

ORIGINAL ARTICLE

The effects of 7 mg levobupivacaine on maternal hemodynamics with side effects in combined spinal-epidural anaesthesia for cesarean section

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ABSTRACT

Background: It has been reported that 10-15 mg local anaesthetic is enough for cesarean sections. Reduced doses of levobupivacaine may decrease the incidence of associated complications e.g. hypotension, nausea, vomiting and the vasopressor use. The primary objective of this study was to compare 7 mg and 10 mg doses of intrathecal levobupivacaine on maternal hemodynamics. The secondary objective was to determine the differences in sensory block, the vasopressor use, associated side effects and a need for additional analgesics between the groups.

Methodology: Following ethical committee approval, thirty three women presenting for elective cesarean delivery were randomly assigned to one of the 2 groups. Group-7 received 7 mg intrathecal levobupivacaine and Group-10 received 10 mg. Women in both groups received 10 ml/kg crystalloids intravenously, at the time of initiation of combined spinal – epidural anaesthesia. Surgery began when a sensory level was at T4. Maternal hemodynamics and sensorimotor levels were recorded at regular intervals. Side effects, additional analgesics and the vasopressor use were documented.

Results: No difference was observed in the incidence of hypotension (p:0.482), bradycardia (p:1.00) or nausea and vomiting (p:0.448) between two groups. Incidence of additional analgesic requirement and vasopressor requirement was also similar in both groups (p:0.383).

Conclusion: Intrathecal levobupivacaine 10 mg and 7 mg yielded similar maternal hemodynamics, sensory block, side effects and additional analgesic requirement during cesarean delivery.

Key Words: Cesarean section; Combined spinal-epidural; Spinal anaesthesia; Hemodynamics; Hypotension; Levobupivacaine.

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INTRODUCTION

Hypotension remains an important side effect of spinal anaesthesia for cesarean delivery¹. Maternal hypotension can be encountered in 20-100% of cases due to the dose of the local anesthetic agent injected into the subarachnoid space.² There is limited evidence that reducing the spinal dose has a favorable effect on maternal hemodynamic stability¹. Aortocaval pressure caused by the enlarged uterus in supine position in the last trimester of the pregnancy deepens the hypotensive effects. There is no definite method to prevent the sympathetic block and resultant hypotension after spinal anaesthesia. Preoperative intravenous bolus infusions of up to 1000 ml of crystalloids, increasing

the fluid infusion rate during the operation, using vasoconstrictors e.g. ephedrine or phenylephrine etc. are several interventions to prevent hypotension.^{3,4} The toxicity of the local anesthetic agent is another complication of regional anaesthesia in addition to the high sympathetic blockage.⁵ Bupivacaine is known to have a narrow therapeutic index. Levobupivacaine is a long acting local anesthetic. It is the S-enantiomer of bupivacaine and has been shown to be less cardiotoxic as compared to bupivacaine in several studies and is now being used in cesarean sections. Rapid development of sympathetic blockade in pregnancy and requirement of keeping sensorial blockade at T4-5 in labor increases its importance.

We hypothesized that a lowered intrathecal dose of this drug could be used safely, satisfactorily but with less side effects. In this study we aimed to compare the maternal hemodynamics, sensorimotor levels, side effects and vasopressor requirement with a lower dose of levobupivacaine (7 mg) with conventionally used dose (10 mg).

METHODOLOGY

This study was approved by General Directorate of Pharmaceuticals and Pharmacy, Ministry of Health of Turkey, Ethical Committee, and performed at Keçiören Training and Research Hospital Anesthesiology and Reanimation Department from 1st January 2011 to 1st March 2011.

Thirty three parturients, ASA I-II, scheduled for elective cesarean section, with no problem in the fetus and mother and no contraindication for regional anesthesia were included in the study. Their written informed consents were obtained. Pregnant women with diabetes, history of allergic reaction to local anesthetic agents, with skin infection at the injection site, pregnancy-induced hypertension, mental disorder, bleeding diathesis or neurologic disorders were excluded.

Age, height, weight and gestational age were recorded for each subject. All subjects received 10 ml/kg colloids intravenously at the time of initiation of combined spinal-epidural anesthesia. Vital signs were monitored before and during the operation (Drager Infinity Delta Monitor TR Danvers, MA 01923, USA).

Subjects were randomly distributed via sealed envelop method into two groups. We used a sample size estimation procedure for diagnostic test studies based on the desired likelihood ratio confidence interval. Group-10 (n = 15) was given 10 mg levobupivacaine 0.5% and Group-7 (n = 18) was given 7 mg levobupivacaine 0.5% by combined spinal epidural method into the subarachnoid space. Preparation of study solutions was performed by an anesthesiologist not involved in data recording. CSE was performed with the patient in sitting position. After IV fluid administration, the epidural space was identified at the L3-4 interspace with an 18 gauge Tuohy needle using the loss of resistance to saline technique. A 27G pencil-point spinal needle was advanced via the epidural needle and after confirming free flow of cerebrospinal fluid, spinal solutions were injected over approximately 30 seconds. A 20G epidural catheter was positioned 4 cm into the epidural space. After the CSE was performed successfully, the patient was positioned to the supine position with left uterine displacement. The operation started after the sensorial blockade reached T4-5. The spinal level was checked by pin prick test. Maternal arterial blood pressure

was recorded noninvasively. Blood pressure, mean arterial pressure, pulse rate and oxygen saturation were recorded at 0, 5, 10, 15, 20 and 30 min for each subject. Maternal hypotension was defined as a 20% reduction in systolic arterial pressure from baseline value and was treated promptly with intravenous ephedrine 10 mg. Presence of nausea, vomiting or need for additional analgesics were also recorded. A pulse rate of fewer than 50 beats/min was regarded as bradycardia and treated with 0.5 mg atropine sulphate intravenously. The time for sensory blockade to reach T4 and the level of motor blockade before and just after the operation according to the Bromage Scale (0-3) were also recorded. The definitions of this scale are: 0=able to straight leg raise (SLR) and flex both feet and knees; 1=unable to SLR but able to flex knees and feet; 2=unable to SLR or flex knees but able to flex feet.

Demographic data were collected and presented as mean(SD). Statistical analysis was performed using SPSS version 11.5. T-test used for continuous variables between groups and Chi-square test for categorical data analysis. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 33 women were recruited. The demographic and obstetric characteristics of the study are shown in Table 1. The weight of the patients in Group-7 was statistically significantly higher than Group-10 (p:0.032). Except weight there were no statistical differences in mean age, height, and parity among women in the two groups. The duration of surgery was similar in both groups.

Table 1: Demographic data; Mean±SD

Groups	Group-7	Group-10	P value
Number	15	18	
Age	28.3±4.1	27.9±5.0	NS
Height	162.87±7.64	161.44±5.19	NS
Weight	82.53±11.17	75.56±6.37	0.032
Baseline SBP(mmHg)*	125±11	128±14	NS
Duration of surgery	45±9	43±17	NS

* SBP = systolic blood pressure

Except the significantly low initial systolic blood pressure in Group-10 (p:0.013), no significant difference was observed between the groups according to hemodynamic parameters (p > 0.05) (Fig. 1). No difference was observed in the incidence of hypotension (p:0.482), there were 9 patients in Group-7 and 10 patients in Group-10, who developed hypotension and were treated with ephedrine. Quantities of ephedrine (11.5 ±

11.3 mg vs 10.9 ± 10.5, NS) and total intravenous fluids (1590 ± 495 ml vs 1498 ± 357 ml, NS) were similar in two groups respectively. Systolic, diastolic and mean arterial pressure and heart rate versus time are depicted graphically in Figure 1, 2 and 3 respectively.

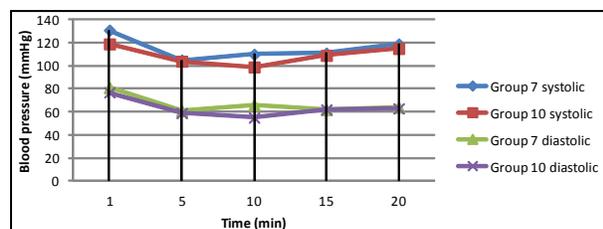


Figure 1: Systolic and diastolic blood pressure versus time following spinal anesthesia. There was no significant difference between groups except first minute systolic blood pressure decrease.

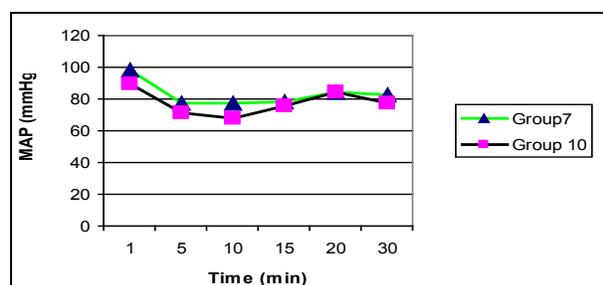


Figure 2: Mean arterial blood pressure (MAP) in patients undergoing cesarean delivery using combined spinal epidural anesthesia using 7 mg or 10 mg intrathecal levobupivacaine. There was no difference between groups.

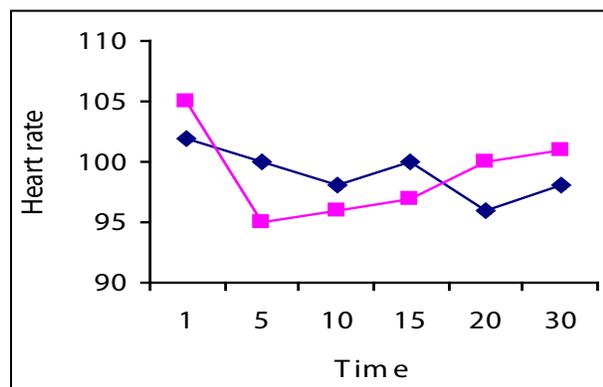


Figure 3: Heart rate versus time following spinal anesthesia

There was also no difference in the incidence of bradycardia (p:1.00) and nausea and vomiting (p:0.488) between two groups. Patients did not complain of pain at skin incision, but some required supplementary analgesia at peritoneal closure. Requirement of additional analgesics was similar in both groups (p:0.383). Epidural supplementation was necessary for 4 patients in Group-7 and 2 patients in Group-10 (Table 2).

Table 2: Comparative Side effects; N(%)

Groups	Group-7 (n:15)	Group-10 (n:18)	P value
Hypotension	10 (66.7)	9 (50)	0.482
Bradycardia	1 (6.7)	1 (5.6)	1.000
Nausea-Vomiting	6 (40)	4 (22.2)	0.448
Additional analgesics	4 (26.7)	2 (11.8)	0.383

There were no statistically significant difference between two groups regarding the level of sensory and motor blockade (Table 3).

Table 3. Comparison of Bromage Scale (% of patients)

Bromage Scale	Group-7		Group-10		P value	
	1 min	30 min	1 min	30 min	1 min	30 min
0	47.6%	0.0	33.3%	5.6%	0.086	0.102
1	26.7%	20%	61.1%	50.0%		
2	26.7%	80%	5.6%	44.4%		

DISCUSSION

Use of smaller doses of local anesthetic agents to prevent maternal hypotension and consequent adverse effects on uteroplacental blood flow during combined spinal epidural anesthesia is an important topic for the safety of fetus and mother.

The primary results of this study suggest that decreasing the levobupivacaine dose from 10 mg to 7 mg does not lead to reductions in hypotension and vasopressor use during cesarean section. Some authors⁶ described hypotension as the most common side effect after spinal injection of levobupivacaine 15 mg. Coppejans et al⁷ compared levobupivacaine with bupivacaine and found less incidence of hypotension with the S-enantiomer. One study determined an ED₅₀ for levobupivacaine of 9.3 mg, but the local anaesthetic was in 8 % glucose.⁸ In addition to this, there was no statistically difference in requirement of additional analgesics and vasopressor use between both groups.

Contrary to the results of the present study, Ben David et al.⁴ 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 anesthetics. In cesarean sections, subarachnoid injection of this agent with CSE technique provides adequate motor and sensory blockade. 0.5% concentration is preferred for this use.⁹

Levobupivacaine, which is S-enantiomer of bupivacaine, was discovered by Aberg in 1972.¹⁰ He showed that cardiac effects of both enantiomers of bupivacaine are different. Levobupivacaine is used less frequently in cesarean operations but epidural use of this agent has

increased recently. Bader et al compared the efficacy of 0.5% levobupivacaine with 0.5% bupivacaine for epidural anesthesia in parturients undergoing elective cesarean delivery,¹¹ the frequency of hypotension was 84.4% in the levobupivacaine group and 100% for the bupivacaine group ($P \leq 0.053$) and levels of sensory block, motor block, muscle relaxation, and overall quality of anesthesia did not differ between groups.

We chose CSE technique in our study in order to be able to give additional levobupivacaine into the epidural space in case of reduction in the level of sensory blockade in the low dose group. 7 mg levobupivacaine provided adequate level of anesthesia and analgesia in 11 patient while in 4 patient additional doses of local anesthetic agent were used. In Group-10, 2 patients required additional analgesic.

In both groups only in the 10 mg group statistically significant hypotension after combined epidural anesthesia was observed at 1 minute. In other studies it has been reported that as the concentration of the injected solution decreases, the level of sympathetic blockade is reduced.¹¹ In another study it has been showed that the dose of the local anesthetic is the major determinant of hypotension after intrathecal use.¹²

There were no statistically significant differences between two groups regarding the level of sensory and motor blockade. We expected to see a difference in the level and total recovery of motor blockade in our

study because in an earlier study, onset of the block was significantly shorter in the groups receiving opioids and less local anesthetic.¹³

We allowed the operation to begin after the sensorial blockade reached T4-5 and time to reach this level was 5 minutes and similar in both groups. This result was different from the findings of Ginosar et al, who reported the time for sensory blockade to reach T6 level as 10 minutes.¹⁴

The need for sedation was similar in both groups and respiratory depression was not observed during sedation. Two women from Group-7 and four women from Group-10 required sedation.

There was no statistically significant difference between the groups regarding complications. Four women from Group-7 and six women from Group-10 suffered from nausea and vomiting. Manullang et al reported that patients receiving intrathecal fentanyl and reduced dose of bupivacaine had significantly less intraoperative nausea and vomiting compared with the patients receiving intravenous ondansetron.¹⁵

CONCLUSION

We conclude that the use of 7 mg of levobupivacaine has no edge over 10 mg of the same drug when used in combined spinal epidural anesthesia for cesarian sections and it cannot prevent the development of hypotension.

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