

Effects of Varying Doses of Plain Bupivacaine with Fentanyl in Patients Undergoing Cesarean Section: Haemodynamics and Neonatal Outcome

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Abstract

Key words:

spinal anaesthesia; cesarean delivery; hypotension; neonatal outcome.

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Aim. The purpose of this study was to evaluate a three different regimes of spinal anaesthesia for caesarean delivery as well the incidence and severity of maternal hypotension and its influence over neonatal outcome.

Material and Methods. Sixty (60) term healthy (ASA I) parturients scheduled for elective or non-elective caesarean delivery without fetal distress under spinal anaesthesia were randomly divided in three groups: group SA F10 (n = 20) received plain bupivacaine 12 mg plus 10 µg fentanyl, group SA F20 (n = 20) received 11 mg plus 20 µg fentanyl and SA LD group (low dose, n = 20) received 8 mg bupivacaine plus 20 µg fentanyl. Ephedrine 5-10 mg i.v. bolus was given when systolic blood pressure (SBP) was < 95 mmHg. Maternal blood pressures, ephedrine dosage, sensory level of anaesthesia, Apgar scores and neonatal umbilical cord blood acid-base (Ua) status were evaluated.

Results. Spinal block provided surgical anaesthesia in all patients. Peak sensory level was higher in the greatest bupivacaine group (4.9 ± 1.33 , 5.0 ± 1.21 vs. 5.4 ± 1.55). Parturient who received 12 mg bupivacaine (SA F10 group) develop significantly decrease of SBP - 97.9 ± 8.9 mmHg (23.8%), after spinal blockade compared with low dose group SA LD - 125.0 ± 12.9 , (6.0 %, $p < 0.05$) and 115.1 mmHg (17.5%) in the SA F20 group. The total amount of ephedrine to treat hypotension was significantly lower in the low dose group (SA LD) compared with two other group (1.75 ± 1.0 mg vs. 13.75 ± 6.5 mg (SA F10) and 11.75 ± 6.2 (SA F20, $p < 0.5$). Neonatal Ua pH was significantly lower with SA F10 group than low dose spinal group-SA LD (7.22 ± 0.07 vs. 7.27 ± 0.04 , $p < 0.05$; 7.23 ± 0.04 SA F20 group).

Conclusion. spinal anaesthesia for caesarean delivery with a low dose bupivacaine of 8 mg in conjunction with 20 µg fentanyl leads to less hypotension and ephedrine requirements with better neonatal outcome when compared with 12 and 11 mg bupivacaine – fentanyl spinal anaesthesia.

Introduction

Spinal anaesthesia for caesarean delivery owns well-established and long use but its superiority for the newborns is often assumed. Twenty-seven studies reporting neonatal acid-base data with different types of anaesthesia and comparing umbilical artery pH and base deficit, found that cord pH was significantly lower with spinal than with both general and epidural

anaesthesia (2). The hypotension is one of the most important mechanism by which spinal anaesthesia may affect fetal well-being (1,12,14). Reducing the dosage and total volume of local anaesthetic have influence over lowering the incidence and severity of hypotension and optimizing of acid-base status of newborns (7,19, 20). Using a minimal dosage of local anaesthetic with opioids (a low dose spinal anaesthesia) Ben-David et al. 200 (18) demonstrated a decrease

incidence of hypotension and a nearly tenfold reduction in the amounts of ephedrine required in patients receiving low dose spinal anaesthetics. As the clinical actions of lipophilic opioid have a very fast onset, the influence of fentanyl on the characteristics of the quality of anaesthesia provided by the combined action of bupivacaine plus fentanyl are well documented.

Thus, we are strongly interested about the low dosage concept could be used to provide spinal anaesthesia while incurring less frequent hypotension and favourable neonatal outcome. In our study we have investigated 12 and 11 mg bupivacaine dosage combined with 10 or 20 µg fentanyl compared with low dosage of bupivacaine (8 mg) with 20 µg fentanyl and influence over spinal hypotension and neonatal short-come parameters – Apgar scores and acid-base status of term newborns delivered with this different types of spinal. Also we wanted to favour the anaesthetic method which can be identified that favours the fetal and neonatal-well being.

Patients and Methods

For that manner, we evaluated sixty (60) healthy ASA I term (> 37 gestational age) parturients scheduled for elective caesarean delivery. Patients were divided randomly into three groups. The demographic characteristics of those completing the study are shown in Table 1. There were no statistical differences among the groups in age, weight, height, parity and physical status.

Table 1: Demographic data of the patients undergoing cesarean section.

	SA F10(n=20)	SA F20(n=20)	SA LD(n=20)
Age (yr)	25.8 ± 5.8	27.0 ± 6.4	26.9 ± 4.7
Weight (kg)	70.2 ± 3.0	75.8 ± 8.0	76.0 ± 8.4
Height (cm)	163.0 ± 4.0	162.0 ± 2.9	162.0 ± 1.9
Length of the operation	72.5 ± 9.5	71.0 ± 9.5	69.0 ± 15.0

The patients were randomly assigned to three groups defined by the spinal injectate. The parturient from SA F10 group received intrathecally 12 mg plus 10 µgr fentanyl, group SA – F20 µg received 11 mg bupivacaine plus 20 µg fentanyl and the parturient from SA LD group received 8 mg bupivacaine with 20 µg fentanyl. The lumbar puncture was performed at the L2-3 or L3-4 interspaces, with a 26 or 27-gauge Braun needle, with the parturient in the sitting position. All the parturient were received 500 ml prehidratation of crystalloids solutions. After completion of the injection the patients were immediately returned to the supine position with left uterine displacement breathing oxygen

2-4 l/min via face mask. IV boluses of 5-10 mg ephedrine and additional IV fluids were given to treat hypotension, which was defined as a systolic blood pressure below 95 mmHg or a decrease in systolic pressure of more than 20% of the baseline value. Heart rate and non-invasive arterial blood pressure were recorded at 3 minute interval during first 15 min after the spinal injection and every 5 minutes thereafter.

The lowest systolic blood pressure, the number of hypotensive measurements and total ephedrine use for each parturient were recorded. The protocol allowed for conversion to general anaesthesia as deemed necessary. The newborns' Apgar scores at 1 and 5 minutes and umbilical artery (uA) pH values PaO₂, pCO₂, BE and bicarbonate were studied. The sensory block progression was assessed with a blunt pin-prick and was assessed 5, 10, 15, 30 and 60 min after intrathecal injection.

Frequency of hypotension were assessed using the Chi-square statistic and haemodynamic variables were compared using repeated measures analysis of variance; peak sensory dermatome levels were compared with the Wilcoxon rank sum test, statistically significant differences were assumed if p < 0.05.

Results

There were 20 patients in each group of total 60 patients and were similar with respect to age, weight and height among the groups (Table 1). Spinal block provided surgical anaesthesia in all patients.

The changes in SAP over time of 60 min are shown in Figure 1. There was a fall of SBP in two groups - SA F10 and SA F20, by 2.5-7 min after subarachnoid block. The maximal decrease of SBP

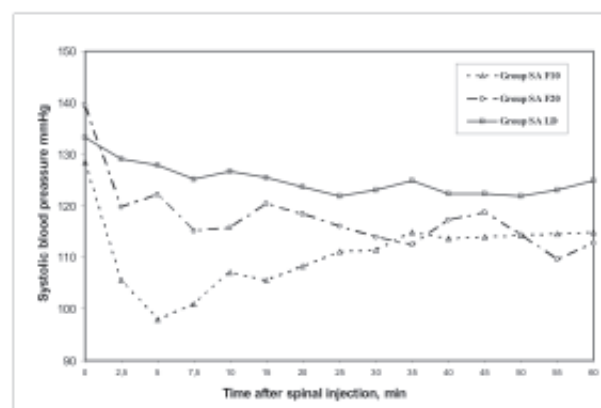


Figure 1: Mean arterial pressure after spinal anaesthesia, expressed as mean ± SD, p<0.05 compared to baseline.

after spinal blockade until delivery was significantly greater in SA F10 group - 97.9 ± 8.9 mmHg (23.8 %) compared with 115.1 mmHg (17.5%) in SA F20 group and 125.0 ± 12.9 (6%) seen with SA LD group ($P < 0.05$). Hypotension requiring treatment was present in 18/20 parturient in the SA F10 group and 17/20 in the SA F20 but only 5 parturient need vasopressor therapy in SALD group. SBP do not continued to fall in the next period after the delivery of the newborn. In our study there was not significant clinical or statistical decrease of SBP from baseline value in the low dose bupivacaine group - SA LD ($p > 0.05$).

Table 2: Measured levels of sensory anaesthesia to pinprick.

Time (min)	SA F10 (n=20)	SA F20 (n=20)	SA LD (n=20)
5	4.9 ± 1.33	5.0 ± 1.21	5.4 ± 1.55
10	4.1 ± 1.02	4.0 ± 1.20	4.5 ± 1.30
15	3.8 ± 0.92	3.9 ± 1.22	4.3 ± 1.32
30	3.8 ± 1.24	4.1 ± 1.15	4.2 ± 1.24
60	3.7 ± 0.94	4.0 ± 0.02	4.3 ± 1.22

Other maternal findings - characteristics of the sensory blocks observed are summarized in Table 2. All patients in both groups SA F10 and SA F20 had sensory blocks above the fifth sixth thoracic dermatome within five minutes of induction. Spinal block provided surgical anaesthesia in all patients. Use of supplemental analgesia to resolve intraoperative discomfort with fentanyl 50 µg iv and midazolam 2 mg in three groups was not significantly different (4/20, 5/20 and 4/20, ns).

Total dosage of ephedrine to treat hypotension was lower in the SA LD groups compared with two other group ($p < 0.05$), Figure 2. The plain bupivacaine groups with 12 and 11 mg were more likely to require treatment for hypotension (mean ephedrine requirements: 13.75 ± 6.5 mg and 11.75 ± 6.2 vs. 1.75 ± 1.0 mg in the SA LD group) and had more persistent hypotension (2.8 vs. 0.6 hypotensive measurements

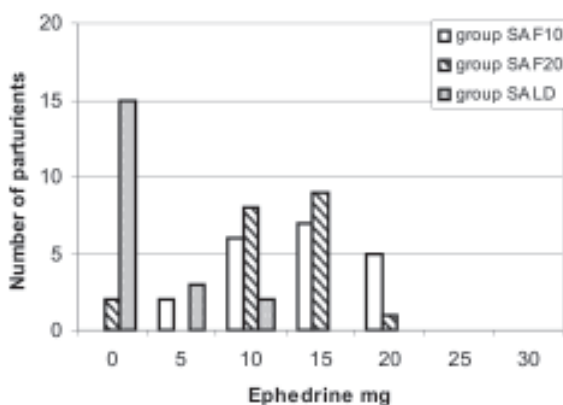


Figure 2: Number of parturient required ephedrine.

per patient) than patients in the low dose bupivacaine-fentanyl group ($p < 0.05$).

Neonatal outcome: median Apgar scores at one minute were 7.8 ± 1.4 and 7.6 ± 1.4 in the SA F10 and SA F20 group respectively but the best scores were obtained in the SA LD group - 8.6 ± 2 (ns). Similarly, Apgar scores were 8.7 and 9.2 ± 1.2 in the low dose group (ns). Four (4) newborn infants in SA F10 group have 7 or less than 7 Apgar score at first minute, but no child had an Apgar of less than 7 (1 min) and 9 at five minutes in the SA LD group (Table3).

Cord pH (UA) at the time of Caesarean delivery was 7.22 (SA F10 group), 7.23 (SA F20 group) and 7.27 (SA LD), Table 3. Median umbilical arterial pH were significantly lower in the SA F10 and SA F20 when compared with UA pH from low dose spinal group SALD (7.27 vs. 7.23, $p < 0.05$). No infant had a cord pH of less than 7.10 at delivery in the SA LD group but there are values of pH < 7.0 in the SA F10 and SAF20 groups – pH 6.93 and 6.91 respectively. The base excess values (BE, mEq/ml) was higher in the SA F10 group.

Table 3: Neonatal outcome.

	SA F10 (n=20)	SA F20 (n=20)	SA LD (n=20)	p
Apgar values				
1 min	7.8 ± 1.4	7.6 ± 1.4	8.6 ± 1.2	
5 min	8.7 ± 1.5	8.7 ± 1.6	9.2 ± 1.2	
Artery (UA)				
Umbilical blood gas tensions				
Ph	7.22 ± 0.07	7.23 ± 0.04	7.27 ± 0.04 *	0.04
(rang)	(6.93-7.34)	(7.0-7.35)	(7.05-7.4)	6*
UA pO2 (mmHg)	21.17 ± 19.5	19.77 ± 18.5	21.66 ± 18.9	0.67
UA pCO2 (mmHg)	53.79 ± 12.0	52.95 ± 11.6	51.76 ± 10.5	0.44
BE (mEq/ml)	5.30 ± 3.6	4.02 ± 3.4	3.46 ± 2.8	0.02

Discussion

Despite such well-established and long use of spinal anaesthesia for caesarean section, hypotension continues to be a problem and the most important common complication. Hypotension under spinal anaesthesia during caesarean delivery is also very frequent - 55 to 90% if not prevented (3). Moya and Smith, 1962 found that after spinal anaesthesia the blood pressure was reduced by more than 10% in 68% of mothers, by more than 20% in 46% of mothers and by more than 30% in 23% of mothers (11).

Because such hypotension readily responds to immediate aggressive treatment with vasopressors, intravenous fluids and left uterine displacement, possibility of adverse effects on the foetus is minimal (2, 3). But when data were analysed according to whether or not hypotension (and ephedrine) occurred, there were differences between infants of hypotensive

and non-hypotensive mothers. Newborns born to mothers with hypotension were significantly more acidotic than controls although acid-base levels were still within normal limits (1, 14). Two recent studies implicate that spinal anaesthesia and hypotension as the cause of fetal acidemia (3, 7). In the study by Roberts et al., 1965 fetal acidemia with umbilical arterial pH < 7.19 was present in 18% of infants exposed to spinal anaesthesia compared with 4 % exposed to general anaesthesia (6). In the study by Mueller et al., 1993 the frequency of fetal acidemia was significantly higher in the spinal anaesthesia group compared with general anaesthesia group (8). It seemed that severe hypotension, defined as a decrease in maternal MAP of 30 % from baseline causes fetal compromise with neonatal metabolic acidosis.

Many factors could minimize or decrease the incidence and severity of hypotension. Methods of managing hypotension include lateral uterine displacement, mechanical leg compression, intravenous (or colloid prehydration), use of vasopressors (3, 15). Uterine displacement is accepted as standard, although the optimal degree of tilt is unknown, and most anaesthetists overestimate the amount of tilt they are applying (21). Leg compression is effective but not popular. In contrast to early reports, recent studies have not shown intravenous crystalloid prehydration to be very effective (9). Colloids are more effective but are expensive and have potential adverse effects. Prophylactic ephedrine is more effective than control for preventing hypotension during spinal anaesthesia for elective Caesarean delivery but a clinically relevant positive effect on neonatal outcome was not observed (5). Therefore, the routine use of prophylactic ephedrine to prevent any adverse effects of maternal hypotension following spinal anaesthesia for Caesarean delivery is not supported by the current systematic review. There is some evidence that slow intrathecal injection and use of plain anaesthetic solutions may decrease the incidence of hypotension (10). So, what can we do to decrease the incidence of hypotension?

The approach of preventing the hypotension with reducing the dosage of local anaesthetic is not unusual in obstetric anaesthesia practice. In terms of neonatal and maternal well-being, prevention of hypotension results in better outcomes than treatment of established hypotension (10). Carvalho B et al., 2005 demonstrated that reduced dose of bupivacaine lead to decreased incidence of hypotension (23). Ben-David et al., 2000 demonstrated a threefold decrease in the incidence of hypotension and a nearly tenfold reduction in the amounts of ephedrine required in those patients receiving lower dose spinal anaesthetics-

decreasing the bupivacaine dose from 12 mg to 4.5 mg does lead to reduction in hypotension and vasopressor use during caesarean delivery (18).

Clinically, the addition of small dose of opioids to a local anaesthetic has allowed a reduction of local anaesthetic dose thus minimizing the incidence of side effects and reaching adequate spinal anaesthesia, with otherwise inadequate doses of local anaesthetic (19, 20). The concept of "low dose" anaesthesia with addition of fentanyl to bupivacaine leads to a decrease in a local anaesthetic doses and so to decrease the incidence of hypotension. The practice of adding fentanyl 10- 25 µg to a low dose anaesthetics (< 10 mg bupivacaine) is characterised with decreasing the hypotension with no adverse effects over neonates. Ben-David et al., 2000 administered bupivacaine 5 mg with fentanyl 25 µg intrathecally for caesarean delivery in order to test the feasibility of low dose local anaesthetic with intrathecal fentanyl and they reported less hypotension and vasopressor requirements (18). Choi et al., 1998 reported that with the addition of 10 µg fentanyl, the dose of bupivacaine could be reduced to 8 mg bupivacaine and the hypotension could be minimized (19). Vercauteren et al., 1998 showed that bupivacaine 9 mg with fentanyl 20 µg offered excellent conditions for caesarean section with reduced hypotension (20).

In our study we demonstrated that this concept could be used to provide spinal anaesthesia for caesarean delivery while incurring less frequent hypotension and favourable neonate values. We demonstrated that using a "low dose" concept with bupivacaine -8 mg in conjunction with fentanyl 20 µg, offers minimal haemodynamic changes (no hypotension) with no adverse effects over neonatal short-outcome. The greater dosage -12 and 11 mg bupivacaine leads to more pronounced hypotension and more compromised neonates. We observed a fall in SAP from baseline nearly 25 % in the 12 mg dosage spinal group (SA F10), but there was not a fall in SBP in the low dose spinal anaesthesia group (only 6% from baseline). Finally, the decreased cephalic spread of anaesthesia in low dose group described in our study may have obscured correlation between lower doses of bupivacaine and decreased maternal hypotension. These findings may be attributable to the smaller volume and low dosage of injectate employed.

The Apgar score is rapid way to evaluate the physical condition of newborn infants, but is not specific for the effects of anaesthesia on the newborn. A median score of 7 or higher indicates that the baby's condition in all three groups is good to excellent. In this

study we couldn't demonstrate that the score was sufficiently sensitive to detect significant differences among newborns whose mothers receive classical vs. low dose spinal although four (4) newborns infants from SA F10 g had Apgar score under 7. We also observed that neonates of hypotensive mothers had significantly longer "times to sustained respiration". We did not observe a score under 7 in the newborn infants from the low dose group (SALD).

We demonstrated that neonatal outcome with a low dose spinal anaesthesia (group SALD) provides better acid-base values than others. The umbilical arterial acid-base values were significantly higher than those parturient in whom hypotension was observed (groups SA F10). The lower acid-based parameters compounded to these groups resulted probably from hypotension and decreased intervillous perfusion and consecutive placental metabolic fetal disturbances. Ebner et al., 1960 found that during vaginal deliveries, fetal bradycardia developed when hypotension (SAP < 80 mmHg) lasted more than 4 minutes (17); Hok and al., 1960 noted the frequent association of "pathological fetal bradycardia of hypoxic type" when maternal systolic arterial pressure had fallen below 100 mmHg (16). But, Clyburn, 2005 mentioned that as ephedrine crosses the placenta it is possible that fetal acidosis is the result of a direct *ephedrine fetal effect* (22). The relatively large doses of ephedrine that are required in the 12 mg bupivacaine dosage (13.75 ± 6.5 mg) when maternal arterial pressure is the goal, probably have direct fetal effects with increasingly rate of pH acidosis (5, 22). We believe this to have been the additional mechanism for the fetal acidosis in our study. There is also evidence that ephedrine owns additional indirect fetal effects via an ephedrine induced increase in fetal metabolic rate (5). In the pregnant ewe there is evidence that a beta-adrenergic induced increase in fetal metabolic rate can increase fetal oxygen demand, leading to anaerobic metabolism and lactic acidosis (4). Increased fetal metabolic rate would also be expected to reduce fetal pH by increasing fetal $p\text{CO}_2$. We also concluded that duration of hypotension was more important than the degree of hypotension in affecting the condition of the newborn although we observed that a short period of brutal hypotension (less than 2 minutes) is frequently associated with altering the neonatal acid-base values. So, prompt diagnosis and treatment of hypotension appear to be very important for the best short-come outcome values.

Our findings suggest that applying a concept of low dose spinal anaesthesia for caesarean delivery with 8 mg bupivacaine in conjunction with 20 μg fentanyl result in anaesthesia with less hypotension

and ephedrine requirements with better neonatal outcome when compared with 12 and 11 mg bupivacaine–fentanyl spinal anaesthesia. Therefore, we favour the routine use of low dose bupivacaine–fentanyl combination as a routine practise following spinal anaesthesia for Caesarean delivery.

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