

Comparison of Efficacy and Hemodynamic Effects of two Different Concentrations of Hyperbaric Bupivacain 0.5% and 0.75% during Spinal Anesthesia

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ABSTRACT

Background: Bupivacaine 0.5% isobaric and 0.75% hyperbaric are most commonly used local anesthetics for spinal anesthesia. In this study two different concentrations of hyperbaric Bupivacaine (0.5% and 0.75%) in same dose are compared for their efficacy and hemodynamic effects during spinal anesthesia.

Aim: To compare the efficacy (onset, duration and intensity of block) and the changes in hemodynamic parameters (heart rate, systolic, mean and diastolic blood pressure) while using two different concentrations of hyperbaric Bupivacaine 0.5% and 0.75% for spinal anesthesia.

Methods: In this comparative study, 100 patients, 20-60 years of age, ASA I & II, were divided into groups of 50 each. After written informed consent, Group-A was given hyperbaric Bupivacaine 0.5% whereas Group-B received Bupivacaine 0.75%. Non-invasive systolic, diastolic, mean blood pressure and heart rate were recorded at 5, 10, 15, 20, 25, 30, 45 and 60 minutes. Before onset of surgery, extent of sensory block was determined using a 3 point rating scale and motor block was assessed using a modified Bromage Scale. Data entry and analysis was done by using SPSS 13.

Results: Heart Rate at 60th minute in Group-A and B was 76.90 and 76.20, systolic blood pressure at 60th minute in Group-A and B was 127.60 and 128.32 and diastolic blood pressures at 60th minute in Group-A and B was 84.18 and 84.24. Sensory block when assessed at 60th minute, was absent in all patients in both treatment groups. At 60th minute Hip, Knee and ankle were completely blocked in both groups.

Conclusion: No statistically significant difference was seen in sensory and motor block and hemodynamics parameters with the use of 0.5% and 0.75% hyperbaric Bupivacaine.

Keywords: Hyperbaric Bupivacaine 0.5%, Hyperbaric Bupivacaine 0.75%, Hemodynamic, Spinal Anesthesia

INTRODUCTION

Spinal anesthesia is a reversible interruption of nerve transmission caused by injection of local anesthetic in the subarachnoid space¹. It is a simple approach providing deep and fast surgical block most suitable for surgeries below the umbilicus².

Dr. August Bier was the first to perform spinal anesthesia in 1899 with Cocaine³. The greatest challenge of the technique is to control the spread of local anesthetic through cerebrospinal fluid (CSF) in order to produce a block that is adequate for the proposed surgery without producing a needless extensive spread⁴.

Many factors affect the spread of injected local anesthetics. Nevertheless, the influence of most of them is small, unpredictable and beyond the clinician's control.⁵ The major factors are represented by the baricity of the injected drug and the posture of the patient. Manipulation of the factors affecting the spread of local anesthetics may be used to produce different types of blocks.⁶ The height of the block largely depends upon the solution's baricity⁷.

The selection of the local anesthetic to be used for spinal anesthesia is usually based on the expected duration of surgery and need for early patient discharge. Many local anesthetics like Lidocaine, Mepivacaine, Cinchocaine, Tetracaine and Bupivacaine have been used for spinal anesthesia. However, in spite of Lidocaine's wide use and long history, the overwhelming evidence of transient neurological symptoms associated with it have raised strong concerns with its use⁸.

Induction of spinal anesthesia has a very significant effect on many organ systems including cardiovascular,

respiratory, gastrointestinal, renal, endocrine and coagulation systems⁹. The cardiovascular effects associated with sympathetic block are more frequent. A high block can lead to adverse hemodynamic changes and in extreme cases, a significant blood pressure drop and severe bradycardia¹⁰. The degree of hypotension correlates with the level of sympathetic block which is generally two segments higher than the level of analgesia¹¹. It has long been known that duration of spinal anesthesia is proportional to the total dose of local anesthetic injected. The result of most of the studies on the effect of volume, concentration or total dose of local anesthetic on spread of spinal anesthesia support the assumption that total dose is more important than the volume¹².

In the last decade Bupivacaine 0.5% Isobaric and 0.75% hyperbaric are the most frequently used agents for spinal anesthesia¹³. Increase in Bupivacaine concentration can cause more adverse effects like hypotension, nausea and vomiting¹⁴. Bupivacaine 0.5% hyperbaric is currently available in our country and is being used for spinal anesthesia¹⁵.

In this study two different concentrations of Bupivacaine i.e., 0.5% and 0.75% of same baricity, dose and injection sites were compared for their efficacy (onset, duration & intensity of block) and hemodynamic effects during spinal anesthesia. The rationale of this study was to find which concentration would achieve adequate block with more hemodynamic stability and hence lesser morbidity and mortality.

MATERIAL & METHODS

This comparative study was conducted in Department of Anesthesia, King Edward Medical University /Mayo Hospital Lahore. Study was consisted of 100 patients of ASA I-II of age 20-60 years scheduled for elective surgical procedure under spinal anaesthesia. Patients with history of hypertension, diabetes, morbid obesity, allergy to local anesthetics,

Received on 03-03-2019

Accepted on 23-07-2019

neurological disease, coagulopathy or taking anticoagulants , alpha, beta blockers, antidepressant and patients with spinal deformity were excluded from the study.

Data collection procedure: Patients were divided into two groups. (Group-A & Group-B). Each group was comprised of 50 patients. The pre-operative assessment was done day before surgery and procedure was explained to the patient and written informed consent was taken. Patient's weight was noted on the chart. On arrival of patient in operation theatre, base line heart rate and non-invasive blood pressure was recorded. Patient's ECG and pulse oximetry was monitored. Intravenous cannula 18 G was passed and patient was given Ringer Lactate infusion 7 ml/kg in 15 -20 minute. Under complete aseptic measures, using a mid-line approach at L3-L4 interspace with a 25 G Quincke spinal needle dural puncture was performed with patient in the sitting position. Patients in group A were given 15 mg (3 ml) of 0.5% hyperbaric Bupivacaine while patients in group B were given 15 mg (2 ml) of 0.75% hyperbaric Bupivacaine. Patients were made to lie down immediately after injecting drug. Non-invasive systolic, diastolic, mean blood pressure and heart rate was recorded at 5, 10, 15, 20, 25, 30, 45 and 60 minutes intervals. Before onset of surgery, extent of sensory block (analgesia) was determined using a 3point rating scale: 0= Normal sensation, 1= Blunted sensation, 2= Absent sensation. Complete sensory block was taken as score of 2. A score of < 2 was considered incomplete sensory block. Motor block was assessed using a modified Bromage Scale whereby patients were asked to flex the limb at the hip, knee and ankle joints and the results were recorded as 0 = no motor block , 1 = hip blocked, 2 =hip and knee blocked, 3 = hip, knee and ankle blocked. Patient was judged ready for surgery when there was complete loss of pin prick sensation at T10 level. After spinal anesthesia as mentioned in methodology, data was collected and entered into attached study proforma.

Statistical Analysis: After the completion of study, data was collected and analyzed by using SPSS version 13. Demographic data, maximum changes in arterial pressure and heart rate were analyzed by t-test. Whereas changes over time were analyzed with a two way ANOVA for repeated measures. Hemodynamic changes between the two groups were considered statistically significant if p-value was ≤ 0.05 .

RESULTS

One hundred patients of ages 20 to 60 with mean age of patients in Group-A and in Group-B was 39.98 ± 10.29 and 39.80 ± 10.53 years respectively. Age range of patients in both groups was 22-60 years (Table 1). In Group-A 42 patients were male and 8 were females. While in Group-B 43 patients were male and 7 patients were females (Graph-1).

Mean systolic BP in Group-A and in Group-B was 139.54 ± 13.31 and 136.02 ± 13.41 mmHg. While diastolic BP in Group-A and in Group-B was 84.46 ± 9.25 and 85.36 ± 9.71 mmHg.

Heart rate of patients was monitored in both groups from base line till 60th minutes. Detailed description is given in above table. Overall heart rate decreases significantly in all patients. i.e. ((p-value=0.025) But change in heart rate was not statistically significant among groups. (p-value=0.966).

Systolic blood pressure of patients was monitored in both groups from base line till 60th minutes. In above figure change in systolic blood pressure from base line till 60th minute monitoring was shown up in both groups. Group wise comparison shows that in both groups drop in systolic blood pressure was not statistically significant. i.e., (p-value=0.217)

At 60th minute average systolic blood pressure in Group-A was 128.32 and in Group-B it was 127.60. Although minor difference in systolic blood pressures was present in both groups at 60th minutes but this was not statistically significant.

Table1: Descriptive statistics for age (years) in treatment groups

	Group A	Group B
N	50	50
Mean	39.98	39.80
SD	10.29	10.53
Minimum	22	20
Maximum	60	60

Group-A= Bupivacaine 0.5% Group-B= Bupivacaine 0.75%

Graph-1 Gender distribution in treatment groups

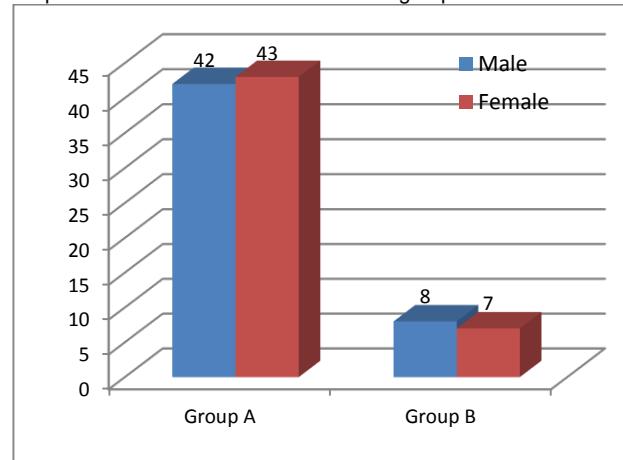


Table 2: Descriptive statistics for systolic & diastolic blood pressure in treatment groups

	Treatment Group			
	Systolic BP		Diastolic BP	
	Group-A	Group-B	Group A	Group-B
N	50	50	50	50
Mean	139.54	136.02	84.46	85.36
SD	13.31	13.41	9.25	9.71
Minimum	119	117	63	65
Maximum	167	159	98	100

Table-3 Heart rate changes over time in treatment groups

	Group	Mean	Std. Deviation
HR-0 (Beats/Min)	Group-B	79.50	12.38
	Group-A	79.52	12.25
HR-5 (Beats/Min)	Group-B	78.88	10.57
	Group-A	79.20	10.30
HR-10 (Beats/Min)	Group-B	81.68	11.80
	Group-A	81.92	11.90
HR-15 (Beats/Min)	Group-B	80.12	11.73
	Group-A	79.08	11.86
HR-20 (Beats/Min)	Group-B	80.58	11.76
	Group-A	81.28	11.98
HR-25 (Beats/Min)	Group-B	82.80	11.87
	Group-A	82.16	12.09
HR-30 (Beats/Min)	Group-B	81.60	12.25
	Group-A	82.64	11.92
HR-45 (Beats/Min)	Group-B	81.48	12.39
	Group-A	80.88	12.46
HR-60 (Beats/Min)	Group-B	76.90	12.44
	Group-A	76.20	12.04

p-value (Overall Change Over Time)= 0.025

p-value (Overall Change Over Time* Treatment Group)= 0.966

Table-4 Sensory block changes over time in treatment groups

Min	Groups	Sensory Block (Sensation)			p-value
		Normal	Blunted	Absent	
0	A	50	0	0	N/A
	B	50	0	0	
5	A	0	4	46	0.695
	B	0	3	47	
10	A	0	1	49	0.315
	B	0	0	50	
15	A	0	0	50	N/A
	B	0	0	50	
20	A	0	0	50	N/A
	B	0	0	50	
25	A	0	0	50	N/A
	B	0	0	50	
30	A	0	0	50	N/A
	B	0	0	50	
45	A	0	0	50	N/A
	B	0	0	50	
60	A	0	0	50	N/A
	B	0	0	50	

Diastolic blood pressure of patients was monitored in both groups from base line till 60th minutes. Group wise comparison shows that in both groups drop in diastolic blood pressure was not statistically significant. i.e. (p-value=0.895) At 60th minute average diastolic blood pressure in Group-A was 84.24 and in Group-B it was 84.18. Although minor difference in diastolic blood pressures was present in both groups at 60th minutes but this was not statistically significant.

Sensory block in both groups was assessed from 0 till 60th minutes. At each interval sensory block was compared in both groups. According to p-value sensory block level was statistically same in both groups from 0 till 60th minute monitoring. At 15th minute sensory block (sensation) was same

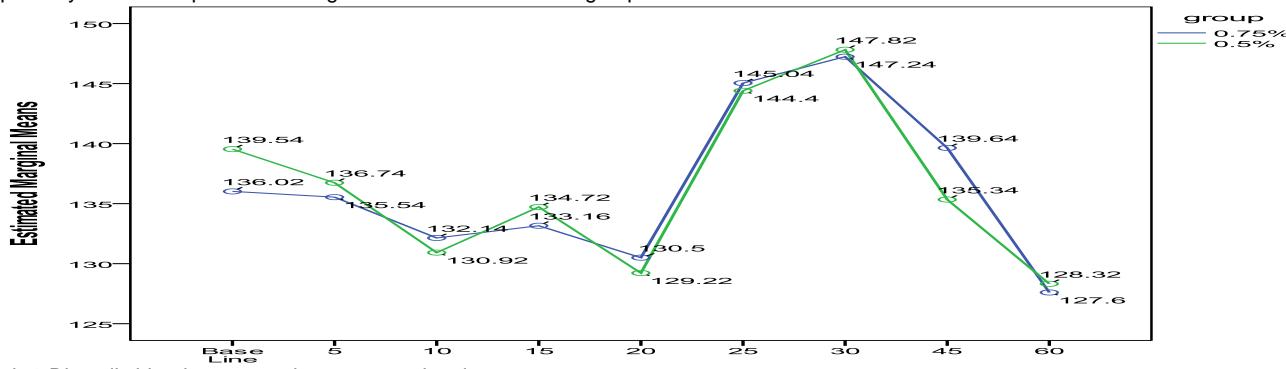
in both treatment groups. p-values for each time interval in both groups is given in Table 4

Motor block in both groups was assessed with the help of Modified Bromage Scale from 0 minute till 60th minutes. At each time interval motor block was compared in both groups. According to p-value motor block level was statistically same in both groups when assessed at 0 and 60th minute. Till 60th minute hip knee and ankle were sblocked. p-values for each time interval is given in Table 5.

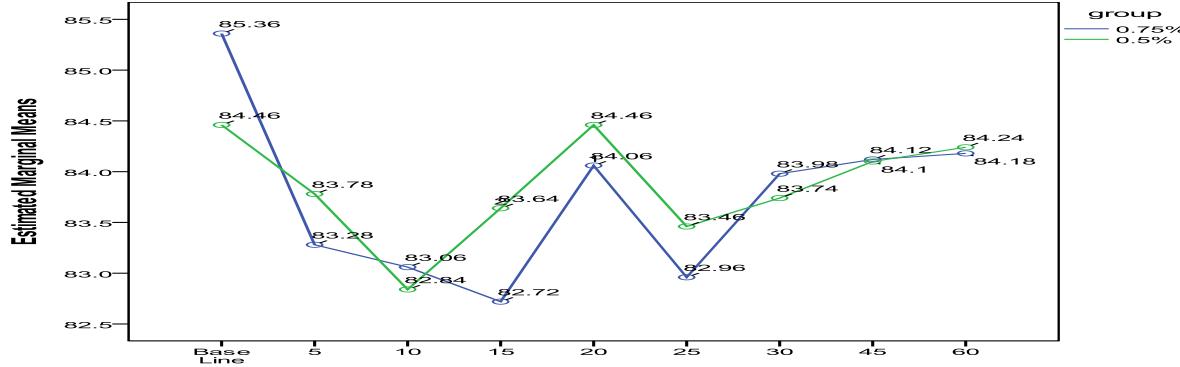
Table-5 Motor block changes over time in treatment groups

Min	Group	Motor block modified bromage scale				P value
		No Block	Hip	Hip & Knee	Hip, Knee & Ankle	
0	A	50	0	0	0	N/A
	B	50	0	0	0	
5	A	1	49	0	0	0.558
	B	2	48	0	0	
10	A	0	50	0	0	N/A
	B	0	50	0	0	
15	A	0	50	46	4	0.928
	B	0	50	47	3	
20	A	0	50	50	50	N/A
	B	0	50	50	50	
25	A	0	50	50	50	N/A
	B	0	50	50	50	
30	A	0	50	50	50	N/A
	B	0	50	50	50	
45	A	0	50	50	50	N/A
	B	0	50	50	50	
60	A	0	50	50	50	N/A
	B	0	50	50	50	

Graph 2: Systolic blood pressure changes over time in treatment groups



Graph-3 Diastolic blood pressure changes over time in treatment groups



p-value (Overall Change Over Time)= 0.909,

p-value (Overall Change Over Time* Treatment Group)= 0.895

DISCUSSION

Spinal anesthesia is a popular regional anesthesia technique used mostly for various surgical procedures below the umbilicus. Its rapid onset and short duration of action, easy application, lower costs, and fewer side effects and complications constitute significant advantages for outpatient procedures¹⁶.

Spinal anesthesia is a reversible interruption of nerve transmission caused by injection of local anesthetic in subarachnoid space. Induction of SAB has a very significant effect on many organic systems, including cardiovascular, respiratory, gastrointestinal, renal, endocrine and coagulation system¹⁷. Effect of SAB on the cardiovascular system is primarily indirect and occurs through blockade of sympathetic nervous system. Most significant easily measurable cardiovascular effects of SA are changes in blood pressure and pulse rate. The more frequent cardiovascular complications of spinal anesthesia are hypotension and bradycardia, with a frequency ranging between 5% and 56%¹⁸. A decrease in venous return and systemic vascular resistance caused by sympathetic nervous system block are the primary causes of spinal anesthesia induced hypotension. Additionally, extension of the sensory block beyond the T4 level will lead to blockade of cardioaccelerator fibers, with subsequent decrease in the heart rate and cardiac output¹⁹. A close correlation between block height and decrease in blood pressure was shown. Sensory blocks at or above T6 increased hypotension risk by 2.4 times, which increased to 3.8 in sensory blocks at or above T5²⁰.

Factors that increase the risk of hypotension include advanced age, female sex, pregnancy, obesity, diabetes mellitus, hypertension, block level at or above T5, use of opioids during premedication, and high local anesthetic dosages²¹⁻²³.

Heart rate variability (HRV) analysis is a noninvasive marker of sympathovagal balance and has been recently used to determine patients who carry a risk of hypotension after spinal anesthesia, especially in cesarean sections. In addition to their role in predicting hypotension due to spinal anesthesia, HRV parameters also undergo significant changes following spinal anesthesia²⁴⁻²⁵.

The aim of all anesthesiologists is to perform the SA with the least deviation in blood pressure and pulse rate. In doing so we are using spinal anesthetics of different baricities. Baricity of anesthetic represents the ratio of the specific density of anesthetic and cerebrospinal fluid at a temperature of 37°C.²⁶ The baricity of a local anesthetic used in spinal anesthesia influences the block level and, as a result, the severity and frequency of hypotension. In practice, the most commonly used anesthetics are 0.5% isobaric and 0.75% hyperbaric bupivacaine. Hyperbaric bupivacaine has a greater tendency for cephalic spread than isobaric bupivacaine; therefore, it has a greater peak sensory block height and, as a result, a greater incidence of hypotension and blood pressure drop in patients undergoing nonobstetric surgery²⁷.

We compared 0.5% and 0.75% hyperbaric bupivacaine and did not find any statistical significant difference in haemodynamic effects among the groups. The changes in heart rate at 60th minute were (Group-A=76.90 vs. Group-B=76.20), systolic blood pressure at 60th minute was (Group-A=127.60 vs. Group-B=128.32) and diastolic blood pressure at 60th minute was (Group-A=84.18 vs. Group-B=84.24). The sensory and motor blocks were also at the same level in both groups with no significant difference. These results clearly indicate that hemodynamic effects, sensory and motor blocks

were same for 0.5% and 0.75% hyperbaric bupivacaine when given intrathecally.

A study conducted by Sikandar et al. compared 0.75% & 0.5% hyperbaric Bupivacaine for haemodynamic stability, level of block and patients comfort. According to the results of their study no statistically significant difference was present between the hemodynamics of two groups but 0.5% hyperbaric Bupivacaine was superior in respect of need for rescue ephedrine, and achieved a higher level of block.¹⁵ These results are consistent with the results of our study in terms of onset of sensory and motor blocks but differ in the use of rescue ephedrine. In contrast to our study, they used ephedrine to treat hypotension in 17 patients who were given 0.75% bupivacaine while we did not use rescue ephedrine in any patient as there was no significant drop in blood pressure. This difference could be due to the fact that they conducted study in obstetrics whereas we did not include pregnant women in our study.

Our literature search revealed very few studies that compared 0.5% hyperbaric bupivacaine with 0.75% hyperbaric bupivacaine for hemodynamic changes as well as for sensory and motor block in patients undergoing spinal anesthesia. Most of the studies have compared isobaric bupivacaine with hyper and hypobaric bupivacaine in certain conditions.

Results similar to our study were also reported by Narejo and his colleagues . They compared different baricities of bupivacaine i.e. 0.5% isobaric and 0.75% hyperbaric in same dose and volume for spinal anesthesia. As in our study they also observed immediate decrease in systolic blood pressure and heart rate with 0.75% hyperbaric Bupivacaine. The onset of sensory and motor block was also similar to our study²⁸.

Recently another study conducted by Toptas et al. in which hemodynamic effects of hyperbaric and isobaric bupivacaine in spinal anesthesia were assessed, also supported our observations. They reported changes in hemodynamic parameters with hyperbaric bupivacain similar to the results of our study²⁹.

Luck in his study compared the clinical effects of hyperbaric bupivacain for spinal anesthesia with those of similar preparations of levobupivacain and ropivacain. Their results with hyperbaric bupivacain were similar to our study with regards to onset of sensory and motor block and hemodynamic parameters³⁰.

A study by Solakovic compared the hemodynamic parameters in 0.5% hyperbaric and isobaric bupivacaine. Results with high statistical significance showed that the baricity has an essential effect on the behavior of the basic hemodynamic parameters in reducing the arterial blood pressure and slowing down the pulse. At the same time isobaric anesthetic gave smaller deviation of these parameters.⁷ Our results contradict this study because we found less deviation with 0.5% hyperbaric bupivacaine in hemodynamic parameters.

Recently Helmi et al compared hemodynamic parameters in 0.5% isobaric and 0.5% hyperbaric bupivacaine when given intrathecally. Contradictory to our results, they observed significant decrease in blood pressure with 0.5%hyperbaric bupivacaine. Most likely this is due to difference in the dose of bupivacane as they had used 20mg of bupivacane while we used 15mg.

Aftab and his associates also reported different results than our study. They compared 0.5% isobaric bupivacaine with 0.75% hyperbaric bupivacaine. In comparison to our study, they observed lesser decrease in the systolic blood pressure with 0.75% hyperbaric bupivacaine which could be due to

preloading with 15ml/kg while we preloaded our patients with 7ml/kg

Previous clinical studies have been comparing hyperbaric and isobaric bupivacaine reporting variable results on spinal anesthesia induced hypotension.¹¹ Limited number of studies have compared the efficacy of 0.5% and 0.75% hyperbaric bupivacaine. Haemodynamic observations did not confer any advantage to use of 0.5% over 0.75% bupivacaine with similar baricity. The sensory and motor block were similar with both drugs. The intrathecal use of either 0.5% or 0.75% hyperbaric bupivacaine can provide excellent surgical conditions with haemodynamic stability.

CONCLUSION

The results of our study concluded that hyperbaric bupivacaine when given intrathecally in different concentration (0.5% and 0.75%) but in same dose (15mg) provided a similar quality of sensory and motor block along with no difference of hemodynamic parameters. However, 0.5% hyperbaric bupivacaine gave more stability in hemodynamics, sensory and motor block functioning as compared to 0.75% hyperbaric bupivacaine but this difference was not statistically significant.

REFERENCES

1. NM. G. Physiology of spinal anesthesia. Baltimore: Williams and Wilkins. 2001:78-108.
2. Boon J, Abrahams H, Meiring J, Welch T. Lumbar puncture: anatomical review of a clinical skill. Clinicsal Anatomy. 2004;17(7):544-53.
3. Di Cianni S, Rossi M, Casati A, Cocco C, Fanelli G. Spinal anesthesia: an evergreen technique. Acta Biomedica Ateneo Parmense. 2008;79(1):9.
4. Atef H, , Omera M, Badr M. Optimal dose of hyperbaric bupivacaine 0.5% for unilateral spinal anesthesia during diagnostic knee arthroscopy. Middle East journal of anesthesiology. 2012;21(4):591-8.
5. McLeod G. Density of spinal anaesthetic solutions of bupivacaine, levobupivacaine, and ropivacaine with and without dextrose. British Journal of Anaesthesia. 2004;92(4):547-51.
6. Hocking G, Wildsmith J. Intrathecal drug spread. British Journal of Anaesthesia. 2004;93(4):568-78.
7. Solakovic N. Comparison of Hemodynamic Effects of Hyperbaric and Isobaric Bupivacaine in Spinal Anesthesia. MED ARH. 2010;64:1.
8. Chan W, Peng P, Chinyanga H, Lazarou S, Weinbren J, Kaszas Z. Determining minimum effective anesthetic concentration of hyperbaric bupivacaine for spinal anesthesia. Anesthesia & Analgesia. 2000;90(5):1135-40.
9. Cindea I, Balcan A, Gherghina V, Nicolae G. Unilateral spinal anesthesia versus conventional spinal anesthesia in ambulatory lower abdominal surgery. European Journal of Anaesthesiology (EJA). 2007;24:10.
10. Solakovic N. Level of sensory block and baricity of bupivacaine 0.5% in spinal anesthesia. Medicinski arhiv. 2010;64(3):158-60.
11. Veering B, Immink T, Burn A, Stienstra R, Van Kleef J. Spinal anaesthesia with 0.5% hyperbaric bupivacaine in elderly patients: effects of duration spent in the sitting position. BJA. 2001;87(5):738-42.
12. Rupam S. Comparison of hypobaric, near isobaric and hyperbaric bupivacaine for spinal anesthesia in patients undergoing knee arthroscopy. Ind J of Anesth. 2002:446.
13. Liu S, McDonald B. Current issues in spinal anesthesia. Anesthesiology. 2001;94(5):888-906.
14. Macarthur A, Riley ET. Obstetric anesthesia controversies: vasopressor choice for postspinal hypotension during cesarean delivery. International anesthesiology clinics. 2007;45(1):115-32.
15. Sikander RI. Comparison of Haemodynamic, block level and patient comfort by using 0.75% & 0.5% Hyperbaric Bupivacaine in Caesarean Section. Ann Pak Inst Med Sci. 2009;5(4):259-62.
16. Wong J, Tan M, Leung P, Tseng K, Cheu W, Tang S. Comparison of the effect of two different doses of 0.75% glucose-free ropivacaine for spinal anesthesia for lower limb and lower abdominal surgery. The Kaohsiung Journal of Medical Sciences. 2004;20(9):423-30.
17. Urmey WF. Spinal anaesthesia for outpatient surgery. Best Practice & Research Clinical Anaesthesiology. 2003;17(3):335-46.
18. D O'Donnell B, Iohom G. Regional anesthesia techniques for ambulatory orthopedic surgery. Current Opinion in Anesthesiology. 2008;21(6):723-8.
19. Stamer U, Wiese R, Stüber F, Wulf H, Meuser T. Change in anaesthetic practice for Caesarean section in Germany. Acta anaesthesiologica scandinavica. 2005;49(2):170-6.
20. Klasen J, Junger A, Hartmann B, Benson M, Jost A, Banzhaf A, et al. Differing incidences of relevant hypotension with combined spinal-epidural anesthesia and spinal anesthesia. Anesthesia & Analgesia. 2003;96(5):1491-5.
21. Mojica JL, Meléndez HJ, Bautista LE. The timing of intravenous crystalloid administration and incidence of cardiovascular side effects during spinal anesthesia: the results from a randomized controlled trial. Anesthesia & Analgesia. 2002;94(2):432-7.
22. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, et al. The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. Anesthesia & Analgesia. 2002;94(6):1521-9.
23. Brenck F, Hartmann B, Katzer C, Brüggemann D, Benson M, Röhrig R, et al. Hypotension after spinal anesthesia for cesarean section: identification of risk factors using an anesthesia information management system. Journal of clinical monitoring and computing. 2009;23(2):85-92.
24. Hanss R, Bein B, Ledowski T, Lehmkuhl M, Ohnesorge H, Scherkl W, et al. Heart rate variability predicts severe hypotension after spinal anesthesia for elective cesarean delivery. Anesthesiology. 2005;102(6):1086-93.
25. Hanss R, Bein B, Francksen H, Scherkl W, Bauer M, Doerges V, et al. Heart rate variability-guided prophylactic treatment of severe hypotension after subarachnoid block for elective cesarean delivery. Anesthesiology. 2006;104(4):635-43.
26. Hanss R, Ohnesorge H, Kaufmann M, Gaupp R, Ledowski T, Steinbach M, et al. Changes in heart rate variability may reflect sympatholysis during spinal anaesthesia. Acta anaesthesiologica scandinavica. 2007;51(10):1297-304.
27. Singla D, Kathuria S, Singh A, Kaul T, Gupta S. Risk factors for development of early hypotension during spinal anaesthesia. Journal of Anaesthesiology Clinical Pharmacology. 2006;22(4):387.
28. Abdul Sattar Narejo , Farida W, Mehboob W. A study to assess the quality of Spinal anesthesia and to observe Hemodynamic changes occurring During cesarean section with spinal Anesthesia, comparing 0.5% isobaric Bupivacaine and 0.75% hyperbaric Bupivacaine in same volume and Dose. Medical Channel. 2012;18(1):58-62.
29. Toptas M, Uzman S, Isitemiz I, Uludag T, Yanaral A, Bican G. A comparison of the effects of hyperbaric & isobaric bupivacaine spinal anesthesia on hemodynamics and heart rate variability.
30. Luck J, Fettes P, Wildsmith J. Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. British Journal of Anaesthesia. 2008;101(5):705-10.

