Type of Article: Original Research Article

HYPERBARIC LEVOBUPIVACAINE VERSUS HYPERBARIC ROPIVACAINE IN SPINAL ANAESTHESIA FOR LOWER LIMB SURGERIES: A RANDOMIZED CONTROL TRIAL

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Abstract

Background: The aim of the study was to compare the efficacy of intrathecally administered hyperbaric Ropivacaine 0.75% and hyperbaric Levobupivacaine 0.5% in surgeries of lower limb.

Material And Methods: After receiving approval from the Institutional Ethics committee and CTRI registration, 64 patients aged between 18-60 years of age with ASA grade I and II physical status, BMI<30 undergoing elective lower limb surgeries were randomly allocated to one of the two groups of 32 patients each. In Group A, patients were given Hyperbaric Ropivacaine 0.75% 3ml (22.5mg) intrathecally, while in Group B, Hyperbaric Levobupivacaine 0.5 % 3ml (15mg) were given intrathecally. A blinded observer assessed onset and duration of sensory block and motor block, peak height for sensory block, hemodynamic changes and any side effects or complications.

Results: Onset of sensory blockade was significantly early in group that received hyperbaric Ropivacaine as compared to the hyperbaric Levobupivacaine, although there was no significant difference in regards to onset of motor blockade amongst both the groups. Duration of sensory as well as motor blockade was found to be prolonged in the group that was administered hyperbaric Levobupivacaine. No remarkable difference amongst the two groups in terms of peak height of sensory block. No significant difference observed in terms of hypotension, bradycardia, shivering or post-op nausea and vomiting.

Conclusion: Hyperbaric Ropivacaine can be used for shorter duration, day care surgeries whereas Hyperbaric Levobupivacaine can be used for longer duration surgeries of lower limb.

Keywords: hyperbaric Ropivacaine, hyperbaric Levobupivacaine, motor blockade.

INTRODUCTION

The most extensively applied regional technique is spinal anaesthesia. Single injection spinal anaesthesia is most regularly employed for lower limb, lower abdominal, pelvic surgeries. Spinal anaesthesia results in either or combined form of sympathetic block, sensory block or motor block.[1]

Bupivacaine is widely used. It has rapid onset, long duration of action and good safety record but there have been reports of central nervous system and cardiovascular complications.[2]It belongs to the category of amino-amide. It is more soluble in lipids.

Ropivacaine in addition to Levobupivacaine are some of the newer local anaesthetic agents that have been introduced, which have a safer profile.[2]Levobupivacaine reversibly blocks the action potential transmission in sensory, motor and sympathetic nerve fibres by inhibiting the passage of sodium through voltage sensitive ion channels in the neuronal membrane.[3] Ropivacaine is a member of pipecoloxylidides. It reversibly blocks the sodium ion influx and thus, hinders the nerve impulse transmission.

Earlier hyperbaric solutions of Levobupivacaine and Ropivacaine were prepared in operating room.The disadvantage of preparing these hyperbaric solutions in operating room was that density of each newly prepared solution was different, so the results could not be reproduced reliably. But now their hyperbaric solutions are available in the market in concentration of 0.5% and 0.75% respectively each combined with 80 mg of dextrose.

In this study, we aim to compare the efficacy, onset and duration of sensory block and motor block, peak height for sensory block, hemodynamic changes and any Side effects or complication of two newly available hyperbaric preparations of Levobupivacaine and Ropivacaine in surgeries for lower limb.

MATERIALS AND METHODS

The present study was carried a tertiary care Hospital. After receiving approval from the Institutional Ethics Committee and CTRI registration, 64 patients aged between 18-60 years of age with ASA grade I and II physical status, BMI<30 undergoing elective lower limb surgeries were included in this study. Patients with contra-indication to Spinal anaesthesia, obesity (BMI>30kg/m2), any neuropathies, allergy or intolerance to Local Anaesthetics and patients who refused for procedure were excluded from this study.

Each patient was randomly allocated to one of the two groups of 32 patients each. In Group A, patients were given Hyperbaric Ropivacaine 0.75% 3ml (22.5mg) intrathecally, while in Group B, Hyperbaric Levobupivacaine 0.5 % 3ml (15mg) were given intrathecally. Drugs were loaded by the anaesthetist who did not participate in the observation.

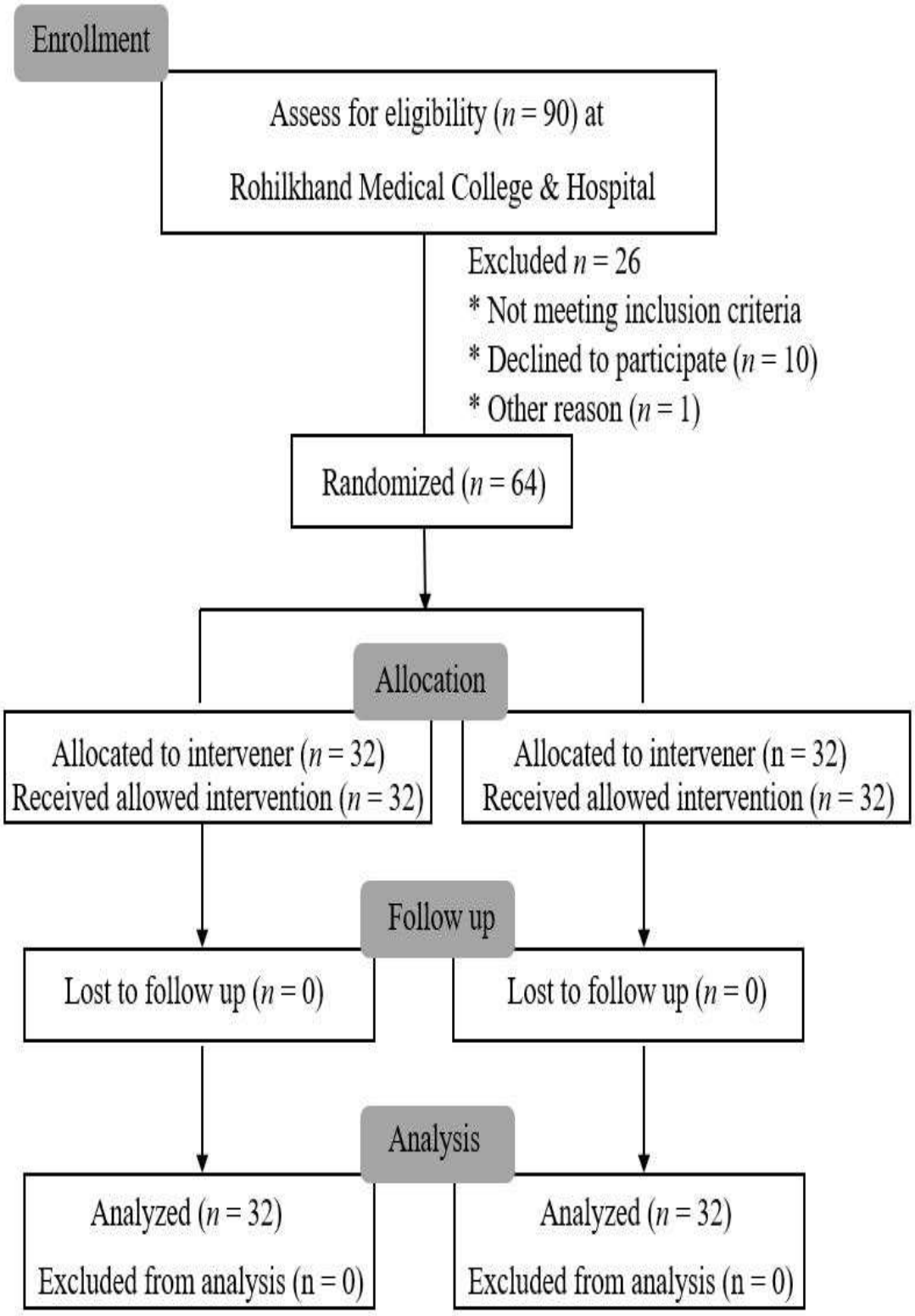
Evaluation of patient was carried out through history taking, clinical examination and routine laboratory investigations. All patients were explained about the procedure of spinal anaesthesia. They were kept nil per orally for 6 hours prior to procedure& Tab Ranitidine 150mg and Tab Alprazolam 0.25mg was given orally, the night before surgery. The multi-channel monitor was connected to the patient to display continuous ECG monitoring for Heart rate (HR), non-invasive arterial blood pressure and peripheral oxygen saturation. Baseline monitoring data was recorded. Procedure of Spinal Anaesthesia was conducted at L2-L3 interspace with patient sitting using a midline approach using 25G spinal needle. After execution of the spinal injection, patient was immediately made to lie supine with operating table horizontal.

Onset time of sensory block was assessed, as well as that of motor block after administration of spinal anaesthesia. The sensory level of the block was assessed in a caudal to cephalad direction, using loss to pin prick sensation, and the C5-C6 dermatome is used as an unblocked reference point. Evaluation of motor block was done using the Modified Bromage Scale.[4]

Grade	Criteria	Degree of block
0	Free movement of legs and feet	Nil (0%)
I	Knee flexion decrease but full flexion of feet and ankle	Partial (33%)
II	Unable to flex knees, but flexion at ankle and feet present	Almost complete (66%)
III	Unable to flex knee or ankle or move toes	Complete (100%)

Patient was considered ready for surgery when they had loss of pin prick sensation ≥ T10 with modified Bromage≥2. Evaluation of the motor block was put on hold until the end of the surgical procedure.

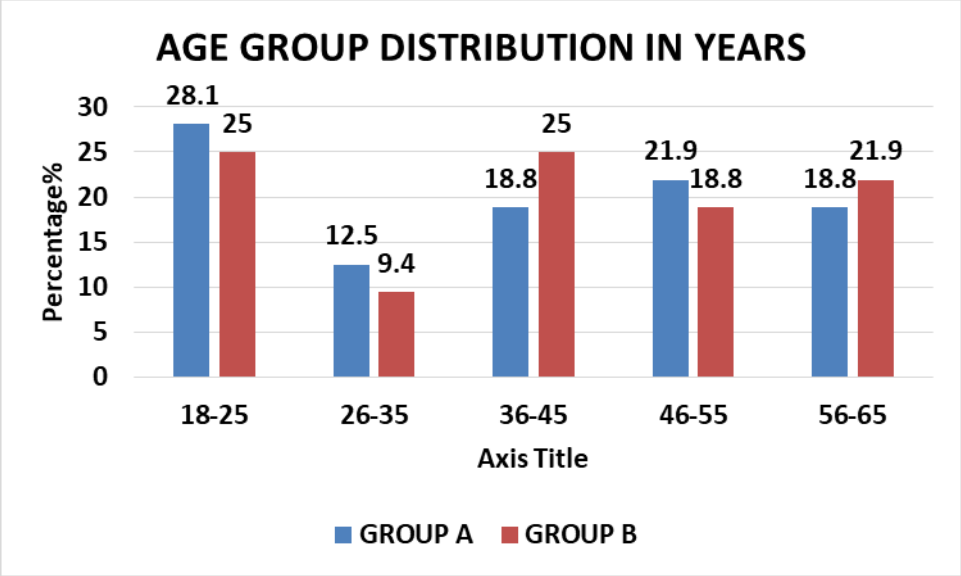
Assessment of Analgesia was done using *Numerical Rating scale.*[5]A. W.A. Crossley and R.P. Mahajan ShiveringScore[6] and Post-Operative Nausea Vomiting Impact Scale Score[7]was used to assess shivering and post-operative nausea and vomiting.

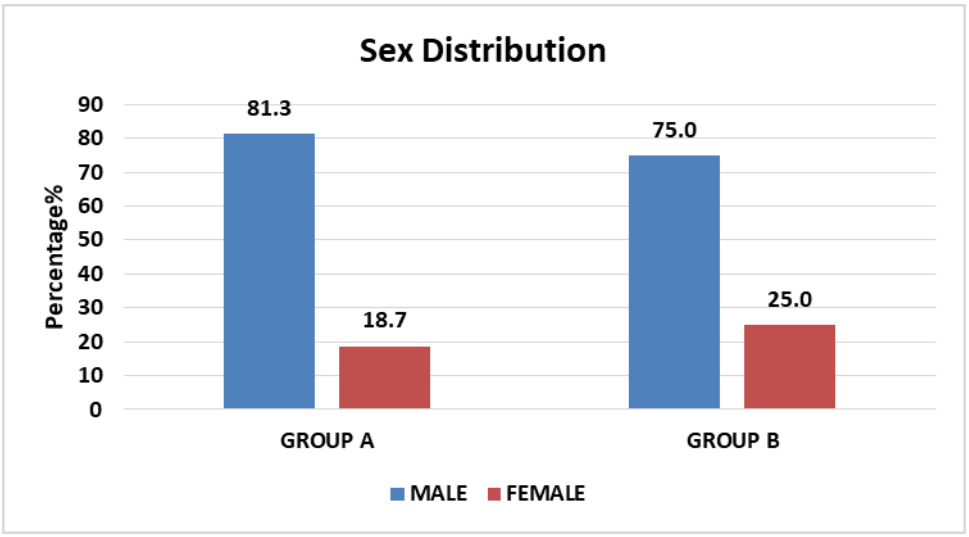


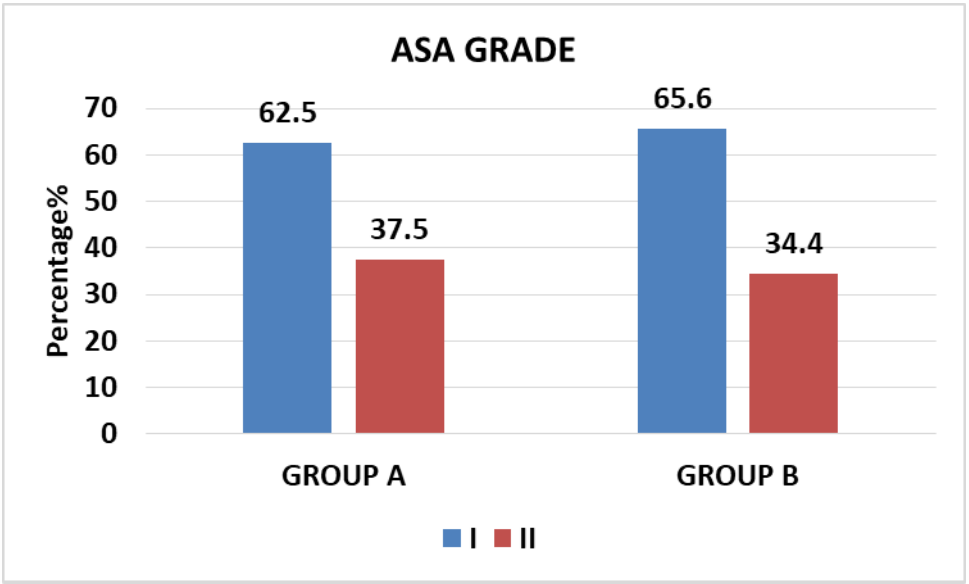
CONSORT FLOW DIAGRAM

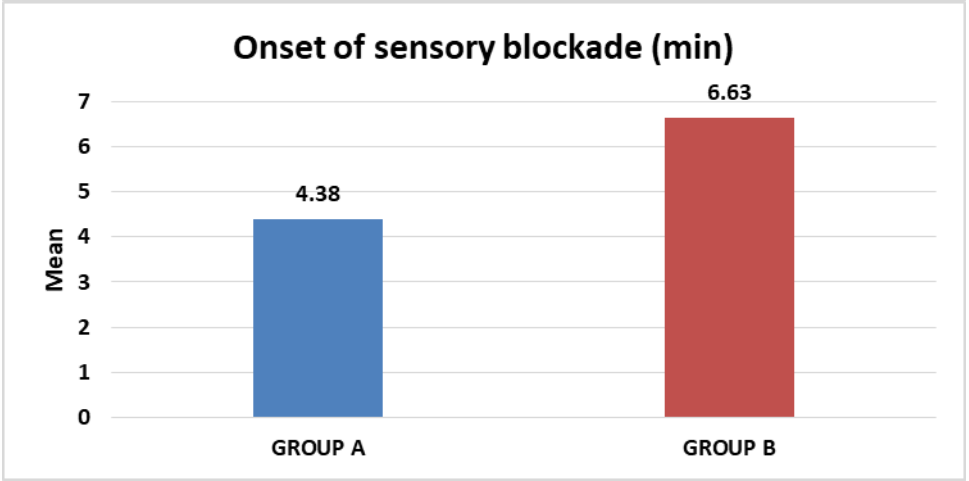
RESULTS

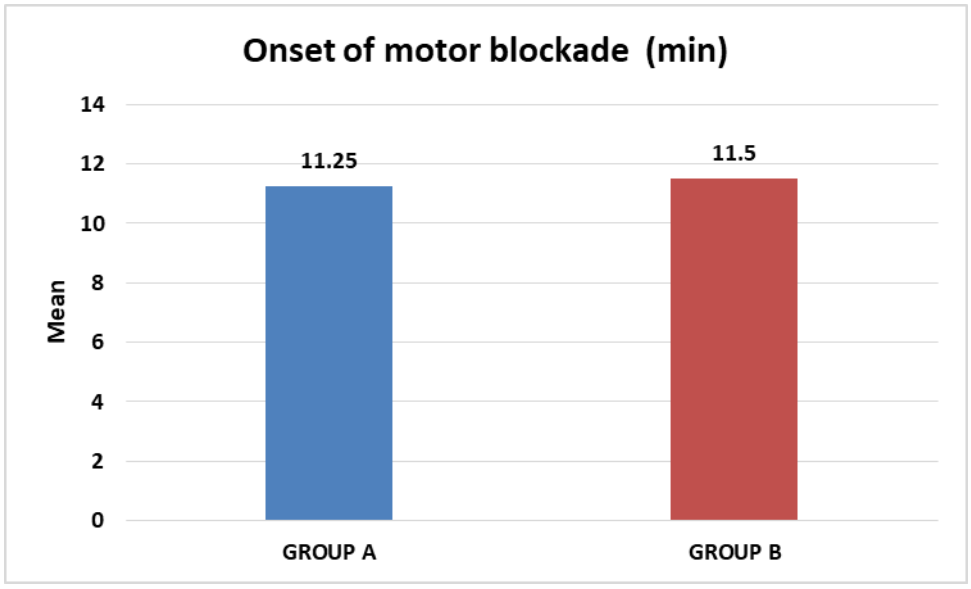
There was no significant difference in age, gender, ASA physical status among the two groups. Mean onset of sensory blockade (in min) in Group A was 4.38 ± 2.12 min and Group B was 6.63 ± 0.94 min. Mean onset of sensory blockade (in min) was more in Group B as compared to Group A and there was significant difference in mean onset of sensory blockade (in min) of patients in between Group A and Group B.Mean onset of motor blockade (in min) in Group A was 11.25 ± 1.78 min and Group B was 11.5 ± 1.16 min. There was no significant difference in mean onset of motor blockade (in min) of patients in between Group A and Group B. Mean duration of sensory blockade (in min) in Group A was 176.38 ± 32.78 min and Group B was 221.88 ± 43.79 min. Mean duration of sensory blockade (in min) was more in Group B as compared to Group A and there was significant difference in mean duration of sensory blockade (in min) of patients in between Group A and Group B. Mean duration of motor blockade (in min) in Group A was 152.53 ± 33.96 min and Group B was 202.44 ± 40.92 min. Mean duration of motor blockade (in min) was more in Group B as compared to Group A and there was significant difference in mean duration of motor blockade (in min) of patients in between Group A and Group B.

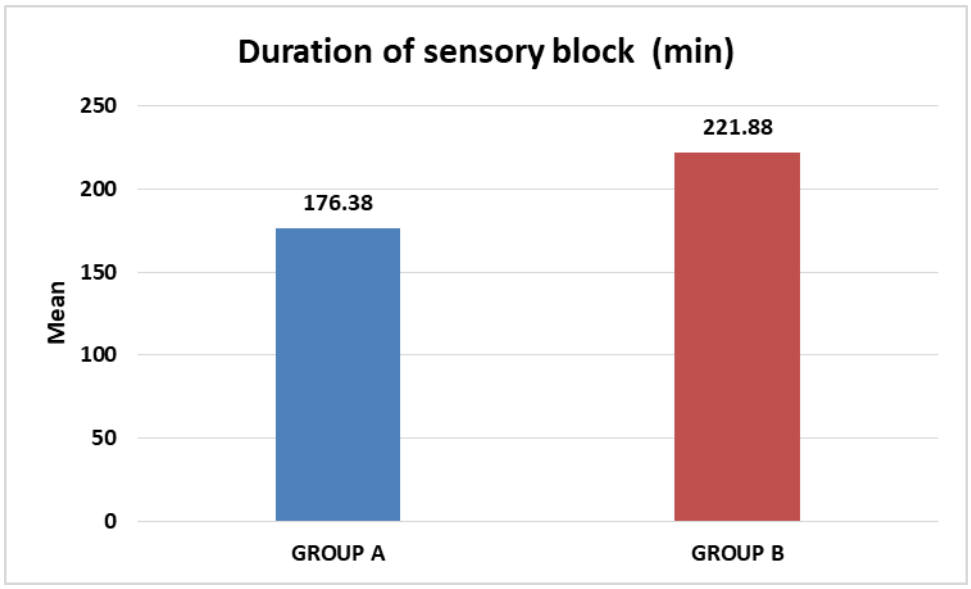


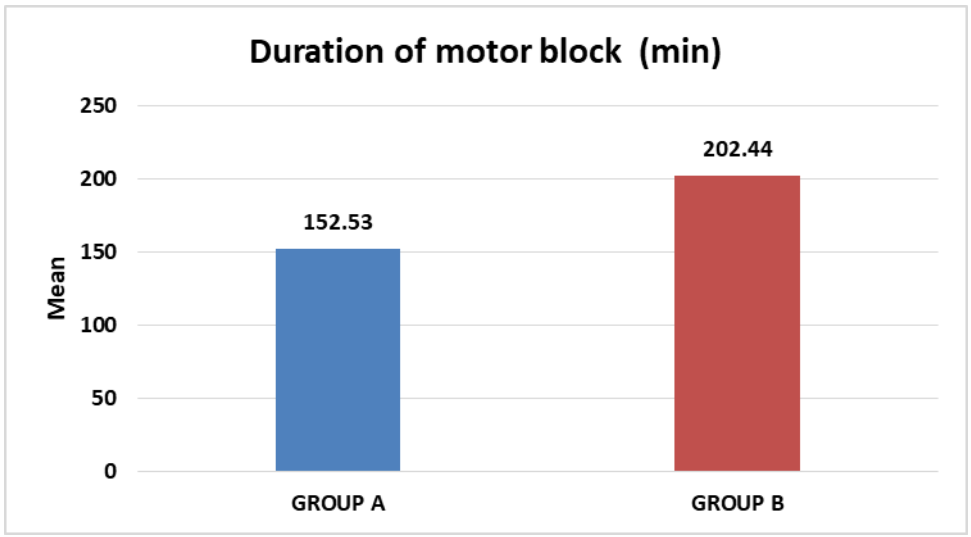

Sex Distribution
Percentage%
90
80
70
60
50
40
30
20
10
0
81.3
18.7
75.0
25.0
GROUP A
GROUP B
MALE
FEMALE

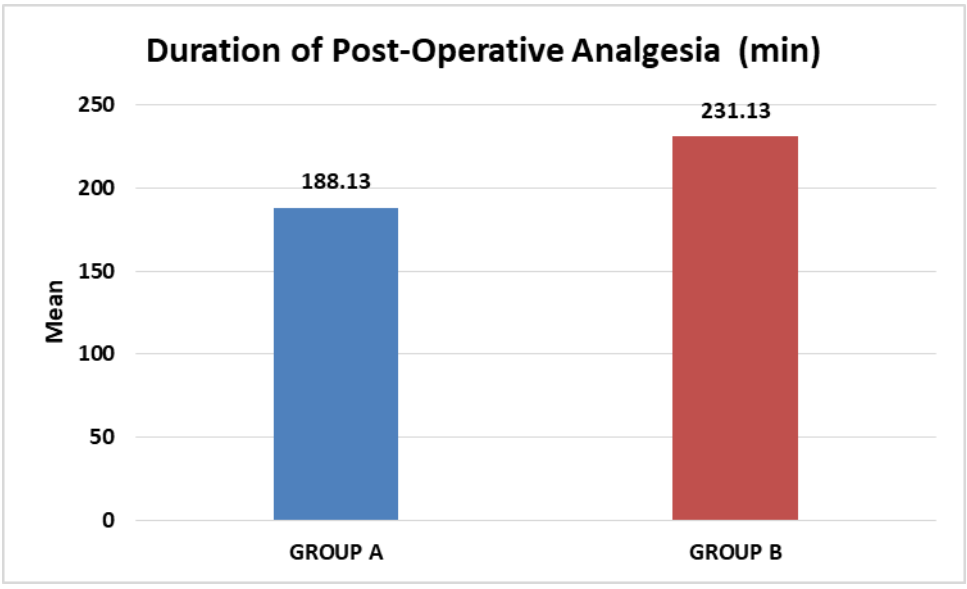

ASA GRADE
Percentage%
70
60
50
40
30
20
10
0
62.5
37.5
65.6
34.4
GROUP A
GROUP B
I
II

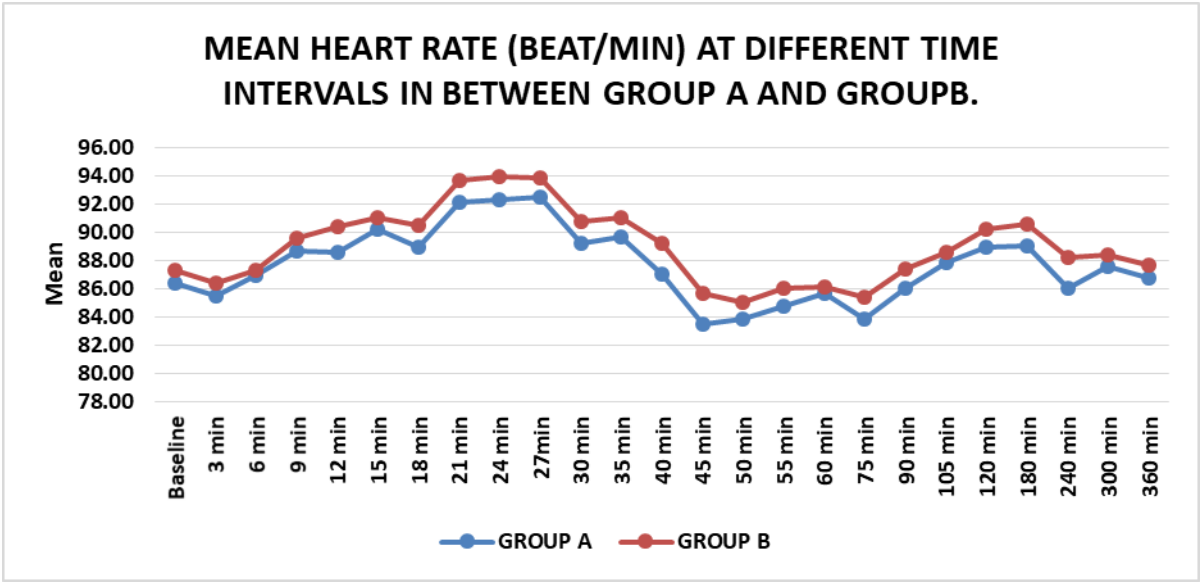

Onset of sensory blockade (min)
Mean
7
6
5
4
3
2
1
0
4.38
6.63
GROUP A
GROUP B

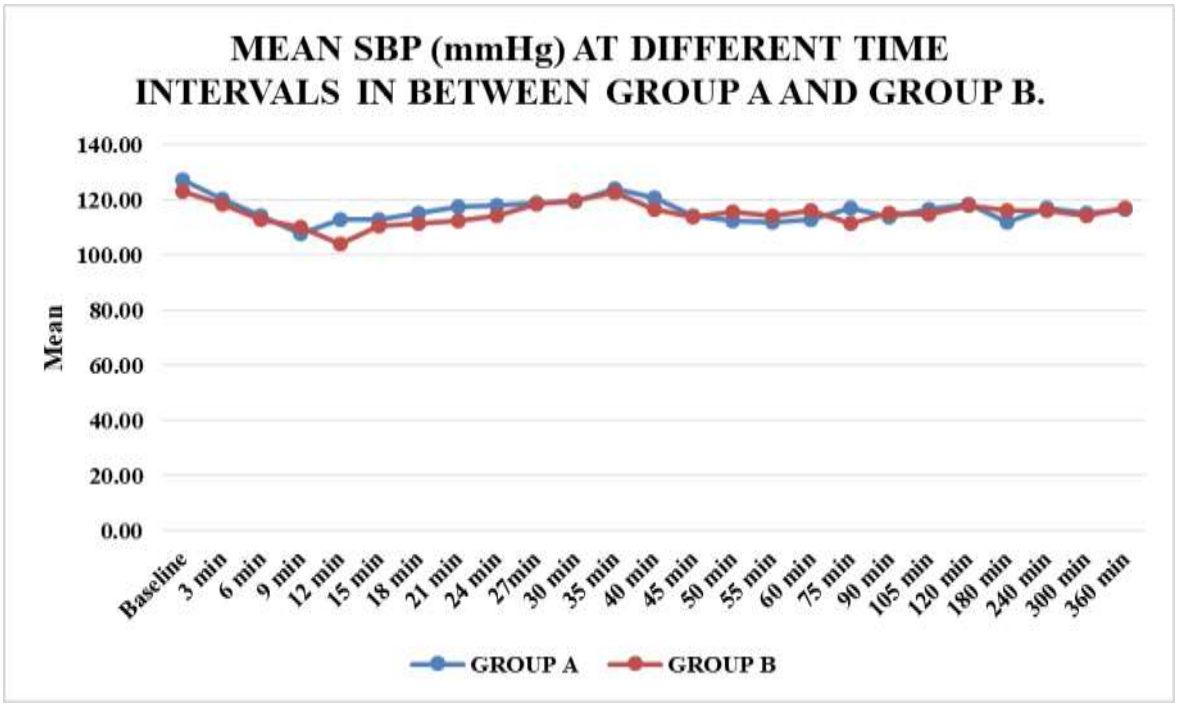

Onset of motor blockade (min)
Mean
14
12
10
8
6
4
2
0
11.25
11.5
GROUP A
GROUP B

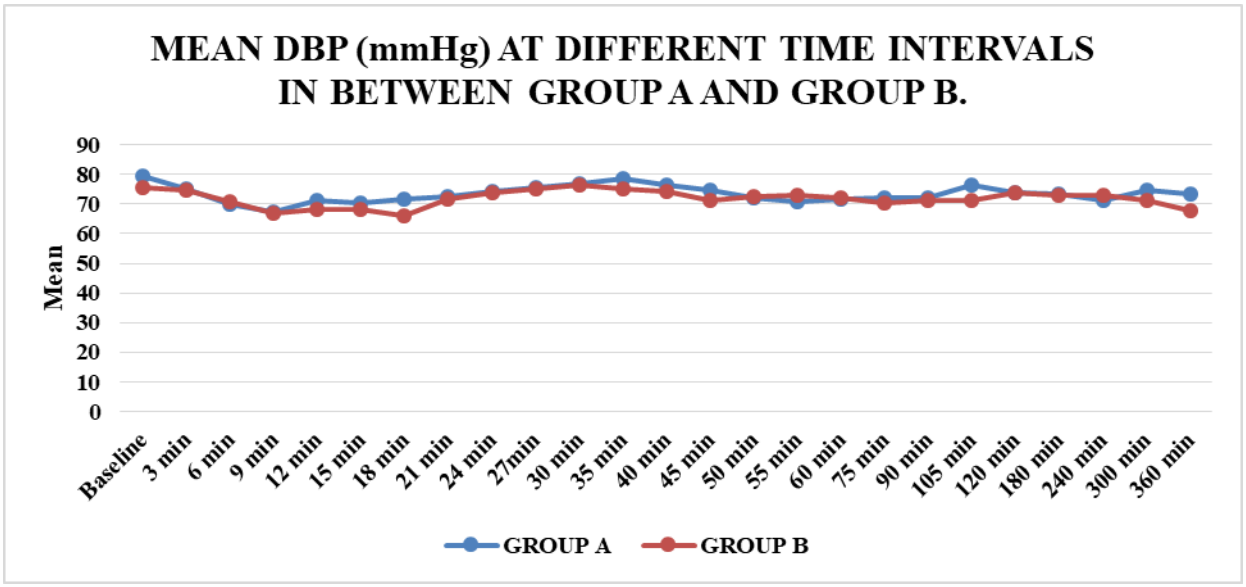

Duration of sensory block (min)
Mean
250
200
150
100
50
0
176.38
221.88
GROUP A
GROUP B

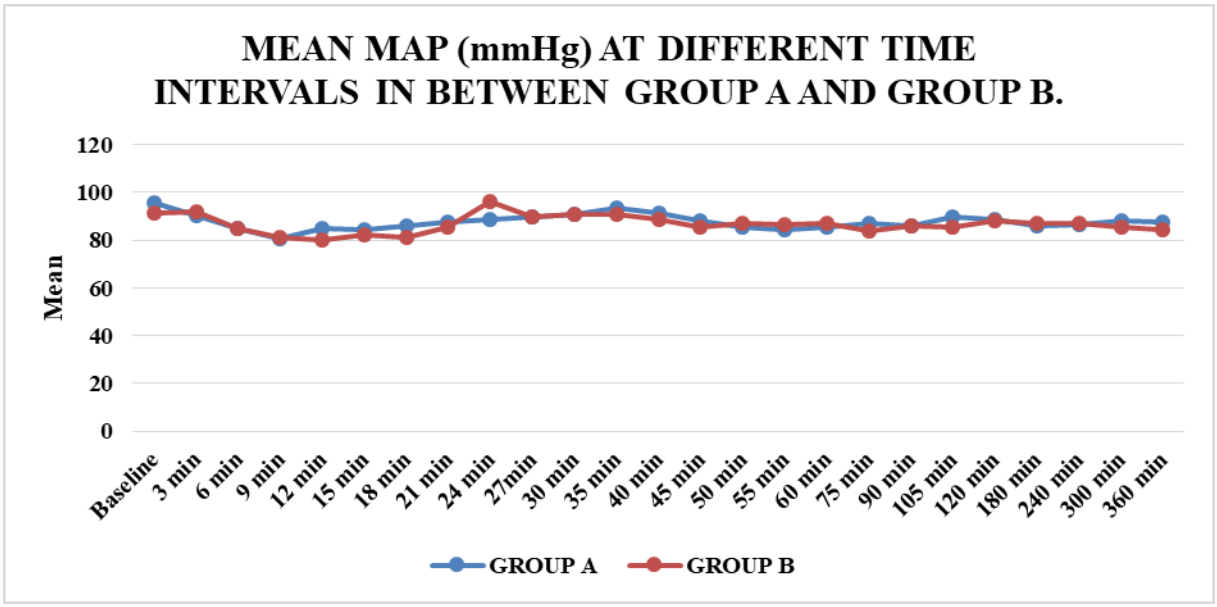

Duration of motor block (min)
Mean
250
200
150
100
50
0
152.53
202.44
GROUP A
GROUP B

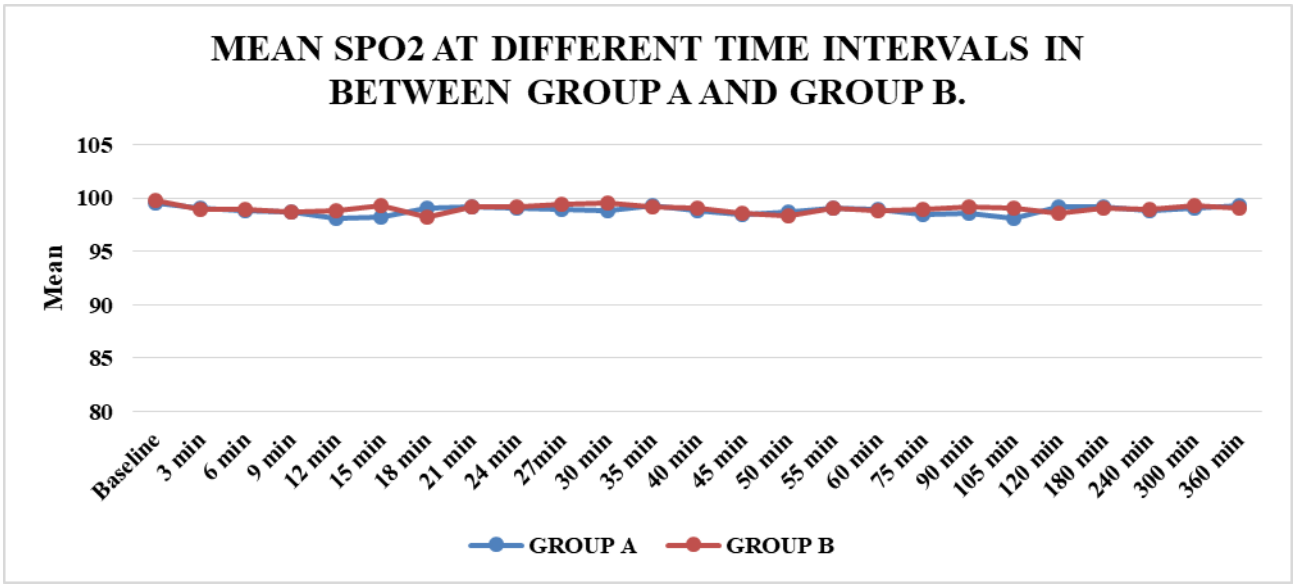

Duration of Post-Operative Analgesia (min)
Mean
250
200
150
100
50
0
188.13
231.13
GROUP A
GROUP B

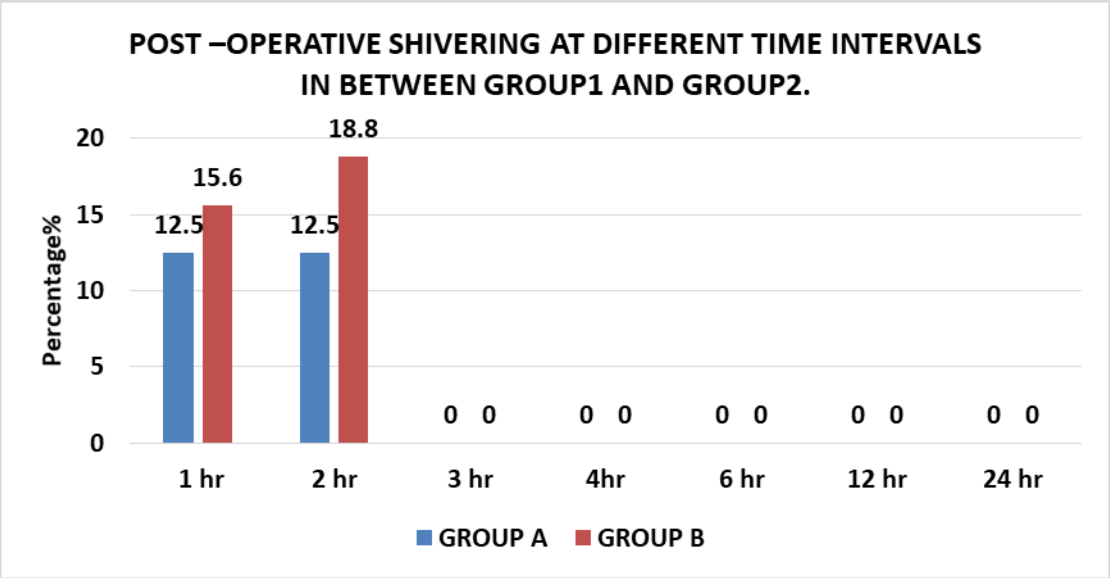

MEAN HEART RATE (BEAT/MIN) AT DIFFERENT TIME INTERVALS IN BETWEEN GROUP A AND GROUPB.
Mean
96.00
94.00
92.00
90.00
88.00
86.00
84.00
82.00
80.00
78.00
Baseline
3 min
6 min
9 min
12 min
15 min
18 min
21 min
24 min
27min
30 min
35 min
40 min
45 min
50 min
55 min
60 min
75 min
90 min
105 min
120 min
180 min
240 min
300 min
360 min
GROUP A
GROUP B

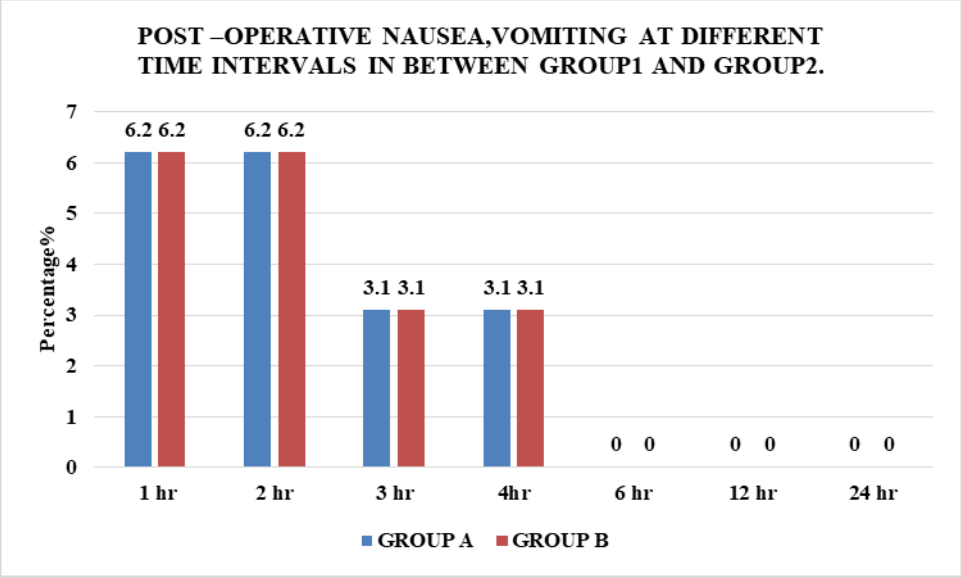

MEAN SBP (mmHg) AT DIFFERENT TIME INTERVALS IN BETWEEN GROUP A AND GROUP B.
Mean
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
Baseline
3 min
6 min
9 min
12 min
15 min
18 min
21 min
24 min
27min
30 min
35 min
40 min
45 min
50 min
55 min
60 min
75 min
90 min
105 min
120 min
180 min
240 min
300 min
360 min
GROUP A
GROUP B


MEAN DBP (mmHg) AT DIFFERENT TIME INTERVALS IN BETWEEN GROUP A AND GROUP B.
Mean
90
80
70
60
50
40
30
20
10
0
Baseline
3 min
6 min
9 min
12 min
15 min
18 min
21 min
24 min
27min
30 min
35 min
40 min
45 min
50 min
55 min
60 min
75 min
90 min
105 min
120 min
180 min
240 min
300 min
360 min
GROUP A
GROUP B


MEAN MAP (mmHg) AT DIFFERENT TIME INTERVALS IN BETWEEN GROUP A AND GROUP B.
Mean
120
100
80
60
40
20
0
Baseline
3 min
6 min
9 min
12 min
15 min
18 min
21 min
24 min
27min
30 min
35 min
40 min
45 min
50 min
55 min
60 min
75 min
90 min
105 min
120 min
180 min
240 min
300 min
360 min
GROUP A
GROUP B


MEAN SPO2 AT DIFFERENT TIME INTERVALS IN BETWEEN GROUP A AND GROUP B.
Mean
105
100
95
90
85
80
Baseline
3 min
6 min
9 min
12 min
15 min
18 min
21 min
24 min
27min
30 min
35 min
40 min
45 min
50 min
55 min
60 min
75 min
90 min
105 min
120 min
180 min
240 min
300 min
360 min
GROUP A
GROUP B





In our study out of 32 patients in Group A, peak height for sensory block T4 in 12.5% ,T6 in 81.3 % and T8 in 6.3 % out of 32 patients and in Group B, peak height for sensory block T4 in 9.4% ,T6 in 68.8 % and T8 in 21.9 % out of 32 patients .There was no significant difference in peak height for sensory block of patients in between Group A and Group B.

Mean duration of Post-Operative Analgesia(in min) in Group A was 188.13 ± 36.85 min and Group B was 231.13 ± 46.68 min, therefore, it was more in Group B as compared to Group A and there was significant difference in mean duration of Post-Operative Analgesia(in min) of patients in between Group A and Group B.

Haemodynamically, there was no significant difference observed between the two groups in terms of Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean Arterial pressure and SpO2. Similarly, there was no significant difference observed among the two groups in terms of post-operating shivering, post-operative nausea and vomiting.

DISCUSSION

The effect of spinal anaesthesia is majorly affected by the baricity of the drug.[1]Previously used isobaric solutions have now been replaced by hyperbaric solutions which are made by adding dextrose to the local anaesthetic agent and it settles to the dependent part, along gravity. The advantage of these hyperbaric solution is that firstly there is very low variations in motor as well as sensory block and secondly less chances of deviation of effect among different patients. Moreover, its spread can be altered by manipulating the operating table as required by the type of surgery.

Previous study conducted by Cappelleri et al[8] and Athar et al[9] have considered an equivalent and equipotent dose of Levobupivacaine versus Ropivacaine and have confirmed 1-1.5 equipotency ratio of Levobupivacaine to Ropivacaine.

All the patients in this study had BMI< 30, there was no difference statistically among the two groups interms of BMI, age, ASA grading and gender distribution.

The onset of sensory block in group Ropivacaine was significantly earlier when compared to group Levobupivacaine in this study.The study conducted by Cappelleri et al compared the use of 7.5mg of 0.5% hyperbaric Ropivacaine and 5mg or 7.5mg 0.5% of hyperbaric Levobupivacaine in patients posted for knee arthroscopy under unilateral spinal anaesthesia and found that the time to readiness for surgery was similar in all three groups.[8] The final density of the solution was less predictable as it was prepared in the operating room, hence the reliability of the result cannot be ascertained. Athar et al, arrived at the conclusion that Levobupivacaine had not only slower onset but also showed greater variability when compared to Ropivacaine, similar to our study.[9]This faster onset of sensory blockade in Ropivacaine group is due to its less lipid solubility in comparison to Levobupivacaine. Casati et al, conducted a study in which they randomly distributed the patients into three groups; they administered 8mg of 0.5% hyperbaric Bupivacaine in first group, second group was administered 8mg of 0.5% hyperbaric Levobupivacaine and third group received 12mg of 0.5% hyperbaric Ropivacaine. As per their study there was no difference in the onset of sensory block among the groups.[10]Moizo et al, conducted a study in which they administered 8 mg of 0.5% hyperbaric Bupivacaine in the first group, 8mg of 0.5% hyperbaric Levobupivacaine in second group and 12mg of 0.5% hyperbaric Ropivacaine in the third group.[11] In their study, it was observed that there was no variation in the onset of sensory block among the two groups in equipotent doses. Our study is not in agreement with the results of above two studies, as we have used ropivacaine in a higher concentration which is 0.75 %. Luck et al, conducted a study in which the first group received 3ml of Bupivacaine, second group was administered 3ml of Ropivacaine and third group was administered 3ml of Levobupivacaineintrathecally, each of 0.5% concentration and 30mg/ml of glucose was added in each drug. They observed that there was no such significant difference in the onset of sensory blockade among the groups because the concentration of glucose that was added to make these solutions hyperbaric, was less as compared to the usual dose and there was slight variation in the concentration of glucose amongst the groups.[12] Moreover, the dose of

Ropivacaine and Levobupivacaine used were not equipotent and thus, the disagreement from the result of our study.

The duration of sensory block in group Ropivacaine was shorter in contrast to Levobupivacaine. It was found in studies by Cappalleriet al[8], Athar et al[9], Casati et al[10], Moizo et al[11] and Luck et al[12], that Levobupivacaine has a longer duration of action than Ropivacaine in equipotent doses. Similar results are reflected in our study.

In this study, there was no statistical difference observed in mean onset time of motor block in group. Athar et al, observed that the onset of motor block can be achieved early with hyperbaric Ropivacaine when they considered time to Bromage 3 as time to maximum motor block.[9] In the study conducted by Casati et al[10], had results similar to our study. Luck et al, in their study observed that the group that was administered 3ml of Ropivacaine with added 30mg/ml glucose had early onset of motor block and was less in intensity when compared to the group that received 3ml of Bupivacaine with added 30mg/ml of glucose and 3ml of Levobupivacaine with added 30mg/ml of glucose.[12] The concentration of glucose that was added to made these solutions hyperbaric, was less than the usual dose and there was slight variation in the concentration of glucose amongst the groups. This might be due to lower lipid solubility of Ropivacaine.

In the current study, we found that the duration of motor blockade was significantly shorter in the group administered hyperbaric Ropivacaine than in the group administered hyperbaric Levobupivacaine. Similar conclusion was arrived at in study conducted byCappelleriet al[8], Athar et al[9], Casati et al[10], Moiz et al[11], and Luck et al[12]. Camoricaet al[13], found hyperbaric Ropivacaine to be less potent than hyperbaric Levobupivacaine in terms of motor block. This may be explained by lower lipid solubility of Ropivacaineleading to lesser penetration into the myelinated nerve fibres.
There was no statistically significant difference in terms of peak height for sensory block in between the two groups. Cappelleri et al, in their study observed that there was no significant difference in the peak height of sensory block on the side to be operated but there was significant variation in the level of sensory block between the side to be operated and not to be operated.[8]Athar et al, found in their study that there was no significant difference among the two groups although peak height was achieved at a faster rate with hyperbaric Ropivacaine.[9]Casati et al[10] and Luck et al[12], also observed similar results in their study,that is there was no remarkable difference in the level of peak height in all the groups.

The time to need for first analgesia in our study was significantly prolonged in group that was administered hyperbaric Levobupivacaine. The study conducted by Casati et al, observed that post-operative period of pain relief was sufficient and for 24 hours post-surgery, no opioid was required in both the groups.[10]Athar et al, in their study found results similar to our study.[9]Only a few studies have assessed postoperative analgesia, hence there is limited literature regarding the same.

Both the drugs hyperbaric Ropivacaine and hyperbaric Levobupicvaine have less cardiovascular toxicity in comparison to hyperbaric Bupivacaine, and thus have lesser

variation in Heart Rate, Systolic blood pressure, Diastolic blood pressure, Mean Arterial Blood Pressure and SpO_2 . Hence, both these drugs lead to greater hemodynamic stability. Cappelleri et al, found similar results in their study.[8]Athar et al, observed in their study that few patients in the group which received 3mg of 0.75% hyperbaric Ropivacaine experienced short-term fall in blood pressure whereas the fall in blood pressure was constant in group that was administered 3ml of 0.5% hyperbaric Levobupivacaine but there was no major variation amongst the two groups in terms of heart rate and SpO_2. The fall in blood pressure in group that received Ropivacaine in their study, could be consequent to the fact that peak height of block was achieved at a faster rate in this group.[9] Study conducted by Casatiet al[10] and Luck et al[12], reported similar results.

SIDE EFFECTS

In current study, we observed that only a small number of patients reported incidences post-operative nausea and vomiting or shivering in both the groups. There were no significant differences in regard to these side effects amongst the two groups. Ahmad dar et al, observed that there was no wide variation in the incidences of nausea, vomiting and shivering amongst the two groups.[9]Kallio et al, noticed that there was no wide variation in the number of patients who experienced shivering in the two groups.[14] Glaser et al, found that there was no difference in the number of patients who experienced nausea and vomiting in between the groups.[15] No such studies have been reported which compared Hyperbaric Ropivacaine with hyperbaric Levobupivacaine in terms of shivering, post-operative nausea and vomiting.

LIMITATION OF PRESENT STUDY

There were certain limitations of this study. This study was conducted on patients of the age group 18-60 years. ASA grade I-II patients were included in this study and therefore, results cannot be anticipated in ASA grade III and IV patients**.**Side effects such as Post-Dural Puncture Headache were not observed in this study.

CONCLUSION

Current study was conducted in order to compare 3ml of 0.5% hyperbaric Levobupivacaine and 3ml of 0.75% hyperbaric Ropivacaine administered intra-thecally, for lower limb surgeries. Onset of sensory blockade was significantly early in group that received hyperbaric Ropivacaine as compared to the hyperbaric Levobupivacaine, although there was no significant difference in regards to onset of motor blockade amongst both the groups. The duration of sensory as well as motor blockade was found to be prolonged in the group that was administered hyperbaric Levobupivacaine. There was no remarkable difference amongst the two groups in terms of peak height of sensory block. When compared hemodynamically, both the groups showed almost equal incidence of hypotension and bradycardia. Incidence of shivering or nausea and vomiting showed no significant difference amongst the two groups. Thus, for shorter duration of surgeries, hyperbaric Ropivacaine may be preferred while for longer duration of lower limb surgeries hyperbaric Levobupivacaine may be preferred.

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