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Original Research Article

Comparison of Intrathecal Hyperbaric 0.5% Bupivacaine, Isobaric 0.5% Levobupivacaine and Isobaric 0.75% Ropivacaine for Lower Abdominal Surgeries

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ABSTRACT

Background: Ropivacaine and levobupivacaine are local anesthetics with better safety profile as compared to bupivacaine regardless of the route of administration. This study was performed to compare the anesthetic efficacy and safety of three local anesthetic agents, Hyperbaric 0.5% Bupivacaine , Isobaric 0.75% Ropivacaine and Isobaric 0.5% Levobupivacaine , in patients undergoing elective lower abdominal surgeries under spinal anesthesia, using 3ml of each (0.5% hyperbaric bupivacaine = 15mg, 0.75% isobaric Ropivacaine 22.5mg, 0.5% Isobaric Levobupivacaine = 15mg).

Materials and Methods: 60 healthy consenting patients meeting our inclusion criteria were selected for the trial. They were randomly allotted into one of three groups of 20 each. The patients were randomized to receive Hyperbaric 0.5% Bupivacaine, Isobaric 0.75% Ropivacaine or Isobaric 0.5% Levobupivacaine respectively intrathecally. Intra-operative hemodynamic parameters, characteristics of sensory and motor nerve block and any adverse effects like such as hypotension, bradycardia, nausea, vomiting and shivering were evaluated.

Results: Hyperbaric Bupivacaine had a significantly faster onset of sensory block at T10 as compared to the both the other groups with isobaric solutions. The onset of Bromage1 motor block was similar in Group Bupivacaine and Levobupivacaine with a median onset of 3 and 2.5 min respectively, their onset was earlier than Group Ropivacaine and this result was statistically significant. (P Value < .05/3 ≈ .02). The onset of Bromage1 motor block was similar in Group Bupivacaine and Levobupivacaine with a median onset of 3 and 2.5 min respectively, their onset was earlier than Group Ropivacaine and this result was statistically significant. (P Value < .05/3 ≈ .02). The difference in onset of Bromage 3 Motor block was significant between all three groups with Group Bupivacaine having the shortest onset with a median time of 4 minutes followed by Group Levobupivacine with a median time of 5 min and them by Group Ropivacaine with a median time of 18 minutes. The duration of sensory and motor block was significantly shorter in Bupivacaine Group as compared to the ropivacaine and levobupivacaine groups

Conclusions: Hyperbaric bupivacaine produces a spinal block which has sensory block with an earlier onset of clinically significant sensory and motor block as compared to isobaric levobupivacaine or isobaric ropivacaine. This sensory and motor block produced by hyperbaric bupivacaine also recovers earlier. However this is also associated with a higher incidence of side effects. Hyperbaric thus seems to be an ideal choice for shorter duration surgeries at the expense of hemodynamic stability.
Key Words: intrathecal, bupivacaine, ropivacaine, levobupivacaine.

INTRODUCTION

Spinal anesthesia is a safe, reliable and inexpensive technique with the advantage of providing surgical anesthesia and prolonged post operative pain relief by using various adjuvant drugs along with local anesthetic agents. It blunts operative pain and autonomic, somatic and endocrine responses; providing a fast onset and effective sensory and motor blockade[1]

The impetus for the development of the newer stereoselective, single enantiomer amide local anaesthetic agents, ropivacaine and levobupivacaine, came from reports of fatal cardiac toxicity in pregnant women receiving epidural bupivacaine and etidocaine for Caesarean section

Both ropivacaine and levobupivacaine have been used successfully for spinal anaesthesia. Ropivacaine is well tolerated after intrathecal use, and was found to have a shorter duration of action than bupivacaine, making it a possible alternative to lidocaine for ambulatory surgery because of the low incidence of transient neurological symptoms (TNS).[2]

Bupivacaine (0.5%) is an amide type of local anesthetic, commonly employed in intrathecal injections for lower abdominal surgeries. Hyperbaric bupivacaine is popular in non-obstetric practice, attaining higher sensory levels of intrathecal anesthesia than equal doses of plain (glucose-free) bupivacaine when anesthesia is induced with the patient in the lateral position.[2-5] Plain bupivacaine, however, is unpredictable in its behavior, often spreading to cervical dermatomal levels. Large doses of intrathecal bupivacaine were associated with severe hypotension and delayed motor block recovery.[3]

Ropivacaine is a long acting amide local anesthetic agent,[4] less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibres, resulting in a relatively reduced motor blockade. Thus, ropivacaine has a greater degree of motor sensory differentiation, which could be useful when motor blockade is undesirable. The reduced lipophilicity is also associated with decreased potential for central nervous system toxicity and cardiotoxicity,[4] and when compared to bupivacaine, the lower lipid solubility of ropivacaine would predict that it is likely to produce a greater differential block of sensory and motor function than bupivacaine[5]

Levobupivacaine is an S (-)-enantiomer of the long acting local anesthetic bupivacaine[6] having less cardiotoxic and central nervous system effects in comparison with both R(+) bupivacaine and bupivacaine. Clinically, levobupivacaine is well tolerated in a variety of regional anesthesia techniques both after bolus administration and continuous postoperative infusion. Reports of toxicity with levobupivacaine are scarce and occasional toxic symptoms are usually reversible with minimal treatment with no fatal outcome. Yet, levobupivacaine has not entirely replaced bupivacaine in clinical practice.[7] Clinical studies show no significant differences in onset, duration and sensory block, but complete regression of sensory block takes longer.

The effects of bupivacaine, ropivacaine and levobupivacaine have been

compared in various clinical trials but to our knowledge there are very few studies comparing the efficacy of hyperbaric bupivacaine which is most commonly used with isobaric ropivacaine and isobaric levobupivacaine in lower abdominal surgeries.[8,9]

MATERIALS AND METHODS

After approval of the Institutional Ethical Committee and written informed consent, 60 patients of ASA physical status I-II between the ages of 18-70, scheduled for elective lower abdominal surgery under spinal anesthesia were prospectively enrolled in our randomized controlled trial. The trial was conducted from August 2012 to August 2013 in Father Muller Medical College, Mangalore. Patients with a contraindication for spinal anaesthesia, morbid obesity (BMI >40 kg/m2), neurological and musculoskeletal disease, with ASA class $\geq$ III, an allergy to amide local anesthetics or a significant history of drug / alcohol abuse were excluded from the study.

Patients were randomized to one of three groups of 20 members each using a sealed envelope technique. Patients in Group A received 15mg of 0.5% Hyperbaric Bupivacaine, Group B 15 mg of 0.5% Isobaric Levobupivacaine and Group C 22.5 mg of 0.75% Isobaric Ropivacaine. All 3-ml solutions were prepared in an adjacent room by an anaesthesiologist not involved in the subsequent evaluation of the study-patient.

Each patient was assessed in detail preoperatively and baseline readings of pulse rate, blood pressure and oxygen saturation were recorded. All patients received Inj. Ranitidine 50mg IV and Inj. Metoclopramide 10mg IV as premedication. Following arrival in the anesthetic room, I.V. access with 18G cannula was secured and an infusion of 500ml Ringer's lactate 10ml/kg over 15 minutes was commenced. Patients were monitored using a multi parameter device with pulse oximetry, ECG, and non invasive blood pressure.

Before the commencement of the procedure, patients were instructed on the method of sensory and motor assessments. The patient was then placed in left/ right lateral position, skin infiltrated with 2% lignocaine after painting and draping, midline lumbar puncture was performed at L3-L4 interspace with a 25G Quincke Babcock spinal needle and after confirming free and continuous flow of cerebrospinal fluid, the test drug was injected intrathecally @ 0.2ml/sec. After the injection of the drug the spinal needle was removed and the patient was placed supine.

Sensory and motor assessment was performed immediately after positioning supine. Sensory level blockade was measured by pin prick in the mid-clavicular line on both sides with a blunt 27 G needle, every minute until the block reached T6 dermatome. Thereafter the level was checked every 2 minutes, until the maximal height of sensory block was achieved. Onset of sensory blockade was defined as the time taken from the completion of the injection of study drug till the patient did not feel the pin prick at T10 level. Surgical incision was commenced when sensory level was at or above T6 dermatome. Time taken for maximum sensory blockade was defined as the time taken from the completion of the injection of the study drug to the maximum sensory blockade attained. Thereafter, the block was assessed until recovery of motor function and sensation at the L1 dermatome. Duration of sensory block; was taken as the time from the onset of sensory block to the time when the patient requires first dose of analgesia for post operative pain.

Quality of motor blockade in the lower limb was graded according to modified Bromage scale, [8] until the return of normal motor functions:

0- no motor blockade, able to lift the leg at the hip
1- Able to flex the knee and ankle but not able to lift the leg at the hip (hip block)
2- Able to move the foot only (hip and knee blocked)
3- Unable to move even the foot (hip, knee and ankle blocked).

The maximum Bromage score reached and onset of block defined as the time from spinal injection until Bromage 1 score were registered after drug's injection. Duration of motor blockade was taken as the time from injection till the patient attained slight motor recovery to < Bromage 3.

Heart rate and blood pressures were recorded before the procedure and immediately after the subarachnoid block, then at 2 minutes interval for 10 minutes, later at 5 minutes interval until 30 minutes and then after every 10 minutes till completion of the surgery, the last reading was taken 10 minutes after the procedure. Bradycardia defined as the pulse rate less than 60 beats/min which was treated with Inj. Atropine 0.6mg IV. Hypotension defined as a decrease in systolic blood pressure less than 100 mmHg or less than 20% from baseline was treated with incremental boluses of Inj. Mephentermine 6 mg IV as and when required**.**

Patients were administered supplementary oxygen through a face mask during the surgical procedure. Side effects such as nausea, vomiting, shivering and pruritus were checked and recorded. Nausea and vomiting if any were treated with Inj. Ondansetron 4 mg IV. Shivering was treated with Inj. Tramadol 75mg IV. Pruritus was treated with Inj. Avil 25mg IV.

Statistical Analysis

All statistical analyses were performed using Statistical software SPSS 15. Tables and graphs were generated using Microsoft Word and Excel. Onset of sensory block at T10, Onset of Bromage 1 motor block, Quality of motor block, duration of sensory blockade and duration of Bromage 3 were analyzed with Kruskal Wallis Test Statistics (Significance was defined as $P < 0.05$) and Mann-Whitney U Test Statistics(Significance was defined as $P < 0.05/3 \approx .02$)

RESULTS

The characteristics of the three groups were comparable in terms of age, height and weight of the patient.

TABLE 1: Demographic Details.

	GROUP					
	A		B		C	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
AGE	40.65	14.04	47.15	16.53	52.60	14.30
HEIGHT	161.20	8.77	163.00	10.34	161.25	8.94
WEIGHT	60.35	7.89	60.25	8.35	59.90	8.64
DURATION	62.50	19.16	52.00	18.74	71.50	18.14

TABLE 2: Kruskal Wallis Test Statistics.

	GROUP								
	A			B			C		
	Median	First Quartile	Third Quartile	Median	First Quartile	Third Quartile	Median	First Quartile	Third Quartile
Sensory Onset@T10(min)	1.50	1.25	2.00	2.50	1.75	2.50	2.50	1.50	3.25
Motor Onset to Bromage1(min)	3.00	2.25	3.50	2.50	2.00	2.50	5.00	4.50	5.50
Onset of Max Sensory(min)	4.50	4.25	5.25	5.50	4.25	6.00	5.25	4.00	6.00
Onset of Bromage 3(min)	4.00	3.50	4.75	4.75	4.50	5.00	18.00	14.00	22.00
Duration of Sensory (Hrs)	3.50	3.25	4.00	4.50	3.75	4.50	4.50	3.50	5.50
Duration of Bromage 3(Hrs)	3.50	3.00	3.50	4.00	3.50	4.50	3.25	0	4.00

As per Kruskal Wallis Test Statistics (Table 2) **t**here is a significant difference among onset of sensory block at T10, onset of Bromage 1 motor block, onset of Bromage 3 motor block, duration of sensory blockade and duration of Bromage 3 motor block between the three treatment groups($P < 0.05$). But there exists no significant difference between the three groups with respect to maximum sensory level attained.

TABLE 3: Post Hoc: Mann-Whitney U Test Statistics.

PAIRED COMPARISION		Sensory Onset @T10	Motor Onset Bromage1	Motor Onset Bromage 3	Duration of Sensory	Duration of Bromage 3
A – B	Z	-2.830	-2.398	-2.538	-2.601	-3.023
	P VALUE*	.005	.020	.012	.010	.003
A – C	Z	-2.812	-4.697	-5.355	-2.573	-.583
	P VALUE*	.005	< 0.001	< 0.001	.010	.583
B – C	Z	-.786	-5.422	-5.361	-.677	-2.751
	P VALUE*	.445	< 0.001	< 0.001	.512	.006

(*P Value < .05/3 i.e. ≈ .02)

Median onset of sensory block at T10 dermatome in Group A was 1.5 min (interquartile range 1.25 – 2 min), median onset in Group B was 2.5 minutes (interquartile range 1.75 – 2 min) and median onset group C was 2.5 minutes (interquartile range 1.5 – 3.25 min). There is a significant difference between the Groups A and B, also between Group A and C with respect to onset of sensory block. However there is no significant difference between Group B and C. (P Value < .05/3 i.e. ≈ .02)

Median onset of Bromage 1 motor block in Group A was 3 minutes (interquartile range 2.25 – 3 min), median onset in Group B was 2.5 minutes (inter quartile range 2 -2.5 min) and in Group C was 5 minutes (interquartile range 4.5 – 5.5minutes).There is a significant difference between Group B and Group C, also between Group A and C, However, there is no difference between Group A and Group B. (P Value < .05/3 i.e. ≈ .02)

Median onset of Bromage 3 motor block in Group A was 4.5 minutes (interquartile range 4.25 – 5.25 min), in Group B was 5.5 minutes (interquartile range 4.25 – 6 min) and in Group C was 5.25 minutes (interquartile range 4 – 6 min).There is a significant difference between Group A and B, Group A and C and Group B and C. (P Value < .05/3 i.e. ≈ .02).

Median Duration of Sensory Block (Hrs) was 3.5 hours (interquartile range 3.25 – 4 hours), in Group B was 4.5 hours (interquartile range 3.75 – 4.5 hours) and in Group C was 4.5 hours (interquartile range 3.5 hours - 5.5 hours). There is a significant difference between Group A and B, Group b and C but no difference between Group A and C.

Median Duration of Bromage 3 motor Block (Hrs) in Group A was 3.5 hours (interquartile range 3 – 3.5 hours), in Group B was 4 hours (interquartile range 3.5 – 4.5 hours) and in Group C was 3.25 hours (interquartile range 0 - 4 hours). There is a significant difference between Group A and B, Group A and C but no difference between Group B and C.

Only 2 patients in Group A (10%) had bradycardia requiring IV Atropine whereas no patients in the other groups had nausea. 2 patients in Group A (10%) and 1 patient in Group C(5%) had nausea. 11 patients in Group A (55%) whereas 4 patients in Group B (20%) and none in Group C had hypotension requiring IV Mephentermine.

DISCUSSION

This study shows that the intrathecal administration of 15 mg hyperbaric bupivacaine, 15 mg isobaric ropivacaine or 22.5mg isobaric levobupivacaine was well tolerated and an adequate block for lower abdominal surgery was achieved in all groups.

It is now well established that, compared with plain solutions, the use of hyperbaric local anaesthetic solutions results not only in a more predictable cephalad spread, but also increases the duration of the clinically useful block (given by duration at the T10 dermatome), and leads to a more rapid regression of sensory block and recovery from motor block[10-13]

In our study Hyperbaric Bupivacaine had a faster onset of sensory block at T10 as compared to the both the other groups with isobaric solutions, however there was no difference between the onset of sensory block with Ropivacaine and Levobupivacaine which was in similar to findings of M. Mantouvalou et al.[1] We could not demonstrate any difference to onset to maximum sensory block height between the three groups in our study.

The onset of Bromage1 motor block was similar in Group Bupivacaine and Levobupivacaine with a median onset of 3 and 2.5 min respectively, their onset was earlier than Group Ropivacaine and this result was statistically significant. Mantouvalou et al[1] in their randomized trial comparing the anesthetic efficacy and safety of racemic bupivacaine and its two isomers: ropivacaine and levobupivacaine, in patients undergoing lower abdominal surgery also similarly demonstrated that the onset of motor block was significantly faster in the bupivacaine group compared with that in the ropivacaine group and almost the same of that in the levobupivacaine group ($P < 0.05$). He had however used isobaric solutions of all three drugs.

We found that the difference in onset of Bromage 3 Motor block was significant between all three groups with Group Bupivacaine having the shortest onset with a median time of 4 minutes followed by Group Levobupivacine with a median time of 5 min and them by Group Ropivacaine with a median time of 18 minutes. This difference in the onset of a dense motor block between hyperbaric bupivacaine and hypobaric levobupivacaine can be attributed to the difference in baricity, the significant difference between the first two groups and the ropivacaine group is due to the differential sensory blockade by ropivacaine, similar results were obtained in studies by Lacassie et al[8] and Mantouvalou et al.[1,2]

Jean-Marc Malinovsky[14] and colleagues conducted a trial studying the effects of volume and baricity of spinal bupivacaine on block onset, height, duration, and hemodynamics. They divided their patients into two groups receiving either isobaric bupivacaine or hyperbaric bupivacaine and demonstrated that time for regression of anesthesia to L2 and offset of motor block were longer with isobaric than with hyperbaric solutions of bupivacaine. Similar findings were also observed by other investigators.[15-17] Similarly in our study the duration of sensory and motor block was significantly shorter in Bupivacaine Group as compared to the ropivacaine and levobupivacaine groups. It was also noted that due to differential blockade by ropivacaine the motor block produced by ropivacaine was less intense and of a shorter duration as compared to levobupivacaine group but motor block if present was of a longer duration as compared to hyperbaric bupivacaine.

Patients in the hyperbaric bupivacaine group also had a greater incidence of adverse effects like nausea, bradycardia and hypotension as compared to

the other two groups. These results correlate well with those reported by other investigators.[10-12]

CONCLUSION

Hyperbaric bupivacaine produces a spinal block which has sensory block with an earlier onset of clinically significant sensory and motor block as compared to isobaric levobupivacaine or isobaric ropivacaine. This sensory and motor block produced by hyperbaric bupivacaine also recovers earlier. However this is also associated with a higher incidence of side effects. Hyperbaric thus seems to be an ideal choice for shorter duration surgeries at the expense of hemodynamic stability. For day care surgeries a hyperbaric solution ropivacaine which is not yet commercially available may be an attractive alternative. However, the currently available isobaric ropivacaine is not suitable due to its prolonged duration of action.

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