



Original Article

Fixed-dose versus height and weight-adjusted dose of intrathecal 0.5% hyperbaric bupivacaine in elective cesarean section: a comparative study

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Abstract

Background: Spinal anesthesia is the preferred anesthetic technique for cesarean deliveries. But there is a dosage dilemma regarding block to the desired level and preventing hypotension. We aim to study effects of fixed dose with height and weight-adjusted dose of intrathecal 0.5% hyperbaric bupivacaine during elective cesarean section.

Methods: Eighty-eight singleton term parturients were enrolled and divided into two groups, Group FD (Fixed Dose) and CD (Calculated Dose) in this prospective, double-blind, randomized controlled trial. Group FD received 2.2 ml and CD received a height and weight adjusted calculated dose based on Harten's chart. Hemodynamic changes, onset time to sensory block to T6, maximum block in 20 minutes, and adverse effects were compared.

Results: There was a significant reduction in median drug dosage of 11mg in FD versus 9 mg in CD group. The decrease in the MAP was less in group CD (14.5±2.98) mmHg compared to (17.6±4.66) mmHg in group FD (P= 0.03). The median onset time of spinal block to T6 in group FD of 2 minutes with IQR (2-3) was faster than Group CD 4 minutes with IQR (3-5). The spinal block extended above T4 in the larger number of parturients 23 (52 %) in Group FD than in three (6.8%) in group CD (p<0.05).

Significantly larger number 20 (45.45 %) in group FD developed hypotension than seven (15.9 %) in Group CD. Bradycardia and vomiting were also found in group FD.

Conclusions: This calculated dose provided the desired level of the spinal block and also restricted spinal block level with a distinct advantage of less hypotension.

Key words: Spinal anesthesia, cesarean section, Harten chart

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Introduction

Spinal anesthesia with hyperbaric bupivacaine is the preferred anesthetic technique for cesarean deliveries¹. The incidence of hypotension following spinal anesthesia for cesarean section is high with trials reporting as high as 80%.². Untreated severe hypotension can pose serious risks to both mother (maternal nausea, vomiting, pulmonary aspiration, apnoea, unconsciousness or even cardiac arrest) and baby (impaired placental perfusion leading to hypoxia, fetal acidosis and neurological injury)³. The preventive measures decrease the incidence and severity of adverse effects rather than treating hypotension once it is established, however, there is no established ideal technique.

Strategies currently used to minimize hypotension include – preloading/co-loading of fluids (crystalloids/colloids)⁴⁻⁶ a maternal position with manual uterine displacement, table tilt 15- 20°, use of vasopressors⁷, use of prophylactic ondansetron⁸, and physical interventions like leg compression.

Studies have also been done by reducing the dose of a local anesthetic agent which is required for producing adequate blockade, yet maintain hemodynamic stability. However, dose selection for the single-injection spinal anesthesia is one of the major difficulties⁹. The dose adjustment study is based on a Caucasian population whose built differs from that of our population but still, we used it to compare the effects on the ground of hemodynamics, block characteristics and adverse effects.

Methods

Following approval from Institutional Review Board of National Academy of Medical Sciences, this prospective, randomized and comparative study was conducted at Paropakar Maternity and Women Hospital, Thapathali, Nepal from December 2015 to February 2016. Sample size calculation was done based on the previous study of Subedi A et al¹⁰ taking 95% confidence interval and of power of 80%. A total of 88 parturient of singleton term gestation, American Society of Anesthesiologists physical status (ASA-PS) class II planned for the elective cesarean section and the combination of height and weight falling in Harten's chart were included. Patients with contraindication to spinal anesthesia, pre-existing and pregnancy-induced hypertension, cardio-respiratory illnesses and patients not falling in inclusion criteria were excluded. The objectives of this study were to compare hemodynamics (SBP, MAP, and HR), time to T6 sensory blockade, extent of sensory blockade at 20 mins, time to complete motor blockade and incidence of adverse effects (hypotension, bradycardia, vomiting) between the groups.

A written informed consent was obtained from the parturient meeting the inclusion criteria for enrollment in the study. Height and weight of the parturient were noted as well as her anesthetic evaluation was done a day before the surgery. She fasted for 6 hours before the operation¹¹. The patient was allocated randomly to one of the following two groups using sealed envelope method by the non-researcher anesthesia provider.

1) Group FD (Fixed dose Group): fixed dose of 2.2 ml 0.5% heavy bupivacaine.

2) Group CD (Calculated dose Group): 0.5% heavy bupivacaine, volume calculated according to height and weight from the mentioned Harten's chart.

Table 1: Harten chart

Patient weight (Kg)	Patient height (cm)								
	140	145	150	155	160	165	170	175	180
50	1.5	1.7	1.8	1.9					
55	1.5	1.6	1.8	1.9	2.0				
60	1.4	1.6	1.7	1.8	2.0	2.1			
65	1.4	1.5	1.7	1.8	1.9	2.1	2.2		
70	1.3	1.5	1.6	1.8	1.9	2.0	2.2	2.3	
75		1.4	1.6	1.7	1.9	2.0	2.1	2.3	2.4
80		1.4	1.5	1.7	1.8	2.0	2.1	2.2	2.4
85			1.5	1.6	1.8	1.9	2.1	2.2	2.3
90			1.4	1.6	1.7	1.9	2.0	2.2	2.3
95				1.5	1.7	1.8	2.0	2.1	2.3
100				1.5	1.7	1.8	1.9	2.1	2.2
105					1.6	1.7	1.9	2.0	2.2
110						1.7	1.8	2.0	2.2

Baseline non-invasive blood pressure, heart rate, and oxygen saturation were measured in the waiting room. Intravenous access was achieved with an 18 Gauge intravenous cannula in either of the hands after consent. The parturient was pre-loaded with 10 ml/kg of Ringer's lactate 30 minutes before the performance of spinal anesthesia. She was pre-medicated with injection metoclopramide 10 mg and injection ranitidine 50 mg intravenously simultaneously while being preloaded. The subarachnoid block was performed by a non-researcher anesthesia provider who was well instructed in the study and the data was collected by the researcher. Both the parturient and the researchers were kept blinded. Under all aseptic technique in sitting position after proper cleaning and draping in the straight operating table, 26 Gauge Quincke's spinal needle was used for subarachnoid block in L4-L5 or L3-L4 level. After confirming correct placement of the needle in the subarachnoid space by witnessing the free flow of cerebrospinal fluid the study drug 0.5% heavy bupivacaine was injected by the non-researcher anesthesia provider using 3 ml syringe at a speed of 0.2ml/sec. The patient was immediately placed back to the supine position with a left lateral tilt with a wedge (folded towel) beneath the right pelvic region to prevent aortocaval compression. Oxygen supplementation was given via nasal prong at 2 liters per minute from the beginning of the procedure. For the assessment of sensory neural blockade, pin prick test with 27-gauge blunt bevel needle was used. Motor blockade was assessed using Bromage scale¹².

Table 2: Bromage scale

Scale	Interpretation
0	no motor block
1	just able to flex knees but not the hips
2	unable to flex knees, free ankle movements
3	no movement possible in any lower extremity

Sensory and motor assessment were done at 1 minute following the spinal block and every min thereafter until complete (Grade 3) motor blockade and T6 level of sensory block were achieved. If the sensory blockade was inadequate even after 10 minutes, the table was positioned in 10-degrees head down tilt and repositioned back to horizontal after sensory block at the T6 level or for next 10 minutes whichever was earlier. Cases requiring head down was noted. The surgery was allowed to commence once T6 sensory and grade 3 motor block was achieved. If the desired level of sensory block was not achieved even after 20 minutes of spinal anesthesia, then the case was performed under general anesthesia. Those cases were noted and included in the study. The maximum height of sensory block achieved in 20 minutes was also noted. Patients complaining of intolerable intraoperative pain and demanding for analgesia were treated with a 0.3 mg/kg intravenous bolus dose of ketamine and fentanyl 0.5 mcg/kg after delivery of the baby. If the pain still persisted, conversion to general anesthesia with a tracheal intubation was done. HR, SBP, and MAP were measured in every 2.5 minutes for 20 minutes following spinal anesthesia, then every 5 minutes after that.

Hypotension was defined as a decrease in noninvasive mean arterial pressure (MAP) > 20% of baseline or mean arterial pressure (MAP) < 60 mmHg (whichever was lower) and was treated with intravenous Ringer's lactate (5 ml/kg); if hypotension was not corrected, mephentermine 6 mg intravenously in increment doses was given. Bradycardia was defined as heart rate < 20% of baseline or < 60 beats/minute (whichever was lower) and was treated with atropine 0.6 mg intravenously. If the patient complained of nausea or vomiting, the cause was ruled out first. If the cause was hypotension, it was treated as mentioned above. If the patient still complained of nausea or vomiting, ondansetron 0.1mg/kg was given intravenously. Any complications were managed according to standard hospital protocols. After delivery of the baby, oxytocin 5 units was given intravenously as a slow bolus. Collected data were analyzed by means of statistical software SPSS 20.0 with appropriate tests. All data were tested for normal distribution using Kolmogorov-Smirnov test. Continuous variables– age, height, weight, SBP, MAP, HR were analyzed by the student's t-test. Categorical data – ASA, parity, adverse effects were analyzed with Pearson Chi-square test or Fisher Exact test as appropriate. Skewed data such as Bupivacaine dosage, time to sensory block T6, maximum block height, time to motor block Bromage-III, dose of mephentermine consumed were analyzed by Mann-Whitney U test. A p value of < 0.05 was considered statistically significant.

Results

A total of 88 parturient who met the inclusion criteria were included in the study. Detail is shown in the figure 1 below.

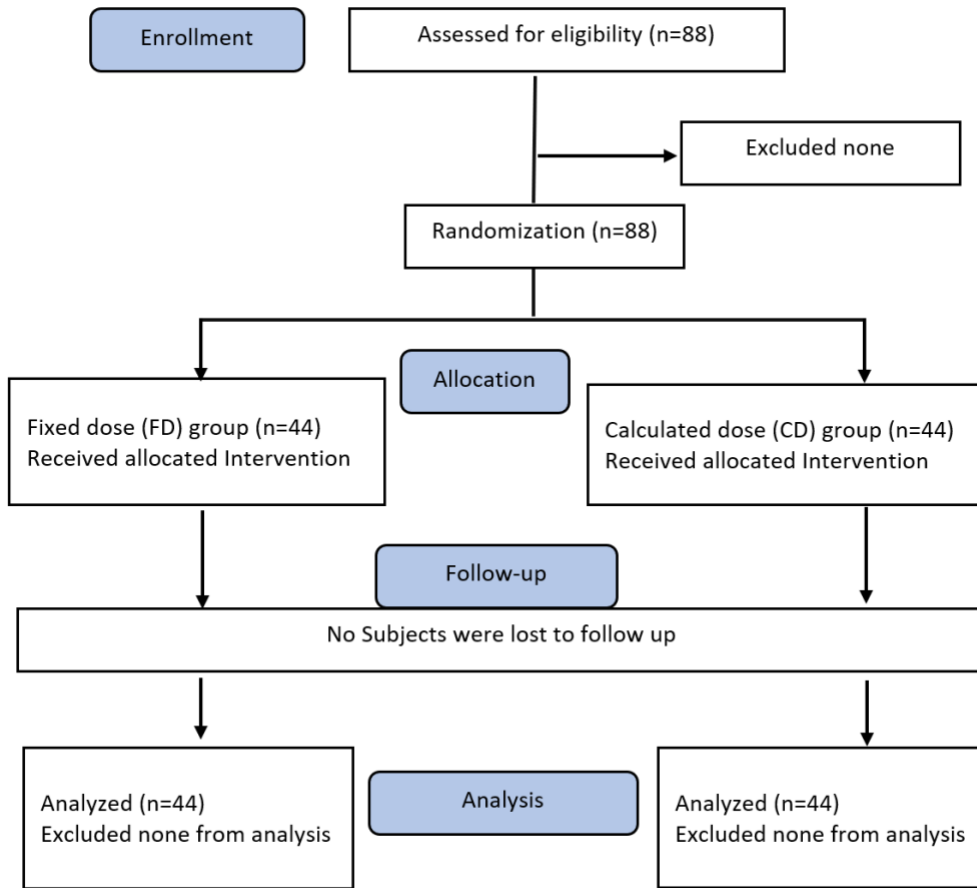


Figure 1: Consort flow diagram

The patients in both the groups were comparable for age, height, weight, ASA-PS, parity, gestational weeks and previous cesarean section as shown in table 3.

Table 3: Demographic data

Variables	Group FD (n=44)	Group CD (n=44)	P value
Age(years)*	27.3±5.31	27.18±2.87	0.90
Height(cm)*	155.66±4.83	155.3±7.10	0.78
Weight(kg)*	66.23±6.54	64.98±8.26	0.43
ASA I/II, N (%) / N (%)**	0 (0) / 44(50)	0 (0) / 44(50)	
Parity Primi/Multi, N (%)**	20(45) / 24(55)	21(47) / 23(53)	0.83
Gestational weeks*	41.00±2.09	40.93±2.17	0.88
Previous C/S, yes/no, N (%)**	15(34) / 29(66)	14(32) / 30(68)	

Values are *mean ± SD or **number(percentage)

The mean baseline MAP, SBP, HR and other parameters like mean duration of surgery, mean blood loss and median consumption of fluids were comparable between the groups. The difference between baseline SBP and minimum SBP 17.93±3.91mm of Hg in group FD and 15.97±2.51in Group CD were also comparable. However, the difference between baseline MAP and minimum MAP 17.60±4.66 mm of Hg in group FD and 14.5±2.98 in Group CD was significant with a p-value of 0.03.

Table 4: Surgical data and hemodynamics

Variables	Group FD(n=44)	Group CD(n=44)	P value
Baseline SBP (mm in Hg) *	125.73±12.10	126.36±13.18	0.81
Baseline MAP (mm in Hg) *	93.84±11.41	93.89±10.77	0.98
Baseline HR (bpm)*	90.25±12.48	89.41±14.27	0.76
Baseline SPO2 (%)*	98±0.43	97.95±0.68	0.70
Duration of Surgery (in minutes) *	39.27±9.97	39.05±7.79	0.90
Maintenance fluid (ml)***	1800 (1700-1800[1500-2000])	1800 (1500-1800[1200-2000])	0.16
Blood loss (ml)*	478.64±23.38	480.91±22.08	0.6
Uterus Exteriorization**	5 (11.3%)	1 (2.27%)	0.2
Difference between baseline and minimum SBP (mm of Hg) *	17.93±3.91	15.97±2.51	.103
Difference between baseline and minimum MAP (mm of Hg) *	17.60±4.66	14.5±2.98	.033

Values are *mean±SD, **number (percentage), or ***median (IQR [range])

The median dosage of 0.5% Hyperbaric Bupivacaine was significantly low of 9(8.5-9.5[7.5-11])mg in CD group in comparison to 11 mg in FD group. The median time to reach T6 sensory block 2(2-3[1-6]) minutes in Group FD was much early in comparison to 4(3-5)[1-12]) minutes in Group CD. The median maximum sensory level achieved in 20 minutes T3(T3-T4[T2-T5]) in Group FD was also significant in comparison to T5(T4-T5[T3-T5]). The maximum sensory level achieved in Group FD was T2 and in Group CD was T3. 15 parturient (34%) in group FD and 3 (7%) in Group CD attained a level of sensory block T3. While 8 parturient (18%) in group FD but none in Group CD attained a level of a sensory block of T2. The values are statistically significant with p-value <0.05. The median time to motor blockage Bromage-III was relatively early 4(3-6[1-12])minutes in Group FD in comparison to 6(5-8[2-14]) minutes in Group CD with a p-value of <0.05. Two parturient (4.5%) in Group CD needed head down position in order to get the desired level of sensory block. One parturient (2.27%) in both groups required supplementary analgesia. None of the cases were converted to General Anesthesia in either groups.

Table 5: Bupivacaine dosage, spinal block characteristics, and efficacy

Variable	Group FD(n=44)	Group CD(n=44)	P value (Significance)
Bupivacaine dosage 0.5% Hyperbaric (in ml) *** (in mg) ***	2.2 (2.2-2.2) 11(11-11)	1.8(1.7-1.9[1.5-2.2]) 9(8.5-9.5[7.5-11])	<0.001
Time to T6 Sensory block (in minutes) ***	2(2-3[1-6])	4(3-5[1-12])	<0.001
Time to motor blockade Bromage -III (in minutes) ***	4(3-6[1-12])	6(5-8[2-14])	<0.001
Maximum Sensory Level achieved in 20 minutes***	T3(T3-T4[T2-T5])	T5(T4-T5[T3-T5])	<0.001
Sensory block above T4- T2 N (%)** T3 N (%)**	8 (18) 15 (34)	0 (0) 3(7)	<0.001
Use of 10-degree head down to get desired block, N (%)**	0	2(4.5)	0.49
Supplementary Analgesia- Ketamine, N (%)**	1 (2.27)	1(2.27)	1.00
Interspace level L4-L5/L3-L4 N (%)**	34(77)/10(23)	38(86)/6(14)	0.26
Conversion to GA, N**	0	0	

Values are *mean±SD, **number (percentage), or ***median (IQR [range])

Hypotension in 20 parturient (45%) was significant in Group FD in comparison to 7 parturient (16%) in Group CD with a p-value of 0.003. Bradycardia in 3 (6.8%) and Vomiting in 2 (4.5%) were also noted in Group FD parturient. The median dose of mephentermine consumed 12(9-18[6-18]) mg in Group FD was statistically significant in comparison to 6(6-9[1-12]) mg in Group CD.

Table 6: Adverse effects

Variable	Group FD(n=44)	Group CD(n=44)	P value (Significance)
Hypotension, N (%)**	20(45)	7(16)	0.003
Bradycardia, N (%)**	3(6.8)	0	0.24
Vomiting, N (%)**	2 (4.5)	0	0.49
mephentermine consumption, N (%)**	20 (45)	7 (16)	0.03
mephentermine consumption (in mg) ***	12(9-18[6-18])	6(6-9[6-12])	0.031

Values are **number (percentage) or ***median (IQR [range])

Discussion

The dose of local anesthetic is reduced by about one-third in pregnant compared to non-pregnant lady for a variety of reasons. Till date, several studies have been conducted to establish the minimal but adequate dose of intrathecal bupivacaine for a cesarean section to limit the adverse effects related to spinal anesthesia but none have quoted for an absolute value.

Bupivacaine dosage: There was a significant reduction in Bupivacaine dosage. A survey of UK practice¹³ showed that the mean (SD) volume of bupivacaine 0.5% usually given is 2.57 ml with a fixed dosage scheme, whereas a median [range] dose of 2.34 [1.2–3.0] ml in a variable dose scheme. Our findings were comparable to study conducted by Harten et al¹², where the fixed dose was 2.4 ml (12 mg) and the median dose received in the dose-adjusted group was 1.9ml (9.5 mg), 1.9 (1.8–2 [1.6–2.2]) ml, p-value<0.001. Asian women are usually shorter in height than European women¹⁴. Nagata et al¹⁵ found that 8 mg of 0.5% Hyperbaric Bupivacaine in SAB was adequate for cesarean section in Japanese parturient. Subedi A et al¹⁰ used a fixed dose of 2.2 ml (11 mg) and the median dose in the adjusted group was 1.8 ml (9 mg), 9 (8 - 9.5 [7.5 - 10]) mg, p-value: 0.001 in Nepalese parturient.

Hemodynamics With higher doses, the level of block attained is higher so are the chances of adverse cardiac consequences. The combined effects of sympathetic inactivity and vagal overactivity, anesthesia of cardio accelerator fibers, activation of cardiovascular reflexes lead to decreased cardiac output and systemic vascular resistance finally causing adverse effects like hypotension and bradycardia¹⁶. There is a decrease in arterial pressures, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure during pregnancy. DBP and mean arterial pressure decrease more than SBP during the pregnancy¹⁷. The difference between baseline MAP and minimum MAP 17.60±4.66 mm of Hg in group FD and 14.5±2.98 in Group CD was significant. 52% of parturient in the fixed-dose group have gained a sensory block above T4. So, the significant difference in the MAP in fixed-dose group can be explained to be a part of this. Harten et al¹² and Subedi et al¹⁰ both found a significant difference between baseline and minimum mean arterial pressure (mmHg) 35.0 ±16.4 as compared to 28.0 ±13.5 and 96.5 ± 6.74 mm Hg as compared to 101.6 ± 6 mm between fixed and adjusted dose groups respectively.

Block characteristics A T6 level of the sensory blockade is usually sufficient for cesarean section¹⁸. The volume of drug is one of the determinants of a local anesthetic spread in SAB¹⁹. Greater the volume greater is the level of sensory block. Thus, in FD group the onset of sensory block was early but the level of block was not confined to the desired one. The spread was more cephalad up to T2. Though, the onset of sensory block was relatively slower in CD group the desired level of block was relatively confined. Two parturient in Group CD needed 10° head down position in order to get the desired level of the block, while none was needed in Group FD. One parturient in each group complained of pain during intraoperative period and was given supplementary analgesia. Subedi et al¹⁰ found that the median onset time for the target spinal block of T5 was significantly (p=0.01) prolonged in Adjusted dose group than in Fixed dose group (6 minutes vs. 4 minutes). In Group FD, the maximum block level extended above T3 in 12 (24 %)patients while it did so in one (2%) patient in Group AD. Six (12 %) patients in Group AD required a head -down tilt after 10 minutes of intrathecal injection to attain T5 block height as compared to one patient in the Fixed Group. Although there were no significant differences between the groups in the quality of intraoperative anesthesia, 4 (8 %) parturient required supplementary analgesia with IV ketamine in Group AD patients. However, none of the patients in either groups required conversion to GA. Harten et al¹²also found that the onset of the sensory block was faster with the fixed-dose than with the adjusted dose (p = 0.02). Though the median time was 6 minutes in both groups, the inter-quartile range was smaller in the Fixed-Dose Group than in the Adjusted-Dose Group. Five patients in the Adjusted-Dose Group and no patients in the Fixed-Dose Group required head-down tilt. No patients in either group required conversion to general anesthesia. Nagata et al¹⁵ found that ten minutes after the spinal anesthesia, in 79% of 8 mg group and in 88% of 10 mg group, sensory block level reached T4. The result of our study correlates with the results of above studies and support that calculated drug doses are sufficient enough to achieve the desired level of sensory block and providing good quality of intraoperative anesthesia and analgesia whereas with fixed doses the level of block achieved is much higher than the desired one. The median time to motor blockage, Bromage-III in Group FD was 4 minutes, 4(3-6[1-12]) minutes. In comparison to 6 minutes, 6(5-8[2-14]) minutes in Group CD.

Adverse effects Hypotension in 20 parturient (45%) was significant in Group FD in comparison to 7 parturient (16%) in Group CD. High level of spinal block is a potential risk factor for the intraoperative hypotension²⁰. Correlating the hypotensive episodes with the level of block attained we found that all 20 parturient in group FD had block height \geq T4 (8-T2, 10-T3, 2-T4). Similarly, in Group CD out of 7, 6 parturient had block height \geq T4 (2-T3, 4-T4, 1-T5). Greater the level of the sensory block, more pronounced are these effects. Greater the incidence of hypotension, greater is the use of vasopressor (mephentermine). Bradycardia in three (6.8%) and vomiting in two (4.5%) were also noted in Group FD parturient but they were comparable. The incidence of vomiting in the fixed-dose group of our study could be attributed to the greater reduction in arterial blood pressure in the fixed-dose intrathecal block²¹. Harten et al¹² found that the incidence of hypotension after spinal anesthesia was 71.7% in the Fixed-Dose Group and 50.0% in the Adjusted Dose Group ($p = 0.035$). More patients in the Fixed-Dose Group were given ephedrine (79.5% vs 56.8%, $p = 0.02$), and a larger median dose was administered (9 mg vs. 6 mg, $p = 0.042$). The percentage of patients in the Fixed-Dose Group who vomited was 17.9%, compared to 4.5% in the Adjusted Dose Group ($p = 0.052$). Subedi A et al¹⁰ found that significantly ($p < 0.01$) large number of patients in Group FD [32 (6%)] had hypotension than in Group AD [15 (30 %)]. The vasopressor requirement was more in the FD group (9 mg versus 6 mg in the AD group; $p = 0.003$). Nausea and vomiting were more frequent in Group FD than in Group AD. One patient in the fixed-dose group developed a very high block above T1 and had difficulty in breathing. The incidence of bradycardia and shivering was similar in patients of both the groups. Ozoagu AM et al²² found that patients in the fixed-dose group had lower intraoperative mean arterial pressure ($p=0.001$), higher incidence of hypotension (62.9% vs 28.6% with $p<0.001$), and so needed more ephedrine (62.9% vs 28.6%), and more patients reported nausea (15.7 % vs 2.9% at $p=0.009$) but there was no vomiting in either group. Nagata E et al¹⁵ found that hypotension occurred in 19 parturient (7 in 8 mg group and 12 in 10 mg group). The incidence of hypotension was significantly lower in 8 mg group (37%) than in 10 mg group (71%). C. Arzola, et al²³ found that in a Lower dose (LD) group exhibited a lower risk of hypotension (RR $\frac{1}{4}$ 0.78, 95% CI $\frac{1}{4}$ 0.65–0.93) and nausea/vomiting (RR $\frac{1}{4}$ 0.71, 95% CI $\frac{1}{4}$ 0.55–0.93).

Conclusion

In conclusion, the spinal anesthetic dose calculated using Harten chart in Nepalese parturients resulted in adequate level of block, and had a distinct advantage of less hypotension following spinal anesthesia.

Conflict of interests

We have no conflict of interests to disclose.

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References

1. Ögün CÖ, Kirgiz EN, Duman A, Ökesli S, Akyürek C. Comparison of intrathecal isobaric bupivacaine–morphine and ropivacaine–morphine for Caesarean delivery. *Br J Anaesth*. 2003 May 1;90(5):659–64. PMID:12697595 DOI:[10.1093/bja/aeg123](https://doi.org/10.1093/bja/aeg123)
2. Mitra JK. Prevention of hypotension following spinal anaesthesia in caesarean section - Then and now. *Kathmandu Univ Med J*. 2010;8(3):415–9. PMID:22610772 DOI:[10.3126/kumj.v8i4.6242](https://doi.org/10.3126/kumj.v8i4.6242)
3. Mueller M, Bruhwilerr H, Schupfer G, Luscher K. Higher rate of fetal acidemia after regional anesthesia for elective cesarean delivery. *Obstet Gynecol*. 1997 Jul;90(1):131–4.. PMID:9207827 DOI:[10.1016/S0029-7844\(97\)00210-X](https://doi.org/10.1016/S0029-7844(97)00210-X)
4. Dahlgren G, Granath F, Wessel H, Irestedt L. Prediction of hypotension during spinal anesthesia for cesarean section and its relation to the effect of crystalloid or colloid preload. *Int J Obstet Anesth*. 2007;16:128–34. PMID:17276668 DOI:[10.1016/j.ijoa.2006.10.006](https://doi.org/10.1016/j.ijoa.2006.10.006)

5. Dahlgren G, Granath F, Pregner K, Rösblad PG, Wessel H, Irestedt LL. Colloid vs. crystalloid preloading to prevent maternal hypotension during spinal anesthesia for elective cesarean section. *Acta Anaesthesiol Scand.* 2005;49:1200–6. PMID:16095463 DOI:[10.1111/j.1399-6576.2005.00730.x](https://doi.org/10.1111/j.1399-6576.2005.00730.x)
6. Nishikawa K, Yokoyama N, Saito S, Goto F. Comparison of effects of rapid colloid loading before and after spinal anesthesia on maternal hemodynamics and neonatal outcomes in cesarean section. *J Clin Monit Comput.* 2007;21:125–9. PMID:17265094 DOI:[10.1007/s10877-006-9066-4](https://doi.org/10.1007/s10877-006-9066-4)
7. Bhardwaj N, Jain K, Arora S, Bharti N. A comparison of three vasopressors for tight control of maternal blood pressure during cesarean section under spinal anesthesia: Effect on maternal and fetal outcome 338. *J Anaesthesiol Clin Pharmacol.* 2013;29:26–31. PMID:23492921 PMCID:PMC3590536 DOI:[10.4103/0970-9185.105789](https://doi.org/10.4103/0970-9185.105789)
8. Wang M, Zhuo L, Wang Q, Shen M, Yu Y, Yu J, et al. Efficacy of prophylactic intravenous ondansetron on the prevention of hypotension during cesarean delivery : a dose-dependent study. 2014;7(12):5210–6. PMCID: PMC4307470 PMID: 25664023
9. Roofthoof E, Van de Velde M. Low-dose spinal anaesthesia for Caesarean section to prevent spinal-induced hypotension. *Curr Opin Anaesthesiol.* 2008;21:259–62. PMID:18458538 DOI:[10.1097/ACO.0b013e3282ff5e41](https://doi.org/10.1097/ACO.0b013e3282ff5e41)
10. Subedi A, Tripathi M, Bhattarai BK, Gupta PK, Pokharel K, Regmi MC. The effect of height and weight adjusted dose of intrathecal hyperbaric bupivacaine for elective caesarean section. *J Nepal Med Assoc.* 2011;51(1):1–6. PMID:22335087
11. Parameters P. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Com. *Anesthesiology.* 2011;114(3):495–511. PMID:21307770 DOI:[10.1097/ALN.0b013e3181fcbfd9](https://doi.org/10.1097/ALN.0b013e3181fcbfd9)
12. Harten JM, Boyne I, Hannah P, Varveris D, Brown a. Effects of a height and weight adjusted dose of local anaesthetic for spinal anaesthesia for elective Caesarean section. *Anaesthesia.* 2005;60:348–53. PMID:15766337 DOI:[10.1111/j.1365-2044.2005.04113.x](https://doi.org/10.1111/j.1365-2044.2005.04113.x)
13. Boyne, I. & Varveris, D. & Harten, Johann & Brown, A.. (2002). National survey of dose of hyperbaric bupivacaine for elective caesarean section under spinal anaesthesia. *International Journal of Obstetric Anaesthesia - INT J OBSTET ANESTH.* 11. 20-20. 10.1016/S0959-289X(02)80039-5. DOI: [10.1016/S0959-289X\(02\)80039-5](https://doi.org/10.1016/S0959-289X(02)80039-5)
14. Roy D, Swarbrick C, King Y, Pye S, Adams J, Berry J, et al. Differences in peak bone mass in women of European and South Asian origin can be explained by differences in body size. *Osteoporos Int.* 2005 Oct;16(10):1254–62. PMID:15702264 DOI:[10.1007/s00198-005-1837-0](https://doi.org/10.1007/s00198-005-1837-0)
15. Nagata E, Yoshimine K, Minoda Y, Kawaguchi Y, Sakamoto M, Takehara A. Comparison of 8 mg and 10 mg hyperbaric bupivacaine during spinal anesthesia for cesarean section in Japanese parturients. *Masui* 2004 Feb;53(2):131-6. PMID:15011419
16. L.A.H Critchley . Hypotension, subarachnoid block and the elderly patient. *Anaesthesia.* 1996 Dec;51(12):1139–43. <https://doi.org/10.1111/j.1365-2044.1996.tb15051.x>
17. Sanghavi M, Rutherford JD. Cardiovascular Physiology of Pregnancy. *Circulation.* 2014;130(12). PMID:25223771 DOI:[10.1161/CIRCULATIONAHA.114.009029](https://doi.org/10.1161/CIRCULATIONAHA.114.009029)
18. Ousley R, Egan C, Dowling K, Cyna AM. Assessment of block height for satisfactory spinal anaesthesia for caesarean section. *Anaesthesia.* 2012 Dec;67(12):1356–63. PMID:23061397 DOI:[10.1111/anae.12034](https://doi.org/10.1111/anae.12034)
19. King HK, Wooten DJ. Effects of drug dose, volume, and concentration on spinal anesthesia with isobaric tetracaine. *Reg Anesth.* 1995 Jan-Feb;20(1):45-9. PMID:7727328
20. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, Hempelmann Ge. The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. *Anesth Analg.* 2002 Jun;94(6):1521–9. PMID:12032019 DOI:[10.1097/00000539-200206000-00027](https://doi.org/10.1097/00000539-200206000-00027)
21. Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. *Cochrane Database Syst Rev.* 2006 Oct 18;(4):CD002251. PMID:17054153 DOI:[10.1002/14651858.CD002251.pub2](https://doi.org/10.1002/14651858.CD002251.pub2)
22. Ozoagu AM, Isamade ES, Akpa FN. Abstract PR212: The Effect of Height and Weight Adjusted Subarachnoid Dose of Bupivacaine on Incidence of Complications Following Spinal Anaesthesia for Caesarean Section. *Anesth*

Analg. 2016;123(3S). doi: [10.1213/01.ane.0000492610.97991.2d](https://doi.org/10.1213/01.ane.0000492610.97991.2d)

23. Arzola C, Wieczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. *BJA Br J Anaesth*. 2011 Jul 14;107(3):308–18. PMID:21764820
<https://doi.org/10.1093/bja/aer200>