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Comparison of spinal anaesthesia characteristics of intrathecal levobupivacaine 0.5% and ropivacaine 0.5% with dexmedetomidine as an adjuvant

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ABSTRACT

Background: Spinal Anaesthesia is widely used in infraumbilical surgeries with bupivacaine used as local anaesthetic.The pure S(-) enantiomers of bupivacaine i.e., levobupivacaine and ropivacaine were introduced into clinical anaesthesia practice because of the significant reduction in central nervous system and cardiac toxicity. The hyperbaric form produced more predictable and reliable sensory and motor block with faster onset than the isobaric forms. Intrathecal dexmedetomidine is used as an adjuvant drugs to local anaesthetics to prolong the duration of both motor and sensory spinal blockade.In the present study we compared the hyperbaric forms of levobupivacaine and ropivacaine with added dexmedetomidine as an adjuvant on spinal anaesthesia characteristics.

Methods: A prospective, randomised, double blind study was conducted in the Department of Anaesthesiology, Critical care and Pain medicine at Sri Venkateswara Institute of Medical Sciences (SVIMS) university teaching hospital, Tirupati .One twenty patients of American society of Anesthesiologists (ASA) physical status Grades I and II of either sex aged between 18 and 60 years undergoing infraumbilical surgeries were randomly allocated into two groups, Group L, who received 3 ml (15mg) of 0.5% isobaric levobupivacaine with 0.4ml of 25% dextrose with 0.1 ml (5µg) dexmedetomidine and Group R, who received 3 ml (15 mg) of 0.5% isobaric levobupivacaine with 0.4ml of 25% dextrose with 0.1ml(5µg) dexmedetomidine. The patients were studied for onset and duration of sensory blockade, onset and duration of motor blockade, haemodynamic parameters and side effects.

Results: The onset of sensory and motor block were faster and the regression of sensory and motor block were also earlier in the ropivacaine group compared to levobupivacaine group. The haemodynamic parameters HR, SBP, DBP, MAP were comparable in both the groups at all time intervals except for DBP at 45 and 120 min after subarachnoid block which was statistically significant.

Conclusions: The addition of dexmedetomidine resulted in earlier onset and prolonged duration of sensory and motor block with both levobupivacaine and ropivacaine. However onset of sensory and motor block was earlier and duration of sensory and motor block was shorter in ropivacaine than levobupivacaine. Earlier regression of motor block with ropivacaine was useful in day care and ambulatory surgeries where prompt mobilization was required.

Keywords: Spinal Anaesthesia, levobupivacaine,ropivacaine,intrathecal dexmedetomidine.

INTRODUCTION

Spinal Anaesthesia is widely used in abdominal and lower extremity surgeries[1, 2]with bupivacaine used as local anaesthetic. The levorotatory isomers of bupivacaine were shown to have a safer pharmacological profile[3] with less cardiac and neurotoxic adverse effects. The pure S(-) enantiomers of bupivacaine i.e., levobupivacaine and ropivacaine were thus introduced into clinical anaesthesia practice.[3] Levobupivacaine tends to induce more sustained sensory and motor block.[4] It blocks nerve

conduction in sensory and motor nerves mainly by interacting with voltage sensitive sodium channels on the cell membrane. It also interferes with impulse transmission and conduction in other tissues[5]. Ropivacaine is a long-acting amide local anaesthetic agent and first produced as a pure enantiomer. Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibres, resulting in relatively reduced motor blockade. The reduced lipophilicity is also associated with decreased potential for central nervous system toxicity and cardiotoxicity.[6]The hyperbaric levobupivacaine and ropivacaine produced more predictable and reliable sensory and motor block with faster onset than isobaric forms of levobupivacaine and ropivacaine.[4,7,8] Intrathecal α_2 agonist, dexmedetomidine is used as an adjuvant drug to local anaesthetics. Its addition to local anaesthetics prolong the duration of both motor and sensory spinal blockade.[9-11] It potentiates the effect of local anaesthetics and allow a decrease in required doses.[10,12] In the present study scompared the hyperbaric forms of levobupivacaine and ropivacaine with added dexmedetomidine as an adjuvant on spinal anaesthesia characteristics.

Materials and Methods

A prospective, randomised, double blind study was performed after obtaining approval from the Thesis Approval Committee and Institutional Ethics Committee. Written informed consent was obtained from the patients who participated in the study. One twenty patients of American society of Anesthesiologists (ASA) physical status Grades I and II of either sex aged between 18 and 60 years undergoing infraumbilical surgeries were randomly allocated into two groups, Group L, who received 3 ml (15mg) of 0.5% isobaric levobupivacaine with 0.4ml of 25% dextrose with 0.1 ml (5µg) dexmedetomidine and Group R, who received 3 ml (15 mg) of 0.5% isobaric levobupivacaine with 0.4ml of 25% dextrose with 0.1ml(5µg) dexmedetomidine. The patients were studied for sensory block characteristics(onset time of sensory block to T_{10} dermatome,maximum block height attained by cold swab method,time to reach maximum sensory block height and regression time to S1 dermatome),motor block characteristics(onset time of motor block,time taken to achieve complete motor block and time to regression),haemodynamic parameters and side effects.

Statistical analysis

All collected data was represented in Excel chart. The data was cross checked twice before analysis.The quantitative data like age, weight, height, HR, SBP, DBP, MAP and block characteristics were expressed in mean with standard deviation and analysed with Unpaired Student-t test.The qualitative data like gender, ASA grade, level of block, hypotension, bradycardia, nausea or vomiting were expressed in frequency and percentage and analysed by Chi Square test.p value < 0.05 was taken as significant.

Results

Both the study groups were comparable with regard to demographic characteristis like age,gender ratio,ASA physical status ,weight,height and duration of surgery.(Table 1)

The mean time of onset of sensory block to T_{10} was earlier in Group R (179.47±49.44 sec) compared to Group L(241.98±61.79 sec) which was statistically highly significant (p=0.000). The mean time to reach maximum sensory block height was little earlier in Group R (9.67±2.23 min) compared to Group L(10.46±2.02 min) but without any statistical significance.The sensory block lasted longer in Group L(315.17±38.29 min) compared toGroup R(227.22±25.06 min) which was a statistically highly significant(p=0.000).(Table 2)

The onset of motor block was earlier in Group R(2.04±1.25 min) compared to Group L (2.69±0.85 min) which was statistically highly significant(p=0.001). The mean time to achieve complete motor block earlier in Group R(5.93±2.21 min) compared to Group L(7.49±1.44 min) which was also statistically highly significant(p=0.000). The motor block lasted longer in Group L(291.42±35.75 min) compared to Group R (201.92±24.34 min) which was also statistically highly significant(p=0.000).(Table 3)

Both the groups were comparable at all time points with regard to heart rate(Graph 1),systolic blood pressure(Graph 2) and mean arterial pressure(Graph 3).With regard to diastolic blood pressure(Graph 4) a lower value was recorded in Group L than Group R at 45 min and 120 min after subarachnoid block

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which was statistically significant with p value 0.044 and 0.043 respectively.There was no significant difference among the study groups with regard to adverse events or the total dose of atropine and ephedrine required to counter these adverse events.

DISCUSSION

Subarachnoid block is one of the most commonly used anaesthetic technique for lower extremities and lower abdominal surgeries because of its simplicity, rapid onset of action, intense analgesia and relatively less complications. Limitation of spinal anaesthesia is that, it cannot be extended beyond a particular time, except with use of spinal catheters which may increase the chances of infection.The use of adjuvant drugs for spinal anaesthesia is intended to improve the success of regional anaesthesia by prolonging the duration and quality of sensory an motor block and preventing untoward complications of high dose of single drug alone. As the number of operations performed in the ambulatory settings increases, our intention was to find an appropriate drug which will provide faster onset and faster recovery without compromising anaesthetic reliability.

Levobupivacaine, the pure S (−)-enantiomer of bupivacaine, emerged as a safer alternative for regional anaesthesia than its racemic parent. Ropivacaine is a long-acting amide local anaesthetic agent and first produced as a pure enantiomer.Its reduced lipophilicity is associated with decreased potential for central nervous system toxicity and cardiotoxicity. Lot of clinical trials have been validated the role of dexmedetomidine in enhancing the quality of spinal blockade with levobupivacaine and ropivacaine. The present study was undertaken to compare the effects of addition of dexmedetomidine intrathecally to hyperbaric levobupivacaine and ropivacaine.

- **Sell A et al** [13] conducted a study to determine minimum effective local anaesthetic dose of isobaric levobupivacaine and ropivacaine administered via spinal catheter in a hip replacement surgery. They found that Minimum Local Anaesthetic Dose (MLAD) of levobupivacaine was 11.7 mg (95% CI, 11.1–12.4) and that of ropivacaine 12.8 mg (95% CI, 12.2–13.4).So we decided to use 15mg of levobupivacaine and ropivacaine for spinal anaesthesia in lower limb surgeries.
- **Djeno IT et al** [14] did a controlled, randomised and double blinded study to determine whether a combined glucose/LA solution can render a clinically significant difference in sensory block distribution and motor block intensity and found a statistically significant difference in sensory block distribution, motor block intensity and recovery time between hyperbaric and hypobaric solutions. So in our study we decided to add glucose to levobupivacaine and ropivacaine to make them hyperbaric for better block characteristics.
- **Esmaoğlu A et al**[15] conducted a study to compare the characteristics of spinal blocks produced by 0.5% levobupivacaine with and without dexmedetomidine and concluded that intrathecal dexmedetomidine addition to levobupivacaine for spinal anaesthesia shortens sensory and motor block onset time and prolongs block duration without any significant adverse effects.
- **Gupta R et al**[16] conducted a study on efficacy and safety of intrathecal dexmedetomidine added to ropivacaine. sixty patients were randomized receive an intrathecal solution (3.5ml) containing isobaric ropivacaine (15mg) with dexmedetomidine 5mcg (0.5ml) or normal saline 0.5ml.concluded that addition of dexmedetomidine to ropivacaine intrathecally produces prolongation of sensory and motor block.

Onset of sensory block:

The mean time to onset of sensory block to T_{10} dermatome in Group L was 241.98±61.79 sec (4 min nearly) and in Group R was 179.47±49.77 sec (3min nearly) in our study. The mean time to onset of sensory block to T_{10} was earlier in Group R than Group L which was statistically highly significant (p=0.000).

The mean time to onset of sensory block in Group L was earlier compared to study done by **Jain S et al**[17]**(**7.1±1.4 min). The earlier onset in our study might be due to 15mg of hyperbaric levobupivacaine rather than 12.5mg.

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The mean time to onset of sensory block in Group R of our study was earlier compared to study done by **Naithani U et al**[18] (4.16±1.59 min) which might be due to hyperbaric ropivacaine rather than isobaric ropivacaine used in our study.

Time to reach maximum height of sensory block:

In our study peak sensory block was attained at 10.46±2.02 min in Group L and 9.67±2.23 min in Group R. The mean time to reach maximum height of sensor block was earlier in Group R than Group L, however there was no statistically significant difference (p=0.46) among the two groups in this regard.

The peak onset of sensory block in Group L was earlier compared to study done by **Esmauglu A et al**[15](12.7±5.0 min) and **swaika et al**[19] (12.9±3.04 min).The earlier onset in our study may be due to increased dose of dexmedetomidine 5µg and hyperbaric levobupivacaine used.

The peak onset of sensory block in Group R was earlier compared to study by **Naithani U et al**[18] (12.17±2.80 min) and **Krishnappa MS et al**[20] (10.70±1.27 min). The earlier onset in our study may be due to increased dose of dexmedetomidine 5µg and hyperbaric ropicaine used.

Time to regression to S_1 :

In our study mean time to regression to S_1 was 315.17±38.29 min in Group L and 227.22±25.06 min in Group R. Sensory block was regressed earlier in Group R than Group L which was statistically highly significant (p=0.000).

The time to regression of sensory block in Group L was earlier compared to study done by **Esmauglu et al**[15] (356.3±35.2 min) and **Jain S et al**[17](472.5±8.7 min). The earlier regression time of sensory block may be due to hyperbaric levobupivacaine and lower volume of drug(3.5ml) used in our study.

In a study by **Nitish kumar parmar et al** [21] addition of 5µg of dexmedetomidine to 22.5mg of isobaric ropivacaine time to regression of sensory block to S_2 was 297.71±34.11 min. The difference in prolonged time taken to regression of sensory block in **Nitish kumar parmar et al**[21] study may be due to 22.5mg of ropivacaine than 15mg of ropivacaine in our study and hyperbaric ropivacaine used in our study compared to isobaric ropivacaine.

Our study was comparable to study by **Luck F.J. et al** [22] where time taken to regression of sensory block was earlier in hyperbaric ropivacaine (210min) than hyperbaric levobupivacaine (270min). However addition of dexmedetomidine resulted in increase in duration of sensory block in both the groups in our study.

Time to onset of motor block:

In our study time to onset of motor block was 2.69±0.85 min in Group L and 2.04±1.25 min in Group R. The onset of motor block was earlier in group R than Group L and it was statistically highly significant (p=0.001).

The onset of motor block in Group L was comparable to the study by **Esmauglu et al**[15] (1.7±0.6 min).When compared to study done by **Swaika et al**[19](9.0±3.2 min), the earlier time taken in our study might be due to hyperbaric levobupivacaine rather than isobaric levobupivacaine.

The onset of motor block in Group R was comparable to study by **Gupta et al**[16](2.23±0.73 min). Addition of dexmedetomidine resulted in earlier onset of motor block in our study.

Time to achieve maximum motor block:

In our study time taken to achieve maximum motor block was 7.49±1.44 min in Group L and 5.93±2.21 min in Group R. The onset of motor block was earlier in Group R than Group L which was statistically highly significant (p=0.000).

When compared to studies done by **Esmauglu et al**[15](13.9±6.9 min) and **Swaika et al**[19](18.1±4.7 min) the earlier onset in Group L of our study might be due to hyperbaric levobupivacaine used rather than isobaric .

The time to achieve complete motor block in Group R of our study was comparable to study done by **Nitish kumar parmar et al**[21](5.54±0.85 min) and earlier when compared to studies done by **Naithani U et al**[18](6.61±2.18min) and **Singh et al**[23] (9.08±2.38 min) because of the hyperbaric ropivacaine used in our study.

Time to resolution of motor block:

In our study time to regression of motor block was 249.42±35.75 min in Group L and 201.92±24.34 min in Group R. Regression of motor block was earlier in

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Group R than Group L which was statistically highly significant (p=0.000).

The time to regression of motor block was earlier in Group L of our study when compared to studies done by **Esmauglu et al**[15](332±36.7min), **Swaika et al**[19] (390.1±9.2 min) and **Jain S et al**[17] (421.6±10.6 min) probably because of usage of hyperbaric levobupivacaine and lower volume of drug used in our study.

The time to regression of motor block was earlier in Group R of our study when compared to studies done by **Nitish kumar parmar et al**[21](258.55±30.46 min) and **Singh et al**[23] (306.21±44.75 min). The difference in the duration of motor block might be due to difference in the drug dosage used and hyperbaric ropivacaine used in our study.

CONCLUSION

From our study we concluded that the addition of dexmedetomidine resulted in earlier onset of sensory and motor block and prolonged duration of sensory and motor block with both levobupivacaine and ropivacaine. However onset of sensory and motor block was earlier in ropivacaine than levobupivacaine and duration of sensory and motor block was shorter in ropivacaine than levobupivacaine. Earlier regression of motor block with ropivacaine was useful in day care and ambulatory surgeries where prompt mobilization was required.

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Table 1: Demographic Characteristics

Demographic data	Group L	Group R	p value
Age(years)	57.10±3.42	57.02±3.61	0.897
Gender M(n) F(n)	27 33	26 34	0.854
ASA physical status I(n) II(n)	 30 30	 37 23	0.198
Weight (Kgs)	68.80±9.61	68.28±9.78	0.771
Height(cms)	161.95±5.82	162.38±6.53	0.702
Duration of Surgery(min)	82.92±8.55	81.92±8.78	0.529

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The data of age, weight, height, duration of surgery were represented as Mean±SD (Standard deviation).The data of ASA(American Society of Anesthesiologists) physical status, sex were represented as n=frequency. F = Female; M = Male.Group L=Levobupivacaine + Dexmedetomidine.Group R = Ropivacaine + Dexmedetomidine.

$p < 0.05$ is considered significant.

Table 2: Comparison of Sensory Block Characteristics

Sensory block	Group L (Mean±SD)	Group R (Mean±SD)	P value
Onset of block to T_{10} (sec)	241.98±61.79	179.47±49.44	**0.000***
Time to reach maximum height of sensory block (min)	10.46±2.02	9.67±2.23	0.46
Regression time to S_1(min)	315.17±38.29	227.22±25.06	**0.000***

The data represented as Mean ± SD.Group L- Levobupivacaine + Dexmedetomidine .Group R- Ropivacaine + Dexmedetomidine

Statistically significant-*

Table 3: Comparison of Motor **Block Characteristics**

Motor block	Group L (Mean±SD)	Group R (Mean±SD)	p value
Onset of block(min) (Bromage 1)	2.69±0.85	2.04±1.25	**0.001***
Time to achieve complete block(min) (Bromage 3)	7.49±1.44	5.93±2.21	**0.000***
Resolution of block (min) (Bromage 0)	291.42±35.75	201.92±24.34	**0.000***

The data represented as Mean±SD.Group L-Levobupivacaine + Dexmedetomidine .Group R –Ropivacaine + Dexmedetomidine

Statistically significant-*****

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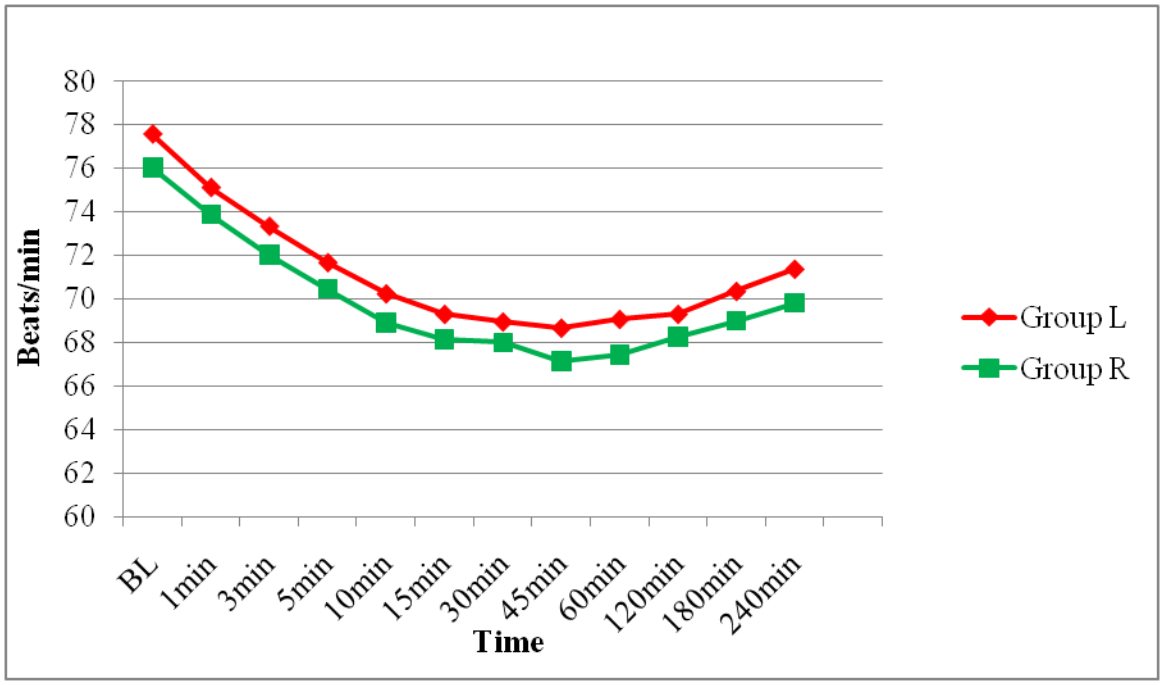
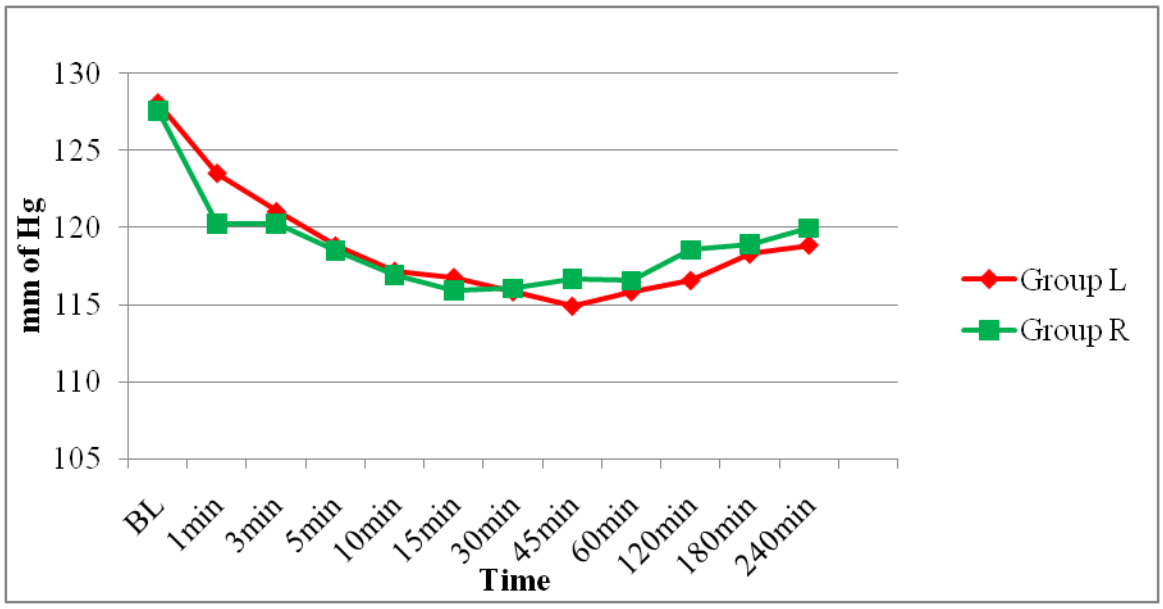
Graph 1: Comparison of Heart rate (HR) between two groups



Graph 2: Comparison of Systolic Blood Pressure (SBP) between two groups



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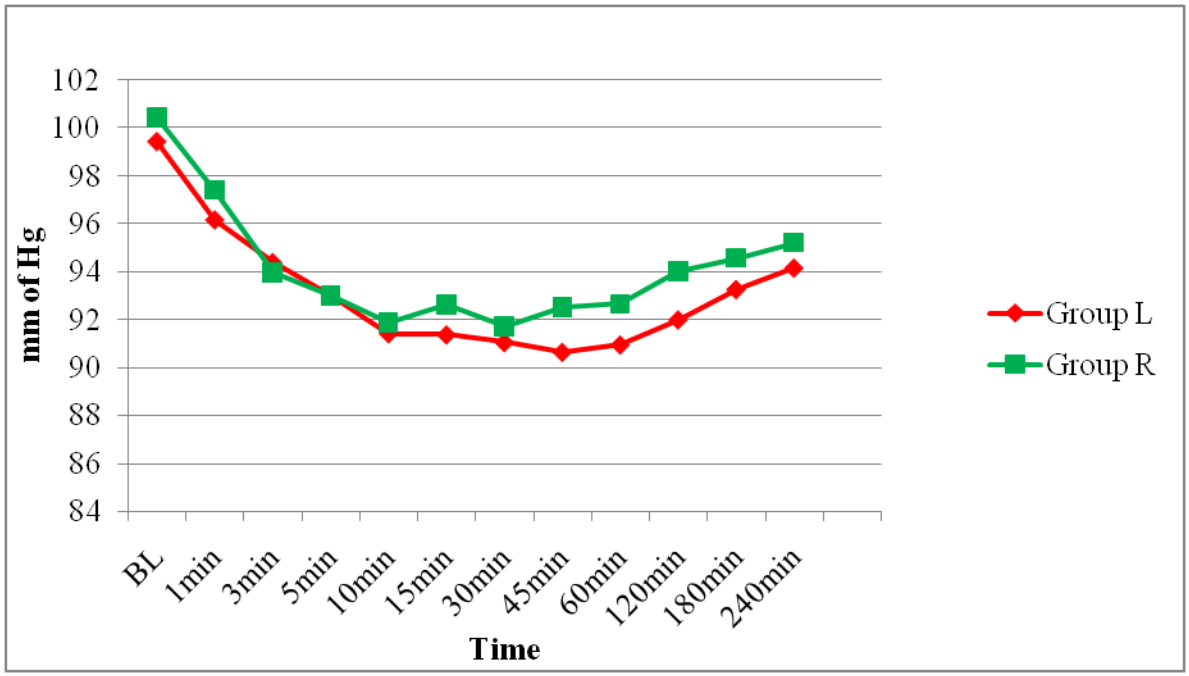
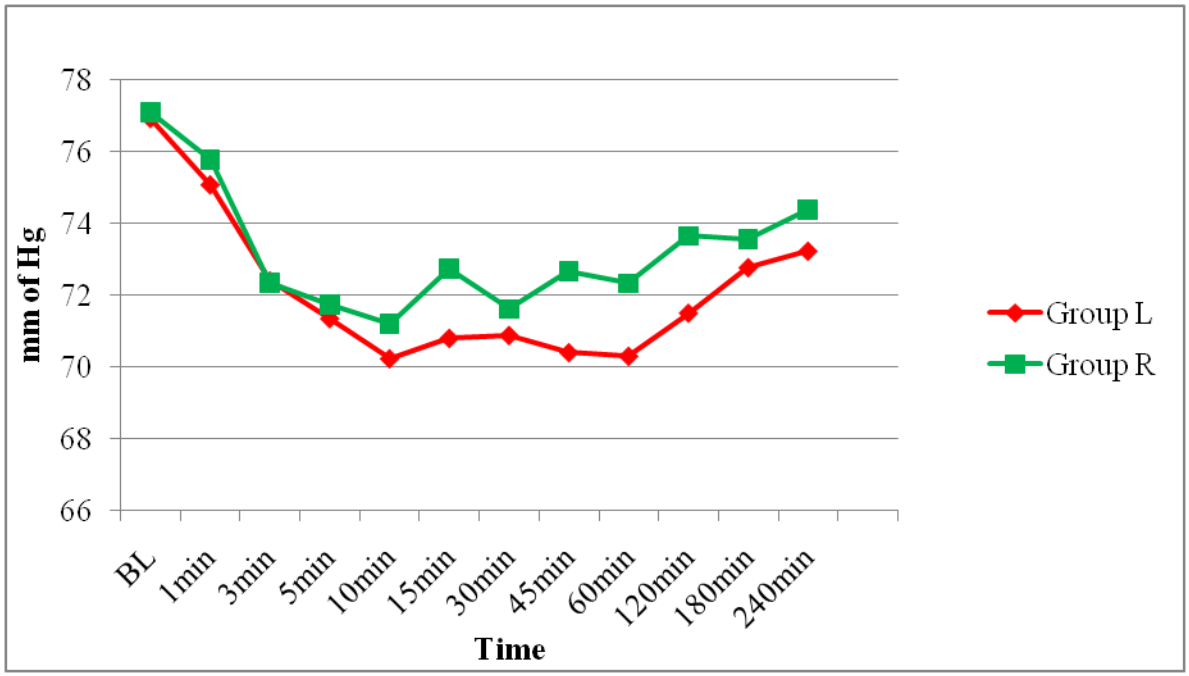
Graph 3: Comparison of Mean arterial pressure (MAP) between two groups



Graph 4: Comparison of Diastolic blood pressure (DBP) between two groups



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