Anesth Pain Med. 2017 December; 7(6):e14426. doi: 10.5812/aapm.14426.

Published online 2017 December 31. **Research Article**

The Effect of Different Doses of Intrathecal Hyperbaric Bupivacaine Plus Sufentanil in Spinal Anesthesia for Cesarean Sections

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Received 2017 July 01; **Revised** 2017 October 09; **Accepted** 2017 October 20.

Abstract

Background: Decreasing side effects and improving the quality of block in caesarean sections by appropriate dosage of local anesthetics and adjuvants could play an important role in the safe management of cesarean section. The present study aimed at comparing the effects of 3 different doses of intrathecal hyperbaric bupivacaine injected with a fixed dose of sufentanil in cesarean sections.
Methods: In a double- blind randomized clinical trial, 105 candidates of elective cesarean section were randomly assigned into 3 groups of 8, 9, and 10 mg of intrathecal bupivacaine plus sufentanil 2.5 μg. The maximum level of sensory block, the intensity of motor block, and vital signs were measured at regular intervals. The incidence of hypotension and bradycardia were also recorded.
Results: No significant difference was found between the maximum level of sensory block and the intensity of motor block in 3 groups. The incidences of hypotension and bradycardia as well as administration of atropine and ephedrine were comparable among the 3 groups ($P > 0.05$).
Conclusions: According to similar effects of different doses of bupivacaine, administration of lower doses of bupivacaine (8mg) is more reasonable for spinal anesthesia for cesarean section.

Keywords: Cesarean Section, Bupivacaine, Sensory Block, Motor Block, Anesthesia

1. Background

Spinal anesthesia is the most common method of anesthesia for caesarean section. Administration of an appropriate dose and combination of local anesthetics could minimize the possible side effects and simultaneously improve the quality of block (1, 2). Hyperbaric bupivacaine with proper use of adjutants has been considered as acceptable common method of spinal anesthesia in caesarian section (3, 4). Several studies have reported that the combination of low dose local anesthetics and opioids in spinal anesthesia have the advantage of shorter onset times and higher quality of the blocks (5, 6).

Spinal anesthesia with any combination is likely to cause adverse effects such as hypotension, bradycardia, and shortness of breath, nausea, and vomiting. However, by adding opioids such as sufentanil to bupivacaine, the required dose of local anesthetic is decreased. This may result in lower side effects and improved quality of spinal anesthesia and postoperative analgesia (7, 8). Earlier studies have examined the effects of adding various amounts of sufentanil to a fixed dose of local anesthetic to find the optimum dose of adjuvant (9-12). This study was conducted to evaluate the effects of different doses of bupivacaine combined with a fixed acceptable dose of sufentanil to find a prescription for a safe and high quality spinal anesthesia for cesarean section.

2. Methods

2.1. Study Protocol

In this double- blind, randomized clinical trial, 126 candidates of elective cesarean section were recruited. Of them, 21 patients were excluded during the study and the remaining 105 were randomly allocated into 3 groups of spinal anesthesia with bupivacaine 8, 9, or 10 mg plus sufentanil 2.5 μg. Block randomization was used to assign equal number of patients in each group. The level of spinal block, duration of sensory and motor block, and hemodynamic variables were compared among the 3 groups. Both the patients and the assessor were blinded to the assignments. The local ethics committee approved the study protocol, and informed consent was obtained from all patients. The study was registered in clinical trials registry (IRCT2017010931852N1).

The inclusion criteria were as follow: candidates of elective cesarean section after 36 weeks of gestation, height more than 150 cm, no history of addiction, no history of pre-eclampsia, eclampsia, or hypertension, and no contraindication for spinal anesthesia. Patients with technical failure were excluded.

2.2. Intervention and Measurements

Standard monitoring was implemented, and then, the patients were hydrated with ringer's lactate solution 5 $mL.kg^{-1}$. Spinal anesthesia was performed at the fowler's position through lower lumbar intervertebral spaces using Quinke needle size 25. Patients were randomly allocated to the spinal anesthesia with 8, 9, or 10 mL of hyperbaric Bupivacaine 0.5% (AstraZeneca Company, France) plus 2.5 μg of sufentanil (Abu Rayhan Company, Iran). Drugs were administered with a 3 mL syringe (3MED, Iran Medical Equipment, Tehran, Iran) to facilitate the dose adjustments. Injection was performed at a constant rate of 0.2 mL/sec. Afterwards, patients were immediately placed in the supine position.

Spinal anesthesia hemodynamic parameters and sensory and motor block were measured at 5, 10, 15, 20, 30, 60, 90, 120, and 150 minutes. Sensory block was evaluated with pin prick method and motor block with Bromage score (Table 1). Assessment for sensory and motor block was continued in 30- minute intervals until full regression of blockade. Side effects such as nausea, vomiting, hypotension, bradycardia, and itching were recorded. Bradycardia was defined as slowing heart rate of more than 30% of individual baseline or less than 60 beats per minute. Atropine 0.5 mg per dose was administered to treat bradycardia. Similarly, hypotension was considered when the mean arterial pressure (MAP) decreased to more than 30% of baseline or less than 70 mmHg. Hypotension was treated with incremental intravenous doses of ephedrine.

Table 1. Description of the Bromage Score

Grade	Criteria	Degree of Block, (%)
I	Free movement of legs and feet	Nil (0)
II	Just able to flex knees with free movement of feet	Partial (33)
III	Unable to flex knees, but with free movement of feet	Almost complete (66)
IV	Unable to move legs or feet	Complete (100)

2.3. Statistical Analysis

Data were presented as mean (standard deviation), median (25, 75 percentile) or frequency (percentage), as appropriate. The normal distribution of quantitative variables was assessed with Kolmogorov-Smirnov test. To compare quantitative variables in the 3 groups, ANOVA or Kruskal-Wallis test were used, as appropriate. Qualitative variables were compared with chi square test. Significance level was set at $P < 0.05$. Data were analyzed using statistical package for social sciences software (SPSS Company, Chicago, Il) Version 22.

3. Results

The demographic variables and the ASA class of patients were comparable among the 3 groups. Patients were 37 ± 7 years on average with the mean gestational age of 37.2 ± 1.2 week. In all 3 groups, spinal block was successful and no high neuraxial block (level higher than T4) was recorded. The patients in the 10 mg group showed higher degrees of motor block. However, the difference was not statistically significant (Table 2). No significant difference was found between the maximum level of sensory block (or duration of recovery from sensory) and motor block in the 3 groups ($P > 0.05$) (Tables 3 and 4). The complication rates including the need for atropine or ephedrine administration, nausea, vomiting, and pruritus were not significantly different among the 3 groups (Table 4). The trend of blood pressure and heart rate was comparable in the 3 groups ($P > 0.05$) (Figures 1 and 2).

4. Discussion

All the 3 doses of intrathecal bupivacaine showed similar satisfactory block profiles. Generally, previous studies yielded comparable results with some trivial differences. An earlier study evaluated the effects of intrathecal bupivacaine (6, 8, and 10 mg plus sufentanil 3 μg) in cesarean section surgery; this study reported similar motor block in the 3 groups, but it was found that with the increase in the dose of bupivacaine, the level of sensory block increased and the time of reaching the maximum motor block intensity decreased. On the other hand, increasing the dose of bupivacaine resulted in higher incidence of nausea, hypotension, and the need for ephedrine (13).

An earlier study suggested that adding sufentanil to intrathecal bupivacaine will reduce the required dose of local anesthetic in parturient. Nevertheless, they examined rather higher doses of bupivacaine (14). Another study reported that the maximum level of sensory block in caesarean patients who received bupivacaine 6 mg plus sufentanil 3.3 μg is comparable to those patients that received bupivacaine 12 mg without adjuvant. This will also reduce the incidence of hypotension and the need for ephedrine

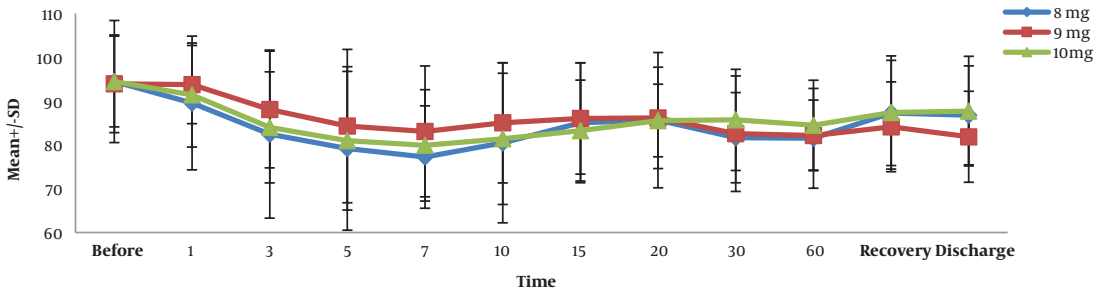

Figure 1. The Trend of MAP in Patients in Three Groups

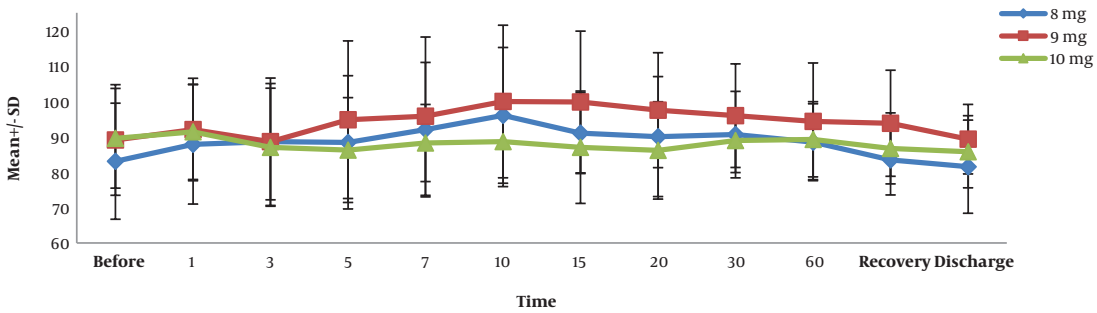

Figure 2. The Trend of Heart Rate in Three Groups

Table 2. Intensity of Motor Block in Three Groups from Spinal Anesthesia Until Discharge[a]

Time, Min	Dose of Bupivacaine			P Value
	8 mg	9 mg	10 mg	
Immediately after spinal anesthesia	2 (2,3)	2 (2,3)	3 (2,3)	0.733
5	4 (3,4)	4 (4,4)	4 (4,4)	0.318
10	4 (4,4)	4 (4,4)	4 (4,4)	0.139
15	4 (4,4)	4 (4,4)	4 (4,4)	0.333
20	4 (4,4)	4 (4,4)	4 (4,4)	0.333
30	4 (4,4)	4 (4,4)	4 (4,4)	0.602
60	4 (4,4)	4 (4,4)	4 (4,4)	0.093
90	4 (3,4)	4 (4,4)	4 (3,4)	0.521
120	2 (2,3)	2 (2,3)	3 (2,3)	0.389
150	2 (1,2)	1 (1,2)	3 (2.5,3.5)	0.137

[a] Data are presented as Median (25,75 percentile).

administration (15). Controversies to our findings may be attributed to the lower prescribed doses of local anesthetic in our patients.

4.1. Study Limitations

Inability to blind the anesthetist who performed spinal anesthesia was a limitation. However, both the assessor and the patients were blinded to the assignments. Another limitation was that we did not evaluate the extra requirement for analgesics in the postoperative period.

Table 3. Maximum Level of Sensory Block in 3 Groups from Spinal Anesthesia Until Discharge[a]

Time, Min	Dose of Bupivacaine			P Value
	8 mg	9 mg	10 mg	
Immediately after spinal Anesthesia	8 (8,10)	8 (8,10)	8 (8,10)	0. 88
5	6 (6,6)	6 (6,6)	6 (6,6)	0.982
10	6 (6,6)	6 (6,6)	6 (6,6)	0.974
15	6 (6,6)	6 (6,6)	6 (6,6)	0.979
20	6 (6,6)	6 (6,6)	6 (6,6)	0.971
30	6 (6,6)	6 (6,6)	6 (6,6)	0.845
60	6 (6,6)	6 (6,6)	6 (6,6)	0.409
90	6 (6,8)	6 (6,7)	6 (6,8)	0.491
120	10 (8,11.5)	8 (8,10)	8 (6,10)	0.166
150	12 (10,12)	11 (10,12)	10 (10,12)	0.252

[a]Values correspond to the level of spinal anesthesia (i.e., 8 represents 8th thoracic level) and presented as Median (25,75 percentile).

Table 4. Duration of Recovery from Sensory and Motor Block, and the Rate of Complications in Three Groups[a]

Variable	Dose of Bupivacaine			P Value
	8 mg	9 mg	10 mg	
Recovery from sensory block, min	110 ± 17	116 ± 15	110 ± 18	0.875
Recovery from motor block, min	107 ± 28	115 ± 17	116 ± 20	0.708
Atropine administration	7 (20)	9 (25.7)	9 (25.7)	0.809
Ephedrine administration	12 (34.3)	12 (34.3)	15 (42.9)	0.826
Nausea	7 (20)	7 (20)	9 (25.7)	0.65
Vomiting	4 (11.4)	5 (14.3)	4 (11.4)	0.92
Pruritus	4 (11.4)	8 (22.9)	5 (14.3)	0.826

[a]Data are presented as mean ± SD or No. (%)

Taken together, it seems that replacing a small amount of intrathecal bupivacaine with sufentanil favorably reduces the incidence of complications; namely, hypotension and nausea, while provides an acceptable profile of spinal anesthesia. The recommended dose of intrathecal bupivacaine ranged from 6 to 12.5 mg in earlier studies. In this study, increasing the dose of bupivacaine from 8 mg to 10 mg, when combined with sufentanil administration, did not considerably affect the maximum level of sensory block, intensity of motor block, or the duration of recovery from sensory and motor block. Thus, a lower dose of bupivacaine seems to be a more reasonable choice. In conclusion, bupivacaine doses of 6 to 8 mg with added sufentanil may provide the best results with minimal side effects in cesarean section surgery.

References

1. Kim JE, Lee JH, Kim EJ, Min MW, Ban JS, Lee SG. The effect of type of anesthesia on intra-and postoperative blood loss at elective cesarean section. *Korean J Anesthesiol*. 2012;**62**(2):125–9. doi: 10.4097/kjae.2012.62.2.125. [PubMed: 22379566].
2. Aksoy H, Aksoy U, Yucel B, Ozyurt SS, Acmaz G, Babayigit MA, et al. Blood loss in elective cesarean section: is there a difference related to the type of anesthesia? A randomized prospective study. *J Turk Ger Gynecol Assoc*. 2015;**16**(3):158–63. doi: 10.5152/jtgga.2015.15034. [PubMed: 26401109].
3. Sivevski A. Spinal anaesthesia for cesarean section with reduced dose of intrathecal bupivacaine plus fentanyl. *Prilozi*. 2006;**27**(2):225–36. [PubMed: 17211305].
4. Desai S, Lim Y, Tan CH, Sia AT. A randomised controlled trial of hyperbaric bupivacaine with opioids, injected as either a mixture or sequentially, for spinal anaesthesia for caesarean section. *Anaesth Intensive Care*. 2010;**38**(2):280–4. [PubMed: 20369760].
5. Olofsson C, Nygards EB, Bjersten AB, Hessling A. Low-dose bupivacaine with sufentanil prevents hypotension after spinal anesthesia for hip repair in elderly patients. *Acta Anaesthesiol Scand*. 2004;**48**(10):1240–4. doi: 10.1111/j.1399-6576.2004.00504.x. [PubMed: 15504182].

6. Labbene I, Gharsallah H, Abderrahman A, Belhadj Amor M, Trabelsi W, Hajjej Z, et al. [Effects of 15 mcg intrathecal clonidine added to bupivacaine and sufentanil for labor analgesia]. *Tunis Med*. 2011;**89**(11):853–9. [PubMed: 22179922].
7. Griffiths JD, Gyte GM, Paranjothy S, Brown HC, Broughton HK, Thomas J. Interventions for preventing nausea and vomiting in women undergoing regional anaesthesia for caesarean section. *Cochrane Database Syst Rev*. 2012;(9):7579. doi: 10.1002/14651858.CD007579.pub2. [PubMed: 22972112].
8. Lamon AM, Habib AS. Managing anesthesia for cesarean section in obese patients: current perspectives. *Local Reg Anesth*. 2016;**9**:45–57. doi: 10.2147/LRA.S64279. [PubMed: 27574464].
9. Vyas N, Sahu DK, Parampill R. Comparative study of intrathecal sufentanil bupivacaine versus intrathecal bupivacaine in patients undergoing elective cesarean section. *J Anaesthesiol Clin Pharmacol*. 2010;**26**(4):488–92. [PubMed: 21547176].
10. Lee JH, Chung KH, Lee JY, Chun DH, Yang HJ, Ko TK, et al. Comparison of fentanyl and sufentanil added to 0.5% hyperbaric bupivacaine for spinal anesthesia in patients undergoing cesarean section. *Korean J Anesthesiol*. 2011;**60**(2):103–8. doi: 10.4097/kjae.2011.60.2.103. [PubMed: 21390165].
11. Azimaraghi O, Marashi SM, Khazaei N, Pourhassan S, Movafegh A. The Effect of adding sufentanil to 0.5% hyperbaric bupivacaine on duration of brachial plexus blockade in chronic opium abusers, a randomized clinical trial. *Anesth Pain Med*. 2015;**5**(3):21960. doi: 10.5812/aapm.21960v2. [PubMed: 26161314].
12. Bang YS, Chung KH, Lee JH, Hong SK, Choi SH, Lee JY, et al. Comparison of clinical effects according to the dosage of sufentanil added to 0.5% hyperbaric bupivacaine for spinal anesthesia in patients undergoing cesarean section. *Korean J Anesthesiol*. 2012;**63**(4):321–6. doi: 10.4097/kjae.2012.63.4.321. [PubMed: 23115684].
13. Moosavi Tekyeh SM, Tabari M, Jahanian V. Investigation the effects and side effects of different dosage of bupivacaine in combination with sufentanil for spinal anesthesia in cesarian section. *Iran J Obstet, Gynecol Infertil*. 2013;**16**(66):1–9.
14. Dourado AD, Filho RLD, Fernandes RAM, Gondim MCD, Nogueira EVM. Sufentanil in combination with low dose hyperbaric bupivacaine in spinal anesthesia for cesarean section, a randomized clinical trial. *Rev Bras Anestesiol*. 2016;**66**(6):622–7. doi: 10.1016/j.bjane.2015.05.002.
15. Rasooli S, Moslemi F, Parish M, Mahmoodpoor A, Sanaie S. Spinal anesthesia with minidose bupivacaine-fentanyl for cesarean section in preeclamptic parturients. *Saudi Med J*. 2008;**29**(3):460–2. [PubMed: 18327382].