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Dose response characteristics of intrathecal hyperbaric bupivacaine (0.5%) by using sequential combined spinal epidural anaesthesia for orthopaedic surgeries of lower limb

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ABSTRACT

Combined spinal epidural anaesthesia (CSEA) technique provides advantages of both subarachnoid block and epidural block. In the present study primary objective was to compare sensory level and degree of motor block achieved with initial intrathecal dose at the end of 10 minutes with peak sensory level achieved with initial intrathecal dose of 7.5 mg and 10 mg hyperbaric 0.5 % bupivacaine respectively whereas secondary objective was to compare adverse events in orthopaedic surgery patients. Sixty patients were included in this randomized controlled study conducted between April 2016 and December 2016. Group A and Group B patients received sequential CSEA with 7.5 mg and 10 mg of 0.5 % hyperbaric bupivacaine respectively intrathecally. Primary outcome measures were mean time required to achieve T 10 levels, mean onset on motor block, mean time to give top up , total number of top ups required whereas secondary outcome measure were adverse events. Comparison of quantitative and qualitative variables between groups was done using unpaired student's "t" test and chi-square test respectively. Sequential CSEA with Group B showed rapid onset, more profound and long lasting block with less number of epidural top ups but more number of adverse events of hypotension. While sequential CSEA with Group A showed requirement of frequent number of top ups to maintain desired anaesthesia but more stability in haemodynamic with less adverse events of hypotension and bradycardia. Sequential CSEA with low dose 7.5 mg bupivacaine is better choice than 10 mg bupivacaine as initial intrathecal dose by using CSEA.

INTRODUCTION

There are various techniques for central neuraxial blockade. Subarachnoid block is relatively simple technique that requires a small dose of local anaesthetic to provide an intense and reliable block with virtually no systemic toxicity, but it has drawbacks such as extensive block, fixed duration of anaesthesia and precipitous hypotension.[1] Epidural block with catheter gives a better control of level of anaesthesia and can be used to extend the duration of anaesthesia; also, it can provide excellent post-operative pain relief with the help of opioids and local anaesthetic agents. However, it has drawbacks of requiring large amount of local anaesthetic, slower onset of action and patchy anaesthesia.[2]

Combined spinal epidural anaesthesia (CSEA) technique provides advantages of both subarachnoid block and epidural block particularly in obstetric and orthopaedic patients. It provides better surgical anaesthesia as well as lower risk of hypotension. The sequential CSEA is now used in elderly high risk patients for orthopaedic surgeries with encouraging result. It has shown the advantages in American society of anaesthesiologist (ASA) grade III-IV, elderly patients, low cardiac output state patients and in high risks patients where avoidance of sudden changes in haemodynamics is of paramount importance.[3] *In the present study primary objective was to* compare sensory level and degree of motor block achieved with initial intrathecal dose at the end of 10 minutes with peak sensory level achieved with initial intrathecal dose of 7.5mg and 10 mg hyperbaric 0.5 % bupivacaine respectively *whereas secondary objective was to compare adverse events* in orthopaedic surgery

patients above 60 years age.

MATERIAL AND METHODS

This randomized double-blind controlled study was conducted between April 2016 and December 2016. After scientific advisory committee and institutional ethics committee approval, written informed consent was obtained from all patients. Patients aged > 60 years of either sex scheduled for planned orthopaedic surgeries of lower limb at Poona Hospital and Research Centre, Pune and ASA grade I,II, and III were included in the study. Patients with known hypersensitivity to local anaesthetics, contraindications for central neuraxial blockade and who refused to participate *were excluded from study.*

Out of the 65 patients assessed for eligibility, after exclusion 60 patients were randomly divided into two equal groups of 30 each, using computer generated randomization code (Fig 1). Group A patients received sequential CSEA with 1.5 cc of 0.5 % hyperbaric bupivacaine i.e. (7.5mg of bupivacaine) intrathecally whereas Group B patients received sequential CSEA with 2cc of 0.5 % hyperbaric bupivacaine i.e. (10mg bupivacaine) intrathecally. *The randomization code was provided to operation theatre nurse who prepared study medication (*1.5 cc of 0.5 % hyperbaric bupivacaine or 2cc of 0.5 % hyperbaric bupivacaine) *under supervision of senior anesthesiologist. Researcher and patients were blind as to group assignment.*

Pre-anesthesia checkup was done one day prior to surgery. The patients were evaluated for any systemic diseases and laboratory investigations were recorded .Details of the procedure was explained to the patients. *In operation theatre (OT), adequate IV access was confirmed. Standard monitors were attached. Noninvasive blood pressure, pulse-oximeter, electrocardiogram, end tidal CO_2 ($ET CO_2$) were monitored after intubation.*

Patient was given sitting position. With all aseptic precautions local infiltration with 2cc of 2 % lignocaine was given in L_2-L3 intervertebral space. Tract was made with 20 gauge needle. Epidural space was identified by using 18 gauge Tuohy's needle. Epidural catheter was inserted and kept at 4 cm in epidural space. A 2 % lignocaine hydrochloride with adrenaline (3cc) was given as a test dose when there was no aspiration of blood and CSF. Subarachnoid block was given by midline approach in L_3-L_4 intervertebral space by using 25 gauge spinal needle. A quantity of1.5 cc and 2cc of 0.5 % bupivacaine hyperbaric was given over 30 seconds for Group A and Group B patients respectively. Patient was then placed in supine position.

If the desired spinal level of T_{10} was not achieved after 10 minutes of subarachnoid block, then top up dose with isobaric 0.5 % bupivacaine according to unblocked segment was given through epidural catheter. If the spinal level receded by two segments, then top up through epidural catheter was given. Sensory block was evaluated by 23 gauge hypodermic needle bilaterally after the end of injection after every 2 minutes till level stabilized for T_{10} level and time was recorded required for achieving T_{10} level. Modified Bromage scale was used to assess motor blockade as follows:

Bromage 0:- Free movement of limb at hip, knee and ankle joint

Bromage 1:- Free movement of limb at knee and ankle joints.

Bromage 2:- Free movement of limb at ankle joints.

Bromage 3:- No movement of limb at hip, knee and ankle joints.

Data were recorded for time required achieving sensory blockade up to T10 after intrathecal dose of bupivacaine, peak sensory level achieved with intrathecal dose of bupivacaine, time to give epidural top up after level receded below T10, modified Bromage score of motor block after initial dose of bupivacaine, maximum modified Bromage score, total dose of epidural initial to get T 10 level, total dose of intraoperative epidural top up, incidence of adverse event, and supplementation of intra operative analgesia and requirement of general anaesthesia.

Primary outcome measures were mean time required to achieve T 10 levels, mean onset of motor block, mean time to give top up , total number of top ups required whereas secondary outcome measure were adverse events. On the basis of previously published study, [4] a sample size of 27 patients in each group was calculated by a formula[5] with 80 % power and 5 % probability of Type I error to reject null hypothesis.

Data collected were entered in the Excel 2007 and analysis of data was done using Statistical Package for Social Sciences (SPSS) version 20, IBM, USA. Continuous variables were summarized by mean, and standard deviation whereas categorical variables were summarized by using frequencies and percentages. The comparison of quantitative variables between the groups such as mean age, mean weight, mean duration of surgery, mean time required achieving T10 levels, mean onset of motor block, mean modified Bromage scale, mean maximum bromage scale and mean time to give top up was done using unpaired student's “t” test, whereas comparison of qualitative variables such as gender , ASA grade ,adverse events, proportion of cases with total number of top ups and peak sensory levels by using chi-square test or Fisher's exact test . The confidence limit for significance was fixed at 95% level with p-value < 0.05.

RESULTS

The present research was randomized controlled study between two dosages of 0.5% hyperbaric bupivacaine used in CSEA in orthopaedic surgeries of lower limbs above 60 years age group patients. The patients were randomly allocated to either of the two groups. Group A and Group B received sequential CSEA with 7.5mg i.e. 1.5 cc of 0.5% hyperbaric bupivacaine and 10mg i.e. 2 cc of 0.5% hyperbaric bupivacaine respectively as initial intrathecal dose.

As depicted in table 1, both groups were comparable with respect to mean age, sex distribution, mean weight, ASA physical status and mean duration of surgery. As shown in table 2, type of surgeries in both groups were comparable. As shown in table 3, mean time required to achieve T10 was significantly more in Group A as compared to Group B. There was no statistically significant difference in sensory levels achieved at 10 minutes after initial intrathecal dose. T10 was achieved in all 30/30 patients in Group B whereas 3/30 (10.0%) patients in Group A could achieve only T12 level at the end of 10 minutes and required supplementation with epidural top ups. There was no statistically significant difference in peak sensory levels achieved, mean modified Bromage scale at 10 minutes after initial intrathecal dose. There was no statistically significant difference in mean time taken to give top up of epidural anesthesia, total number of top ups required, mean top up

Table 1 : Demographic profile

Demographic characteristic	Group A (N = 30)	Group B (N = 30)	p value
Mean age in years (SD)	68.13(± 4.58)	67.07(± 4.51)	0.370
Gender, no (%) Male Female	 18(60.0) 12(40.0)	 20(66.7) 10(33.3)	0.763
Mean weight in kg (SD)	58.97± (4.94)	57.30±(5.21)	0.207
ASA Grade (%) I II III	 14(46.7) 9(30.0) 7 (23.3)	 11(36.7) 12(40.0) 7(23.3)	0.944
Mean Duration of surgery in min (SD)	131.23 ± 14.40	131.40± 15.75	0.965

Table 2 : Types of surgeries

Types of surgeries	Group A (N=30)		Group B (N=30)	
	No.	%	No.	%
T-F for external fixation	4	13.3	4	13.3
Shaft femur for open reduction and internal fixation	3	10.0	3	10.0
Open reduction and internal fixation tibial condyle	3	10.0	3	10.0
Proximal femoral nailing	4	13.3	4	13.3
Dynamic hip screw	4	13.3	4	13.3
Ilizaros external fixation	2	6.7	2	6.7
Femur interlock	2	6.7	2	6.7
Open reduction and internal fixation For supracondylar femur	3	10.0	3	10.0
Tibia Interlock	3	10.0	3	10.0
V nail For Tibia	2	6.7	2	6.7

required, total dose of bupivacaine required for top up intra-operatively, mean dose bupivacaine required, after initial levels were achieved between the two groups. Percentage of patients who had bradycardia was significantly more in Group B than Group A.

DISCUSSION

In the present study, we compared low dose (7.5 mg) and (10mg) of hyperbaric bupivacaine for spinal anesthesia in sequential combined spinal epidural anesthesia technique.

Median peak sensory level in both groups was T8, in Group B (T6 to T9) and in Group A (T6 to T10). This kind of high median peaks sensory level might be due to old age group patients in our study. Bhattacharya D. et al. [3] in 2007, using 5mg of hyperbaric bupivacaine with 20 ugm of fentanyl in sequential CSE technique in high risk geriatric patients age group 60-85 years reported median sensory level of T10 (T6-S5) . This is comparable to our study.

In the present study mean time required to achieve T10 was significantly more (8.43 minutes) in group A as compared to 4.37 minutes in Group B.

Table 3 : Comparison of outcome variables

Variable	Group A (n= 30)	Group B (n = 30)	P value
Mean time required to achieve T 10 in minutes(SD)	8.43 (± 2.56)	4.37 (± 1.27)	0.001
Sensory levels at 10 minutes after initial intrathecal dose (%)			
T 8	2(6.7)	5(16.7)	0.796
T 9	10(33.3)	9(30.0)	
T 10	15(50.0)	16(53.3)	
T 12	3(10.0)	0(0.0)	
Peak sensory level achieved after initial intrathecal dose (%)			
T 6	1(3.3)	5(16.7)	0.085
T 7	6(20.0)	6(20.0)	
T 8	17(56.7)	17(56.7)	
T 9	3(10.0)	2(6.6)	
T 10	3(10.0)	0(0.0)	
Mean modified Bromage scale at the end of 10 minutes(SD)	2.47 (± 0.51)	2.47 (± 0.50)	0.760
Mean time in minutes to give top up of epidural anaesthesia after initial level achieved(SD)	95.6 (± 8.22)	100.3 (± 10.81)	0.063
Total intraoperative top ups required (%)			
0	15(50.0)	20(66.67)	
1	8(26.67)	6(20.0)	0.075
2	3(10.0)	4(13.33)	
3	4(13.33)	0(0.0)	
Mean top up required (SD)	1.73 (± 0.88)	1.40 (± 0.52)	0.126
Total dose in mgm of bupivacaine required for top up (%)			
0	15(50.0)	20(66.67)	0.075
15	8(26.67)	6(20.0)	
30	3(10.0)	4(13.33)	
45	4(13.33)	0(0.0)	
Mean dose in mgm of bupivacaine required (SD)	26.00 (±13.26)	21.00 (± 7.75)	0.126
Adverse event Bradycardia (%)	1(3.3)	6(20.0)	0.044

While comparing motor blockade in groups, we found modified Bromage score of grade III was achieved in both the groups. Our findings of motor blockade were similar to the study conducted by Bhattacharya D et al. [3] and Hamdani GA et al. [1] They reported Bromage score of Grade III in all their patients even with 5 mg of spinal dose along with epidural top up. Hamdani GA. et al. [2] concluded in their study that all patients in sequential group achieved Bromage III motor blockade. Study conducted by Gupta P.et al.[6] between sequential CSE and epidural anesthesia reported that all patients in sequential group achieved 100 % motor blockade of Bromage III as compared to 70 % in epidural Group.

Hamdani GA et al. [1] who gave sequential CSEA to high risk geriatric patients for elective orthopaedic surgeries with 1cc of

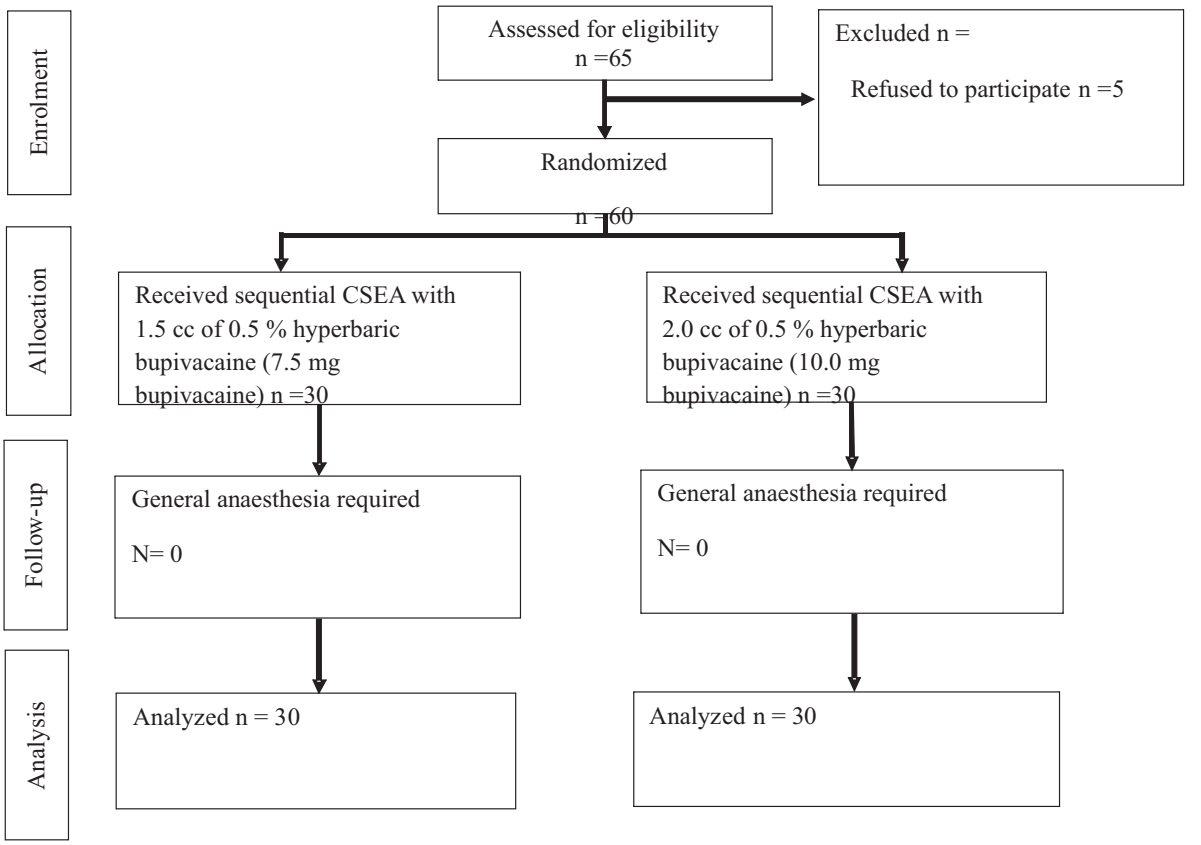

Fig. 1 : CONSORT Diagram

0.75% hyperbaric bupivacaine as initial spinal anaesthesia reported that they required to give top up to all patients to reach T10 level whereas in the present study only 3/30 (10.0%) patient in Group A required top up. In a study conducted by Bhattacharya D. et. al. [3] epidural top up of 25mg of 0.5 % bupivacaine was given to all patients after 90 to 120 minutes of spinal anesthesia to extend intraoperative anesthesia. In our study, we had given epidural top up after two segment regression. This was to avoid intraoperative higher sensory level with its haemodynamic disturbances and to maintain spinal level to T10. In our study the mean time required to give first top up after initial level achieved was 100.3±10.81 minutes and 95.60±08.22 minutes for Group B and Group A respectively. The average top up of epidural required intraoperatively was more in Group A (1.73) compared to Group B (1.4) also the average bupivacaine dose required for top up was 26 mg in Group A and 21 mg in Group B. Our results are comparable to the study conducted by Hamdani GA et al, [1] and Bhattacharya D et al. [3] They used 45 mg of bupivacaine in CSE and 10 mg of bupivacaine in SSS respectively. In the present study there was supplementation of epidural top ups intraoperative to maintain T10 level but there was no case of supplementation with analgesia or general anaesthesia in both the groups. This result was similar to study conducted by Bhattacharya D et al. [3] in which patients with SSS required supplementation with general anaesthesia while in SCSEA anaesthesia could be prolonged with epidural avoiding use of general anaesthesia.

Various studies reported safety of CSEA in elderly patients as well as in ASA III patients. [3,4,7] Studies conducted by Bhattacharya D.et al.[3], Marc Van De Velde et al. [8], Teoh WHL et al. [9], Fan SZ. et. al. [10], and Hamdani GA et al.[2] used low dose of hyperbaric bupivacaine initially to restrict acute high sympathetic blockade and thereby reducing the chances of hypotension. In a study conducted by Bhattacharya D. et. al [3], using sequential CSE technique reported that the incidence of hypotension was 10 %. Similarly Gupta P et al.[6] in 2002 , evaluated the cardiovascular effects of sequential CSE reported that only two patients had episodes of hypotension because of less extensive spinal block due to sequential CSE technique combined with slower onset of epidural block. This allows more time for compensatory mechanisms to be effective. Similarly in a study conducted by Hamdani GA et al.[1] by using sequential CSE technique reported that only four out of thirty patient developed hypotension and two out of them required double dose of ephedrine for treatment. These patients had T10 sensory level.

We had no failed blocks in both the groups. Similarly in a study conducted by Bhattacharya D et. al [3] reported no cases of failed block.

CONCLUSIONS:

Sequential CSEA with 2cc group bupivacaine (10mg) showed rapid onset, more profound and long lasting block with less number of epidural top ups but more number of adverse events of hypotension. While sequential CSEA with 1.5cc group bupivacaine(7.5 mg) showed requirement of frequent number of top ups to maintain desired anaesthesia but more stability in haemodynamic with less adverse events of hypotension and bradycardia. Sequential CSEA with low dose 7.5 mg bupivacaine is better choice than 10mg bupivacaine as initial intrathecal dose by using combined spinal epidural anaesthesia without

compromising quality of block, safety and without requiring any supplementation with analgesics or general anaesthesia.

Conflict of interest

Dr. Sudhir Patil, Dr. Sandeep Mutha, Dr. Deepak Phalgune and Dr. Ajit Gaikwad declare that they have no conflict of interest

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