 3 groups are summarized in Figure 3. Larger doses of ropivacaine were associated with earlier T6 block to pinprick ($R=0.696$, $p < 0.001$).

Table 1. Patient characteristic and obstetric data by study group (values are presented as mean (standard deviation or median)).

Group	Group S		Group M		Group L		P values
Age (yr)	30	(4)	31	(4)	30	(4)	P=0.10
Height (cm)	161	(5)	161	(5)	161	(5)	P=0.759
Weight (kg)	61	(4)	70	(5)	81	(6)	P<0.001
BMI	23.4	(1.0)	27.1	(0.9)	31.4	(1.2)	P<0.001
Gestational age (wk)	39	(1)	39	(1)	39	(1)	P=0.11
Parity	1	(1-2)	1	(1-2)	1	(1-2)	P=0.574
Neonatal weight (kg)	3.25	(0.45)	3.27	(0.46)	3.33	(0.43)	P=0.278
Duration of surgery (min)	44	(11)	45	(13)	47	(15)	P=0.156

Table 2. Data pertaining to successful blocks, epidural blocks and use of ketamine.

Dose of ropivacaine	The successful block	Epidural blocks	Ketamine use
15 mg (n, group S: M: L)	15: 15: 15	0: 0: 0	0: 0: 0
14 mg (n, group S: M: L)	15: 15: 15	0: 0: 0	0: 0: 0
13 mg (n, group S: M: L)	14: 12: 15	1: 3: 0	0: 0: 0
12 mg (n, group S: M: L)	10: 12: 14	5: 3: 1	0: 0: 0
11 mg (n, group S: M: L)	10: 10: 11	5: 5: 4	0: 0: 0
10 mg (n, group S: M: L)	10: 8: 11	5: 7: 4	0: 0: 0
9 mg (n, group S: M: L)	8: 6: 8	7: 9: 7	0: 0: 0
8 mg (n, group S: M: L)	5: 3: 3	10: 12: 12	2: 3: 2
7 mg (n, group S: M: L)	2: 1: 2	13: 14: 13	2: 3: 3

Table 3. The height of the block and the number of high block in three groups.

The highest block level	T1 and above	T2	T3	T4	T5	T6
15 mg (n, group S: M: L)	1: 1: 1	3: 3: 4	4: 3: 4	4: 5: 4	2: 2: 2	1: 1: 0
14 mg (n, group S: M: L)	0: 1: 1	3: 3: 3	4: 4: 4	3: 4: 4	3: 2: 2	2: 1: 1
13 mg (n, group S: M: L)	0: 0: 0	3: 2: 3	3: 3: 3	3: 3: 3	4: 5: 4	2: 2: 2
12 mg (n, group S: M: L)	0: 0: 0	2: 2: 2	3: 2: 3	4: 4: 4	3: 4: 3	3: 3: 3
11 mg (n, group S: M: L)	0: 0: 0	2: 2: 3	3: 3: 3	3: 4: 3	4: 4: 4	3: 2: 2
10 mg (n, group S: M: L)	0: 0: 0	2: 2: 3	2: 2: 3	3: 4: 4	4: 3: 3	4: 4: 2
9 mg (n, group S: M: L)	0: 0: 0	2: 1: 2	2: 2: 1	3: 3: 3	4: 3: 3	4: 6: 6
8 mg (n, group S: M: L)	0: 0: 0	1: 2: 2	2: 2: 2	3: 4: 4	3: 3: 3	6: 4: 4
7 mg (n, group S: M: L)	0: 0: 0	1: 2: 1	2: 2: 2	3: 3: 3	4: 3: 4	5: 5: 5

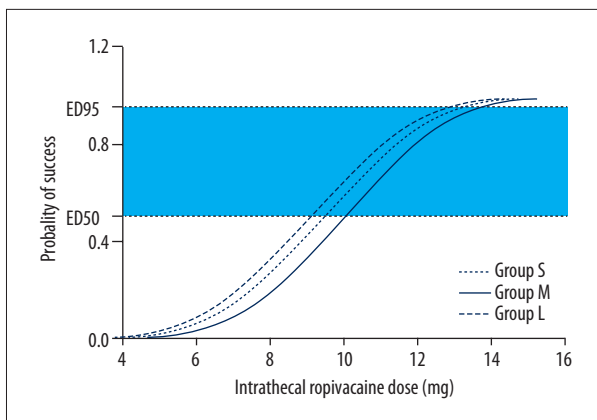


Figure 2. The success ED₅₀ and ED₉₅ values for intrathecal ropivacaine for cesarean delivery in the 3 groups using Probit regression.

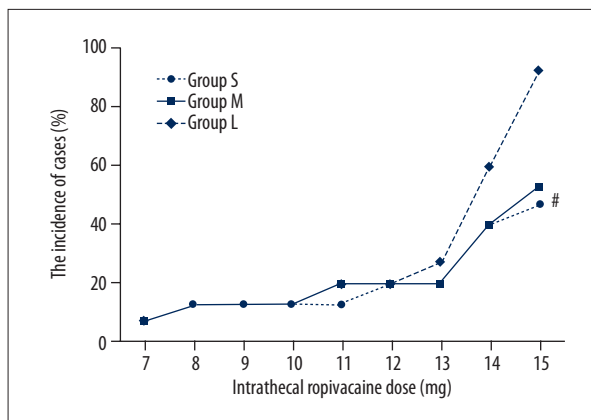


Figure 4. The incidence of hypotension in the 3 groups. # Compared with group L15, p=0.015.

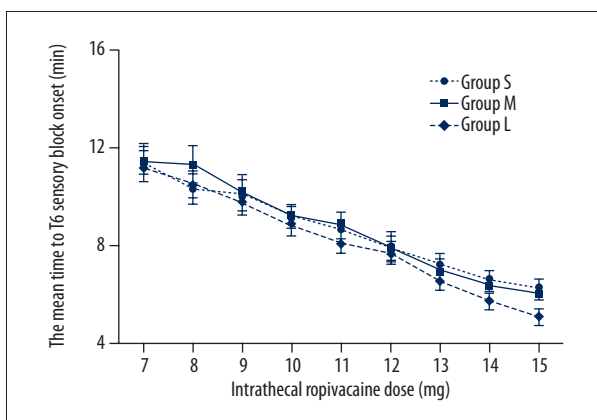


Figure 3. The mean time to T6 sensory block of different intrathecal ropivacaine doses in the 3 groups.

The incidence of hypotension in Group L was significantly higher than that in both Groups S and M with 15 mg of spinal ropivacaine (group S: M: L= 47%: 53%: 93%, p=0.015), but not with other doses (Figure 4). Increasing the dose of ropivacaine with each BMI group resulted in a significant difference in the incidence of hypotension in all 3 groups using the trend chi-square test. The incidence of hypotension had a positive correlation with the dose of ropivacaine (OR=1.453, 95% CI: 1.30–1.626, p<0.001) and gestational age (OR=1.894, 95% CI: 1.383–2.628, p<0.001).

Group L had greater changes in MAP after spinal anesthesia compared to the other 2 groups, and also required more doses of ephedrine than the other 2 groups with 15 mg of spinal ropivacaine, but not with other doses of ropivacaine. There were no significant differences in the same dose of ropivacaine among the 3 groups in the incidence of postoperative nausea and vomiting.

Discussion

In this study, we quantified the ED₅₀ and ED₉₅ of ropivacaine used in spinal anesthesia for cesarean delivery in women with different BMIs. Our results suggest that ropivacaine dose requirements were not different in the normal BMI range. However, the incidence of hypotension was increased with higher intrathecal doses, and the difference was the most pronounced in women with higher BMIs.

Previous studies on BMI and spinal local anesthetic doses showed conflicting findings. Some showed that the spinal local anesthetic dose should be reduced in morbidly obese patients [3,12,13], and some suggested there was no need to reduce the spinal local anesthetic dose [6,14,15]. The lumbosacral cerebrospinal fluid (CSF) is the diluent for local anesthetic delivered by a subarachnoid route, and it is thought to be the primary determinant factor during spinal anesthesia [16,17]. The studies showed that lumbosacral CSF volume was widely variable among patients by using magnetic resonance imaging [18–20]. Other factors, such as the different populations chosen for the study, the racial difference [21], body habitus [22], the bevel direction of the pencil-point needle [23], the baricity of local anesthetic solution [24], the use of opioids [26], the punctured interspace of spinal anesthesia [26], and varied definitions of a successful block [27] may all play a role. When all these factors are considered, the differences in spinal dose requirements for local anesthetics in different BMI patients may not be evident unless the BMI is in the extreme range.

We found that the incidence of hypotension had a correlation with gestational age in our study. A previous study determined that the mean physiological intra-abdominal pressure increased with the increased gestation weeks [28]. Magnetic resonance imaging was used to examine pregnancy-induced changes and showed that gestational week (between 31 and

39 week) was correlated significantly with the reduction in CSF volume and dural sac surface area [19]. Therefore, with longer gestation, the intra-abdominal pressure increased and the CSF volume in the lumbar region decreased [29]. Both of them contributed to the correlation between gestational age and the incidence of hypotension.

We also found that the incidence of hypotension in group L was higher than that in the other 2 groups when 15 mg of ropivacaine was given, but not with other doses. The height of sensory or sympathetic block was detected as an independent factor for hypotension after spinal anesthesia in women undergoing cesarean section [10]. Theoretically, the quality or density of the block, which is related to dosage, is more important for the incidence of hypotension. It is known that higher BMI is associated with higher intra-abdominal pressure [30,31], which can cause a decrease in the CSF volume and exaggerate hypotension. Such an effect may be more pronounced when a high spinal dose of local anesthetic is used. Therefore, the minimum sample size used to determine the difference in the incidence of hypotension in the 3 groups at the dose of 15 mg ropivacaine is smaller than that at the dose of 14 mg ropivacaine. A study with adequate sample sizes is needed to confirm the significant difference in the incidence of hypotension at ropivacaine dosage less than 15 mg.

One limitation of our study is that there were 2 different variables (BMI and weight) in the 3 groups. We initially planned to use only 1 variable and assign patients to the 3 groups according to maternal BMI. In general, patients with higher BMI are likely to have a greater weight when compared with non-obese patients in a large population. It's practically difficult to collect a large study population of pregnant women with different mean BMIs but similar mean weights or heights in the 3 groups. A further limitation of our study was the small

differences in BMIs among the 3 groups (S vs. M vs. L: 23.4 vs. 27.1 vs. 31.4; range: 19.92–36.85, and only 1 woman with BMI ≥ 35 Kg/m²). Pregnant women with a BMI ≥ 35 kg/m² are uncommon in China, so it is difficult to enroll a large study population of pregnant women with BMI ≥ 35 Kg/m² in China. At some point below 23.39 Kg/m² and above 31.36 Kg/m², the mean BMI in these patients may develop a significant difference in ED₅₀ and ED₉₅ values of intrathecal ropivacaine. However, the range of demographic variables in our study encompasses the majority of pregnant women in China.

Conclusions

In summary, we have shown that, within the normal BMI range, the dose requirements of ropivacaine were similar in pregnant women with different BMIs. The incidence of hypotension, however, increased with larger doses, and the difference was the most pronounced in women with high BMIs. When using a larger intrathecal dose, particularly more than the ED₉₅, we should pay more attention to the incidence of maternal hypotension and other adverse effects, especially for obese patients. When using a lower intrathecal dose, particularly near the ED₅₀, they should be administered under a CSE technique to provide reliable anesthesia.

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Conflict of interest

None.

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