ISSN : 0259-1162

Vol 10 / Issue 2 / May-August 2016

Anesthesia: Essays and Researches

www.aeronline.org

Official publication of Pan Arab Federation of Societies of Anesthesiologists

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Anesthesia: Essays and Researches

Original Article

Two syringe spinal anesthesia technique for cesarean section: A controlled randomized study of a simple way to achieve more satisfactory block and less hypotension

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Abstract

Background: Multiple trials have been tried to prevent hypotension during spinal anesthesia. However, the drug choice and mode of administration is still a matter of debate.

Objectives: To compare the outcome of spinal injection of hyperbaric bupivacaine and fentanyl separately to standard injection of mixed fentanyl with hyperbaric bupivacaine.

Settings and Design: A randomized, controlled clinical trial.

Patients and Methods: One hundred twenty-four parturient scheduled for elective cesarean section were randomly allocated into two groups, each 62 parturient: Group M received spinal anesthesia using 10 mg bupivacaine 0.5% premixed with 25 μg fentanyl in the same syringe and Group S received 25 μg fentanyl in one syringe and 10 mg bupivacaine 0.5% without barbotage in a second syringe.

Results: Patients with intraoperative pain that was controllable without the need for a shift to general anesthesia was significantly lower in Group S (3.2%) than in Group M (16.1%). The frequency of hypotension was significantly lower in Group S compared to Group M ($P < 0.05$). Time till the onset of sensory block was nonsignificantly shorter with nonsignificantly higher mean level of maximal sensory block in Group S compared to Group M ($P > 0.05$). There was no significant difference in the time till occurrence of hypotension, duration of hypotension, mean dose of ephedrine used for the treatment of hypotension and frequency of patients developed itching between the groups ($P > 0.05$).

Conclusion: Separate intrathecal injection of fentanyl and hyperbaric bupivacaine provided a significant improvement in the quality of sensory block and significant reduction of the frequency of hypotension compared to injection of mixed medications.

Key words: Bupivacaine, cesarean section, fentanyl, separate, spinal anesthesia

Access this article online		
Website	DOI	Quick Response Code
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How to cite this article: Keera AA, Elnabtity AM. Two syringe spinal anesthesia technique for cesarean section: A controlled randomized study of a simple way to achieve more satisfactory block and less hypotension. Anesth Essays Res 2016;10:312-8.

INTRODUCTION

Regional anesthesia techniques are increasingly preferred for cesarean section (CS). Spinal anesthesia, irrespective of medication used, is now the safest and most popular method for CS.[1,2]

Hypotension is the commonest problem with spinal anesthesia. It is mainly due to sympathetic blockade leading to peripheral vasodilatation and pooling of blood in dilated vascular bed with subsequent decrease of venous return and cardiac output. This problem is magnified in parturient who is liable to develop hypotension by her virtue due to positional causes wherein the supine position, the gravid uterus compresses the aorta and the inferior vena cava against the bodies of the lumbar vertebra resulting in decreased venous return, which may decrease maternal cardiac output and blood pressure leading to a compromised uteroplacental perfusion.[3-5]

Multiple trials to prevent or combat hypotension using positional changes during or immediately after spinal injection were made.[6,7] Fluid therapy was another therapeutic option, but still there is a debate about the administration of crystalloids or colloids;[8] preloading or coloading.[9] The use of vasopressors was tried to induce vasoconstriction so as to combat vascular bed dilatation; however, the drug choice and mode of administration as either bolus or infusion is still a matter of debate.[10,11]

Fentanyl is a lipid soluble opioid with rapid onset of action, within 5 min, after intrathecal injection.[12] It significantly reduces pain during CS when added to bupivacaine. Meanwhile, intrathecal administration of fentanyl 25 μg in no laboring term parturient does not produce clinically important maternal hemodynamic changes.[13]

The current study aimed to compare the effect of spinal injection of hyperbaric bupivacaine and fentanyl separately to the standard injection of mixed fentanyl with hyperbaric bupivacaine.

PATIENTS AND METHODS

The current prospective double-blind randomized controlled study was conducted at Dr. Soliman Fakeeh Hospital, KSA, from 5/2013 to 10/2014. After approval of the study protocol by the Local Ethical Committee and obtaining fully informed written patients' consents, 124 parturient at full-term scheduled for elective CS with uncomplicated pregnancy were included in the study. Exclusion criteria included parturient with body weight <50 kg or >90 kg, height <150 cm or >170 cm, preeclampsia, any major systemic disease, contraindication to regional anesthesia or allergy to used medications. All patients attended the theater fasting at least 6 h and without administration of premedications or preoperative intravenous (IV) fluids.

Patients (parturient primi or multigravid) were randomly allocated into two groups (62 parturient in each group): Group M included parturient received spinal anesthesia using 10 mg bupivacaine 0.5% premixed with 25 μg fentanyl in the same syringe and Group S included parturient received the same medications sequentially without premixing using two different syringes; the first was lodged by 25 μg fentanyl and the second was lodged by 10 mg hyperbaric bupivacaine 0.5% without barbotage. All medications were prepared before insertion of the spinal needle. Timing between the first and second syringes was kept as low as possible to prevent CSF loss with part of the fentanyl dose. Demographic data including age, height, and weight were determined preoperatively. Drugs were injected through Quincke spinal needle, 25-gauge, inserted in the L3-4 interspace. Spinal anesthesia was done in sitting position then the parturient asked to lie down immediately after bupivacaine injection. Envelopes containing the two techniques were placed in a box. One anesthesiologist in our hospital gave spinal anesthesia to all the cases, and he is not from the research team and not sharing in postspinal management and recordings. He randomly picked an envelope and followed the technique written inside without informing the parturient about it. The research anesthesiologist entered the room immediately after spinal anesthesia and was unaware of the technique used. He recorded the results on a paper labeled with the patient's file number. IV fluid co-load was given in a dose of 15 ml/kg warm lactated ringer solution started as fast drip during and continued after spinal anesthesia application through 18-gauge IV cannula.

Patients monitoring included the following

1. Blood pressure and heart rate were monitored noninvasively every 2 min for 30 min then every 5 min and hypotension (systolic blood pressure < 100 mmHg) was treated with ephedrine (doses 5–10 mg). Electrocardiogram and oxygen saturation were monitored continuously
2. Sensory level was checked with ice cube every minute until the level reached T6 to determine the onset of sensory block. Then the height of maximum sensory block was recorded after 30 min
3. The intraoperative quality of surgical anesthesia was estimated using Ochsner Health System which measures patient satisfaction in four grades: Excellent – The patient felt comfortable during operation, no complaints; Good – A little discomfort but no need for additive medication; Fair – Discomfort, but controlled by nitrous oxide mask with or without fentanyl; and Poor – Unable to be controlled even with additive medication and shift to general anesthesia was mandatory[14]
4. Motor blockade of the lower limbs was tested and scored according to the modified Bromage scale[15] where 0: No motor block, 1: Unable to raise an extended leg (able to

flex the knee), 2: Unable to flex the knee (able to move the foot only), 3: Unable to flex the ankle (unable to move the foot or knee). Motor block was assessed every 5 min for 30 min. Time of onset of motor blockade, time lapsed from start of spinal anesthesia till Bromage grade 0 changed to grade I and duration of motor blockade, the time elapsed since start of motor block till complete recovery of muscle strength were determined
5. Neonatal outcome in the form of Apgar score at 1 and 5 min
6. Itching was graded and managed as: Mild – No treatment, Moderate was treated with IV chlorpheniramine maleate, 10 mg; if not responding or in the case of severe itching IV naloxone was given in a dose titrated according to the effect. As regards spinal anesthesia-related side-effects; nausea, vomiting, respiratory depression, or shivering were recorded and managed
7. Demographic data including age, height, and weight were determined preoperatively.

Statistical analysis

Sample Power was calculated according to Kraemer and Theimann[16] using the proposed figure showed the sample size for 60% power would require an N of more than 30/group, 80% power would require an N of 50/group. Thus, the power to be >80% for assuring an effect, thus the current study sample size was chosen, after conducting a pilot study and collecting data from other studies, to be 62 patients per group to reach a point of significance of <0.05. Obtained data were presented as a mean ± standard deviation, ranges, median, numbers, and ratios according to requirement. Results were analyzed using Wilcoxon; ranked test for unrelated data (*Z*-test) and Chi-square test (χ^2 test). Statistical analysis was conducted using the SPSS (version 15, 2006, SPSS Inc., Chicago, IL.) for Windows statistical package. P <0.05 was considered statistically significant.

RESULTS

From 139 consecutive parturient assessed for eligibility, 12 did not fulfill inclusion criteria and were excluded. Three more parturient refused participation in the research. Finally, 124 parturient were randomized into two groups 62 in each group. All parturient enrolled in the study were closely followed up. All the 62 parturient in each group were considered for analysis [Figure 1]. Among the 124 parturient; 82 women were primipara, while 42 women were multipara. All were full-term with a mean gestational age of 37.8 ± 0.8; range:

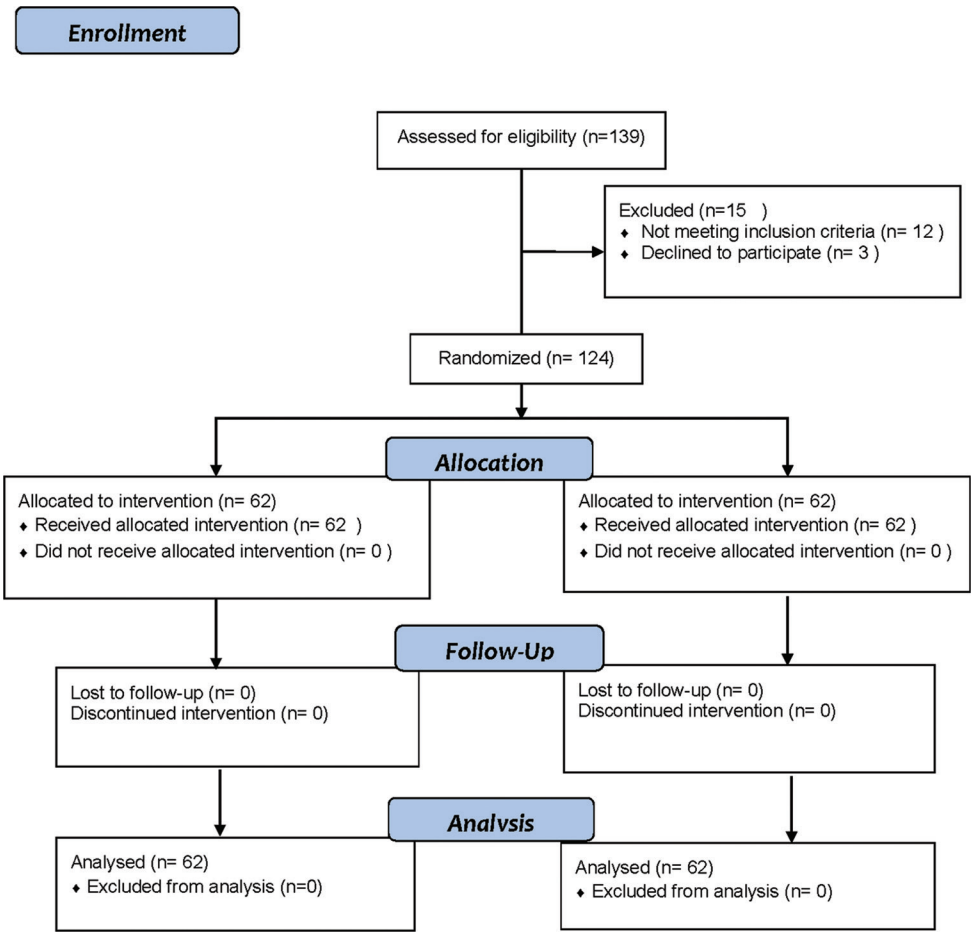

Figure 1: CONSORT flow diagram

37–39 weeks. The mean age of enrolled parturient was 28.2 ± 2.4; range: 23–33 years, 104 were of the American Society of Anesthesiologists (ASA) grade I and 20 were ASA II grade. Parturient inclusion data are shown in Table 1, there was nonsignificant difference between both groups of enrolled parturient. All patients passed smooth intraoperative course without complications within a mean duration of surgery 45.6 ± 7.2; range: 30–55 min with no significant difference between both studied groups.

Hypotension was recorded in 50 patients (40.3%): 32 in Group M and 18 in Group S with significantly lower (χ^2 = 6.56, P < 0.05) frequency of hypotension in Group S compared to Group M. Early hypotension occurred in 11 patients (17.7%) in Group S which is significantly lower than those in Group M (28 patients 45.2%). However, Late hypotension was nonsignificantly more in Group S, 7 (11.3%) compared to 4 (6.5%) in Group M. Meanwhile, mean lowest systolic blood pressure was nonsignificantly (Z = 0.643, P > 0.05) higher in Group S compared to Group M [Figure 2]. Time of occurrence of hypotension since spinal injection was nonsignificantly (Z = 1.444, P = 0.19) longer in Group S compared to Group M. Duration of hypotension was nonsignificantly (Z = 0.441, P = 0.671) shorter in Group S compared to Group M [Figure 3]. Mean dose of ephedrine used for the treatment of hypotension was nonsignificantly (Z = 0.745, P = 0.462) lower in Group S compared to Group M [Table 2].

Two patients (3.2%) had intraoperative pain that was controllable without the need for shift to general anesthesia which was significantly lower in Group S (P = 0.002) than those in Group M (10 patients 16.1%) [Figure 4]. No patients in both groups required conversion to general anesthesia. However, time till the onset of sensory block was nonsignificantly (Z = 1.157, P > 0.05) shorter in Group S compared to Group M. Mean level of maximal sensory block was nonsignificantly (Z = 9.321, P > 0.05) higher in Group S compared to Group M. Time till onset and recovery of motor block and Bromage grades were nonsignificantly different between both groups [Table 3].

Table 1: Parturient inclusion data

Data	Group M (*n*=62) (%)	Group S (*n*=62) (%)	Statistical analysis
Maternal data			
Age (years)	28±2.4	28.3±2.3	*Z*=0.689, *P*>0.05
Parity			
Primi	43 (69.4)	39 (62.9)	χ^2=0.608, *P*>0.05
Multi			
1 offspring	10 (16.1)	12 (19.4)	
2 offspring	6 (9.7)	7 (11.3)	
3 offspring	3 (4.8)	4 (6.5)	
Weight (kg)	89.3±7.3	88.3±5.6	*Z*=1.782, *P*>0.05
Height (cm)	164.3±3.3	165±3.1	*Z*=1.452, *P*>0.05
ASA grade			
I	51 (82.3)	53 (85.5)	χ^2=0.36, *P*>0.05
II	11 (17.7)	9 (14.5)	
Fetal data			
Gestational age	38.2±0.7	37.8±0.8	*Z*=0.723, *P*>0.05

Data are presented as mean±SD and numbers; percentages are in parenthesis. SD=Standard deviation, ASA=American Society of Anesthesiologists

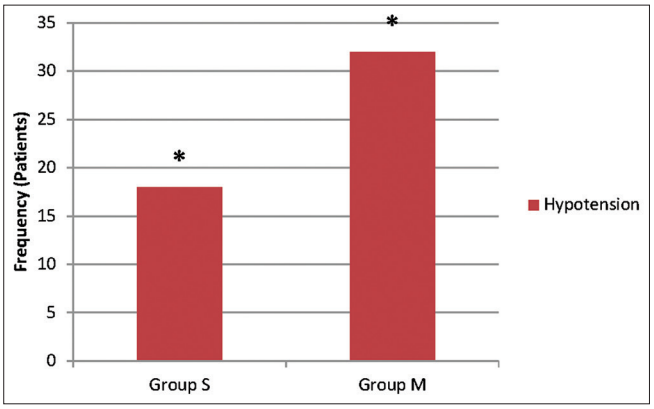

Figure 2: Frequency of hypotension in both groups. *Means statistically significant

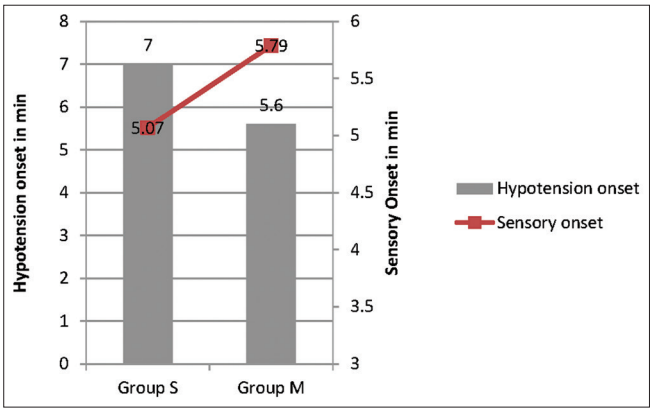

Figure 3: Time till the onset of hypotension and sensory onset in both study groups

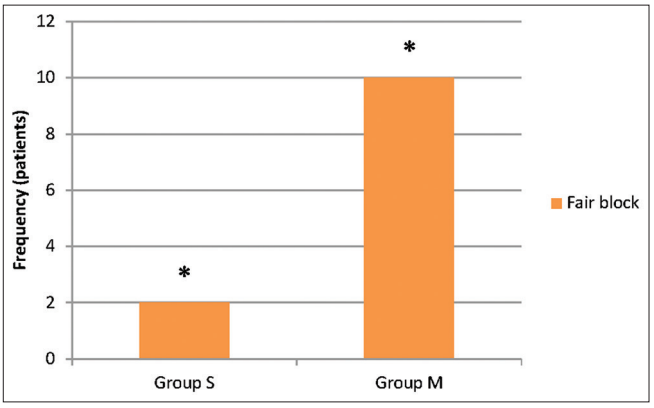

Figure 4: Patients with fair block needed supplemental analgesics. *Means statistically significant

Mean 1-min and 5-min Apgar score was nonsignificantly (Z = 1.204 and 1.508, respectively, $P > 0.05$) different between both groups. Thirty patients (48.4%) in each group developed itching. However, only 6 patients (9.7%) in Group S required treatment, which is insignificantly lower than 14 patients (22.6%) in Group M. However, all patients responded well to IV chlorpheniramine maleate except two patients in Group M, who required naloxone. None of the patients of Group S required naloxone. Fifteen patients developed nausea; 8 in Group M and 7 in Group S, and 7 patients had a vomiting attack; 3 in Group M and 4 in Group S without significant difference between both groups. Patients developed vomiting responded to IV metoclopramide. Twenty patients had mild shivering; 11 in Group M and 9 in Group S with no significant (χ^2 = 2.638, $P > 0.05$) difference. No respiratory depression or any other complications, other than what mentioned above, was recorded in either group [Table 4].

Table 2: Blood pressure data

	Group M (*n*=62) (%)	Group S (*n*=62) (%)	Statistical analysis
Frequency of hypotension (<100 mmHg)			
Hypotension total	32 (51.6)	18 (29)	χ^2=6.56, *P*<0.05
Hypotension (early)	28 (45.2)	11 (17.7)	χ^2=10.81, *P*<0.05
Hypotension (late)	4 (6.5)	7 (11.3)	χ^2=0.898, *P*>0.05
Blood pressure measures (mmHg) (systolic)			
Baseline	120.5±4	118.9±4.9	*Z*=0.935, *P*>0.05
Mean lowest blood pressure	82.0±10.1	83.3±8.4	*Z*=0.643, *P*>0.05
Time of occurrence of hypotension since injection (min)	5.6±3.4	7±4.4	*Z*=1.444, *P*=0.19
Duration of hypotension (min) (with treatment)	6.5±4.26	6.38±2.3	*Z*=0.441, *P*=0.671
Dose of ephedrine used (mg)	21.5±17.2	17.2±4.9	*Z*=0.745, *P*=0.462

Data are presented as mean±SD and numbers; percentages are in parenthesis. SD=Standard deviation

Table 3: Spinal block data

	Group M (%)	Group S (%)	Statistical analysis
Sensory block			
Time till sensory onset (min)	5.79±3.08	5.07±2.4	*Z*=1.157, *P*>0.05
Maximum level			
C5	0	1 (1.6)	χ^2=9.321, *P*>0.05
C7	2 (3.2)	1 (1.6)	
T1	2 (3.2)	1 (1.6)	
T2	4 (6.5)	3 (4.8)	
T3	14 (22.6)	21 (33.9)	
T4	30 (48.4)	30 (48.4)	
T5	4 (6.5)	5 (8.1)	
T6	6 (9.7)	0	
Mean	3.65±1.392	3.4±1.273	
Surgical anesthesia			
Excellent	52 (83.9)	60 (96.8)	χ^2=5.905, *P*<0.05
Fair	10 (16.1)	2 (3.2)	
Poor	0	0	
Motor block			
Time till onset (min)	5±1.3	4.7±1.8	*Z*=1.157, *P*>0.05

Data are presented as mean±SD and numbers; percentages are in parenthesis. SD=Standard deviation

DISCUSSION

The current study aims to compare the effect of spinal injection of fentanyl and hyperbaric bupivacaine sequentially to the standard injection of mixed fentanyl with hyperbaric bupivacaine in CS.

We found that separate intrathecal injection of fentanyl and hyperbaric bupivacaine provided significant improvement in the quality of sensory block and significant reduction of the frequency of hypotension compared to injection of mixed medications.

Understanding the mechanisms of intrathecal drug spread can explain our results. When the patients are turned supine immediately after injection in the lumbar region, a hyperbaric solution will spread under the influence of gravity down the slope created by lumbar spinal curvature. However, plain solution being less viscous, mixes rather freely with CSF, and thus moves easily through compressed subarachnoid space and will not have gravity dependent spread.[17,18]

As regards the outcome; the incidence of hypotension is significantly lower in Group S compared to Group M. In my opinion, the mixture of hypobaric fentanyl and

Table 4: Spinal anesthesia-related side-effects

	Group M (%)	Group S (%)	Statistical analysis
Itching			
Frequency			
Yes	30 (48.4)	30 (48.4)	χ^2=0.0, *P*>0.05
No	32 (51.6)	32 (51.6)	
Need for therapy			
Yes	14 (22.6)	6 (9.7)	χ^2=3.815, *P*>0.05
No	48 (77.4)	56 (90.3)	
Nausea and vomiting			
No nausea and vomiting	54 (87.1)	55 (88.7)	χ^2=0.076, *P*>0.05
Nausea	8 (12.9)	7 (11.3)	
Vomiting	3 (4.8)	4 (6.5)	χ^2=0.151, *P*>0.05
Shivering			
Frequency			
Yes	11 (17.7)	9 (14.5)	χ^2=0.36, *P*>0.05
No	51 (82.3)	53 (85.5)	
Respiratory depression	0	0	

Data are presented as numbers; percentages are in parenthesis

hyperbaric bupivacaine sank down, then they crept up together when the patient lay down acting synchronously on the same level. However, hyperbaric bupivacaine, which was injected separately without mixing, was denser than bupivacaine fentanyl mixture and sank more down and took a longer time to reach the final level which delayed the onset of the sympathetic block and gave time for a compensatory mechanism to prevent hypotension. The delayed mean onset of hypotension in Group S (7 min) compared with Group M (5.6 min) may prove this theory. This delayed onset of sympathetic block match the results of Helmi *et al*. and Martin *et al*., who concluded that isobaric bupivacaine produced more rapid onset of hypotension compared to hyperbaric bupivacaine.[19,20]

Late hypotension, occurring more than 30 min after spinal anesthesia, is observed in both groups with nonsignificantly more patients in Group S. It was first described by Kyokong *et al*., and the mechanism of this late-onset hypotension remains unidentified.[21] In my opinion, some patients have moderately weak compensatory mechanisms in the upper half of the body which is exhausted after more than 30 min. Those patients tend to develop early hypotension in Group M, because of the more rapid sympathetic block and late hypotension in Group S.

The most significant outcome of our work is the great improvement in the quality of sensory block in Group S comparing to Group M. We believe that separate injection of fentanyl allows it to work on higher levels in the spinal cord preventing visceral pain. It is known a long time ago that fentanyl and sufentanil improve neuraxial anesthesia, decrease trans-operative pain, and moderately prolong sensory block.[22,23]

The response to intrathecal medications with different baricity given sequentially was first studied by Cesur *et al*., who compared parturient received 10 mg hyperbaric bupivacaine with those who received 5 mg of plain and 5 mg of hyperbaric bupivacaine sequentially for spinal anesthesia. They found that parturients who receive 5 mg plain and 5 mg hyperbaric bupivacaine sequentially have lower incidence of hypotension compared with those who receive 10 mg hyperbaric bupivacaine.[24] Serhan *et al*. studied spinal anesthesia with hyperbaric bupivacaine (10 mg), sequential administration of hyperbaric and isobaric bupivacaine (5 mg each), and isobaric bupivacaine (10 mg). They found no significant difference between all groups.[25]

Desai *et al*.[26] studied two groups each 24 parturients received spinal injection for CS. The first group received 10 mg hyperbaric bupivacaine plus morphine 100 μg plus fentanyl 15 μg, mixed in a syringe prior to administration. The second group received 10 mg bupivacaine through one syringe, followed by morphine 100 μg plus fentanyl 15 μg through a separate syringe. They reported that patients received mixed medications had higher levels of sensory block to cold than those received separate injections and may be associated with the higher postoperative opioid requirement. In our work, there was no significant difference in levels. This difference could be because they injected hyperbaric bupivacaine before opioids, which went down to lower levels during injection of opioids and gave lower level in the separate group. In their study, the incidence of hypotension was insignificantly lower in Group S. They did not study the incidence of unsatisfactory block which is rare and needs a larger group number.

Atalay *et al*. compared 10 mg hyperbaric bupivacaine intrathecally with 5 mg plain bupivacaine plus 35, 30, or 25 mg of meperidine administered sequentially. They concluded that sequential administration of 5 mg plain bupivacaine and 25 mg meperidine intrathecally provided better blood pressure stability and a lower incidence of side-effects than 10 mg hyperbaric bupivacaine alone.[27] However, they did not compare the same medications mixed and sequentially.

According to our knowledge, we are the first to compare mixed and sequential intrathecal hyperbaric bupivacaine with fentanyl using the same doses in CS.

It will be better in the future studies to specify the temperature of the injected medications as it can affect baricity, also the rate of injection of medications should be specified.

CONCLUSION

It could be concluded that separate intrathecal injection of fentanyl and hyperbaric bupivacaine provided significant improvement in the quality of sensory block and significant reduction of the frequency of hypotension compared to injection of mixed medications.

Acknowledgments

The authors thank Dr. Hassan Ali Al Saleh, McMaster University, for generous support and valuable helping in statistical analysis. The authors also thank Dr. Essam Abo Baker, Anesthesia Consultant, Dr. Soliman Fakeeh Hospital, for helping with the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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