

# Comparison of Different Concentration of Dextrose as an Adjuvant to Levobupivacaine in Lower Limb Surgeries: A Randomised Double-Blinded Controlled Trial

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## ABSTRACT

**Background:** We compared the block characteristics and adverse effects along with the hemodynamic changes, following intrathecal administration of three different volume of dextrose to levobupivacaine in lower limb surgeries.

**Material and methods:** Seventy five patients were randomly allocated to three groups. In group I 50 mg dextrose, in group II 75 mg and in group III 100 mg was added to 0.5% levobupivacaine 1.5 ml (7.5 mg), total volume was made 2 ml by adding normal saline and injected intrathecally. The onset of sensory and motor blockade, duration of sensory and motor blockade, height of sensory block, two segment of regression time of sensory block hemodynamic changes and side effects were recorded.

**Results:** The onset of sensory block (to reach T12) was early in group II and III in comparison to group I ( $p=0.007$ ,  $p<0.0001$ ). The onset of motor block was  $11.52\pm 2.02$  minute in group I,  $9.64\pm 1.11$  minute in group II and  $8.84\pm 2.19$  minute in group III. The mean time to reach maximum height of sensory block was less in group II and group III, in comparison to group I. The full recovery from sensory block was significant prolonged in group II and III compared to group I ( $p<0.0001$ ). The total duration of motor block and time to urination was prolonged in group III compared to group I and II ( $p<0.0001$ ).

**Conclusion:** Levobupivacaine with higher baricity had a faster sensory and motor onset as well as longer duration of sensory and motor block.

**Key words:** Spinal anaesthesia, dextrose, hyperbaric levobupivacaine, lower limb surgery.

## INTRODUCTION

Subarachnoid blockade is the most commonly used modality of regional anaesthetic technique for lower limb surgery. Intrathecal use of hyperbaric 0.5% bupivacaine is being used as standard for surgeries and may lead to early analgesic intervention in the postoperative period. <sup>[1]</sup>

In search for newer longer acting intrathecal drugs with less side effects, hyperbaric levobupivacaine is being tried recently. <sup>[2]</sup> In spinal anaesthesia, greatest

challenge is to control the spread of local anaesthetic (LA) in the cerebrospinal fluid (CSF) and to provide adequate height of block without increasing the risk of complications. <sup>[3]</sup> Baricity, position of the patient during and immediately after drug administration, dosage, site of injection is the important factors for determining the final extent of block. <sup>[4]</sup> Local anaesthetic solution can be made hyperbaric by adding glucose. <sup>[5,6]</sup> Due to neurotoxic effects of other substances, addition of glucose is the

only method of altering baricity to remain in routine use. [7,8] Commercially available solutions contain up to 8% of glucose, but evidence shows that any concentration in excess of 0.8% will produce a solution that behaves in a hyperbaric manner. [9,10]

In view of few literature about efficacy of various concentration of dextrose to levobupivacaine [2,11] a double blind randomized control study was planned to find out the effect of addition of different amount of dextrose on the spinal block characteristics and side effects along with hemodynamic changes following intrathecal levobupivacaine administration in patients scheduled for day care lower limb orthopaedic surgery.

## MATERIALS AND METHODS

This randomized, prospective, double blind, placebo controlled trial was conducted at a tertiary care centre in western Rajasthan, India after ethical approval and informed consent from all patients. Seventy five American Society of Anaesthesiologist (ASA) I-II patients aged between 18-65 years undergoing lower limb surgery were participated in the study. The Consolidated Standards of Reporting Trials (CONSORT) recommendations for reporting randomised, controlled clinical trials were followed. (Fig. 1) Patients with contraindication to regional anaesthesia, history of significant coexisting diseases like ischemic heart disease, hypertension, diabetes, impaired renal functions, left ventricular failure, valvular heart disease, rheumatoid arthritis, severe liver disease, body weight more than 120 Kg, height less than 140 cm, patient on adrenergic receptor agonist or antagonist therapy, with known hypersensitivity to local anaesthetic, drugs, pregnant patients, chronic alcoholics and malnourished patients were excluded from the study.

Thorough preoperative check-up of all patients for anaesthesia fitness and to familiarized with visual analogue scale [12] (VAS) were done, a day prior to surgery, for measuring the postoperative pain.

Preoperative fasting advised as per standard guideline. Sedatives and hypnotics were avoided in premedication drugs as well as during intraoperative period. In operating room, all routine monitors were attached to the patient. Baseline haemodynamic parameters heart rate (HR), oxygen saturation (SpO<sub>2</sub>) and mean blood pressure (MBP) were recorded. Ringer lactated solution 10 mL/kg of was infused over 20-30 minute through 18-gauge cannula to all patients. The randomization was done with computer generated random number sequence into three groups of equal number. The allocated intervention was written on slip of paper, placed in serially numbered opaque envelopes and sealed. As consecutive eligible subjects got enrolled, the envelopes were serially opened and the allocated intervention was implemented. All three groups received injection 0.5% levobupivacaine 7.5 mg (1.5ml). In addition to levobupivacaine Group I patients received 0.2 ml of 25% dextrose (50.0mg), Group II patients received 0.3 ml 25% dextrose (75 mg) and Group III patients received 0.4ml of 25% dextrose (100 mg). The total volume for intrathecal injection was made 2ml by adding normal saline. One anaesthesiologist, who was not involved in further patients care, prepared the intrathecal drugs just prior to positioning the patient for spinal anaesthesia. The spinal anaesthesia was applied at L3 and L4 level in lateral decubitus position with 25G Quincke spinal needle, without barbotage at a rate of 0.1 ml/second to all patients. Patient and anaesthesiologist who collected the data intraoperatively and postoperative period, were blinded to the study group.

The patients were placed supine after injection and the sensory level was assessed by pinprick sensation using a blunt 25-gauge hypodermic needle along the mid-clavicular line bilaterally at two-minute intervals for 30 minutes and then every 15 minutes thereafter. The onset of sensory block (time to reach T12 dermatome), maximum height of sensory block, time to reach the highest dermatomal level of

sensory block were recorded. All durations were calculated in relation to the time of subarachnoid block. The motor block was assessed according to the modified Bromagescale (MBS) [13] (0–3) for onset (time to reach Bromage 3). The hemodynamic parameters heart rate (HR), mean blood pressure (MBP) and oxygen saturation (SpO<sub>2</sub>) were recorded at 1, 3, 5, 7, 10, 12, 15, 20, 25, 30, 45, 60 and every 30 minutes up to 6 hours and hourly thereafter till 24 hours. On achieving T12 sensory blockade level, surgery was allowed. Hypotension (fall in mean blood pressure more than 30 % of baseline) was treated with fluid bolus of 200 ml lactated ringer solution and mephentermine 6mg IV. Bradycardia (pulse rate <50 bpm) was treated with IV atropine 0.6 mg.

The pain score was recorded in post anaesthesia care unit (PACU), by anaesthesiologist who was unaware of the group assignment. For first 8 hours every hour, then every 2 hours till 24 hours pain score was recorded. The time to two segment sensory regression, time to full recovery of sensory block (no feeling of numbness), duration of motor block (time to reach Bromage 0 ) and time of the first urination were also recorded. Duration of pain relief was defined as the time from spinal injection to the first request for rescue analgesics or VAS was  $\geq 4$  and treated with tramadol 2mg/kg IV.

Patients shifted from PACU after full sensory recovery and Bromage score reached to zero. Side-effects such as nausea, vomiting, bradycardia, hypotension, respiratory depression (RR <8/min) and pruritus were noted and treated accordingly.

#### **Statistical analysis:**

We took a sample size of 75 patients with 25 patients in each group, to detect mean difference of 20 minutes in complete regression of spinal anaesthesia with an effect size to standard deviation of 0.9 with two tailed  $\alpha$  error of 5% and  $\beta$  error of 20%. It was based on complete regression of spinal block with hyperbaric levobupivacaine reported in study of

Özgür Yağcı et al [2] with power of 80%. Continuous variables were presented as mean and standard deviation. Analysis of variance (ANOVA) test was used to compare the quantitative variables in the three groups which were independent of each other. Chi square test was used to compare categorical variables. All the data was analysed using SPSS vs. 22 (IBM SPSS Statistics, Chicago IL, USA). The p value of <0.05 was considered as statistically significant.

#### **RESULTS**

Ninety six patients posted for lower limb surgeries were enrolled in the study. Ten patients refused to participate in the study and eleven patients found to be on beta blockers, anticoagulation drugs and had uncontrolled diabetes mellitus, were excluded from study. The remaining 75 patients that fulfilled the inclusion criteria were randomly assigned to one of the three groups. (Figure: 1) There was no statistical difference in patients' demographics or duration of surgery in all three groups. (Table:1) Perioperative haemodynamic parameters were comparable in all the three groups. (Figure: 2a, 2b) The onset time of sensory block was early in group II and in group III in comparison to group I which is statistically significant. (p=0.007, p<0.0001) The motor block (time to reach bromage 3) was also rapid in group II and III in comparison to group. (p=0.0002, p<0.0001) The mean time to reach maximum height of sensory block was less in group II and group III, in comparison to group I. The height of sensory level in group I was T12 (in 80% patients), at T11 (in 60 % patients) in group II and at T10 (in 52% patients) in group III. (Table: 2) The p value of mean time of two segment sensory regression was statistically significant in all the groups. (Table: 2) The time to full recovery of sensory block and duration of motor block also statistically significant in group II and III (p<0.0001) the time of the first urination was prolonged in group III compare to group I and II. The

time to first rescue analgesia was comparable in all three groups. (Table: 2)

In our study, vomiting in two cases, shivering in one case, hypotension in one case, bradycardia in one case in group I, vomiting in two cases, shivering two cases, hypotension in one case in group II and vomiting in one case, shivering in two

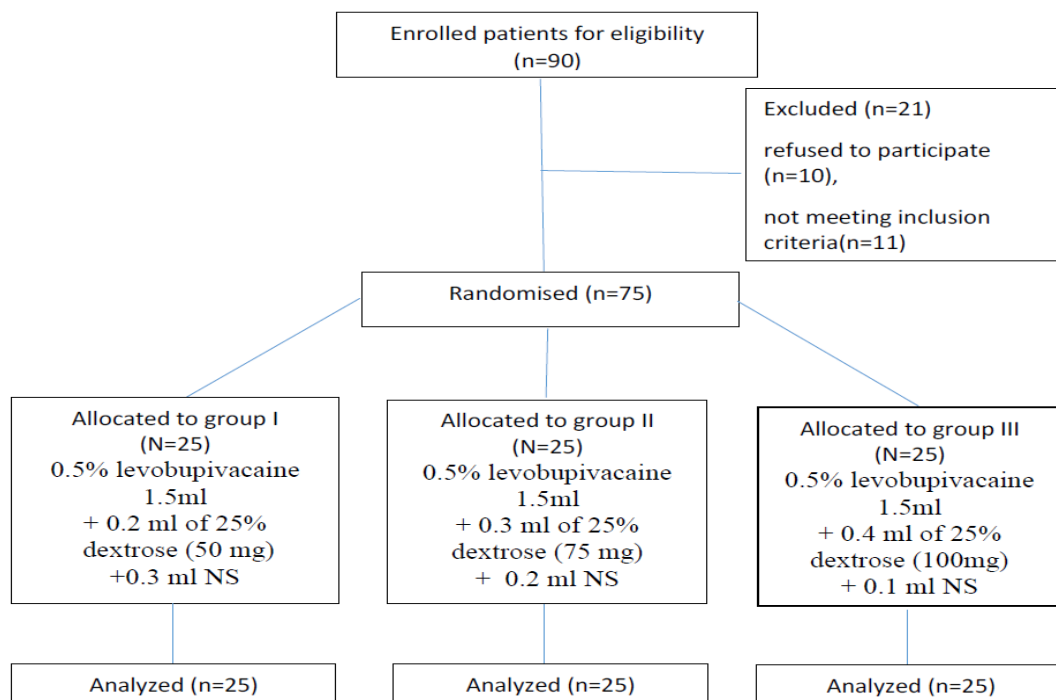
cases, hypotension in one case in group III were observed.

**Table 1: Patients' demographics and duration of surgery**

Variable	Group I (Mean ±SD)	Group II (Mean ±SD)	Group III (Mean ±SD)
Age(years)	34.96±16.67	37.28±12.71	40.2±17.59
Sex(male/female)	21/4	20/5	20/5
ASA I/II	17/8	19/6	19/6
Duration of surgery (min)	49.84±5.74	52.16±6.89	52.96±6.66

**Table 2: Characteristics of spinal block**

Variable	Group I (Mean±SD)	Group II (Mean±SD)	Group III (Mean±SD)	P value
Time of onset of sensory block (up to T12) (minute ±SD)	10.04±0.93	9±1.08	7.84±0.94	I v/s II=0.007 I v/s III=<0.0001 II v/s III= <0.0002
Time of onset of motor block (Bromage score 3) (minute±SD)	11.52±2.02	9.64±1.11	8.84±2.19	I v/s II=0.0002 I v/s III=<0.0001 II v/s III= <0.110
Maximum cephalad spread (dermatome)	T12 (L1-T10)	T11 (L1-T9)	T10 (T12-T8)	I v/s II = 0.123 I v/s III = 0.036 II v/s III = 0.568
Time to reach maximum height of sensory block (minute±SD)	23.48±1.53	21.28±1.37	19.72±2.13	I v/s II=<0.0001 I v/s III=<0.0001 II v/s III= <0.0001
Two segment sensory regression time (minute±SD)	49.2±3.09	56.76±3.68	59.08±4.17	I v/s II=<0.0001 I v/s III=<0.0001 II v/s III= <0.042
Duration of motor block (regression to Bromage score zero) (minute±SD)	83.16±4.35	110.48±7.4	124±7.6	I v/s II=<0.0001 I v/s III=<0.0001 II v/s III= <0.0001
Full recovery sensory block (minute±SD)	126.48±4.94	153.56±4.41	185.12±9.74	I v/s II=<0.0001 I v/s III=<0.0001 II v/s III= <0.0001
Time to first urination (minute±SD)	181.84±6.68	202.04±35.05	239.36±28.26	I v/s II=0.017 I v/s III=<0.0001 II v/s III= 0.0001
Time to first rescue analgesia (minute±SD)	287.76±24.51	288.32±20.54	296.88±23.15	I v/s II=0.930 I v/s III=0.182 II v/s III= 0.173



**Figure1: Consort diagram of study**

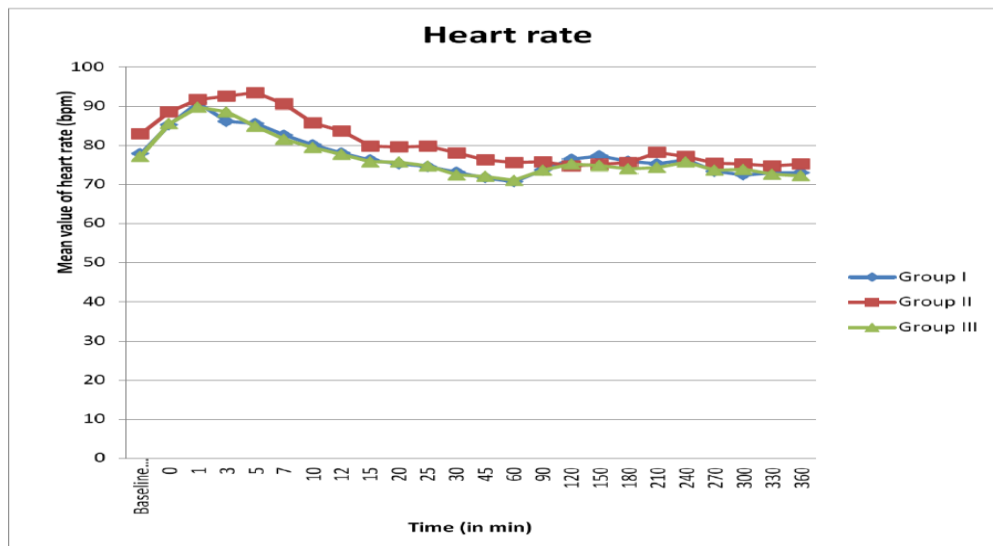


Figure2a: Trend of heart rate

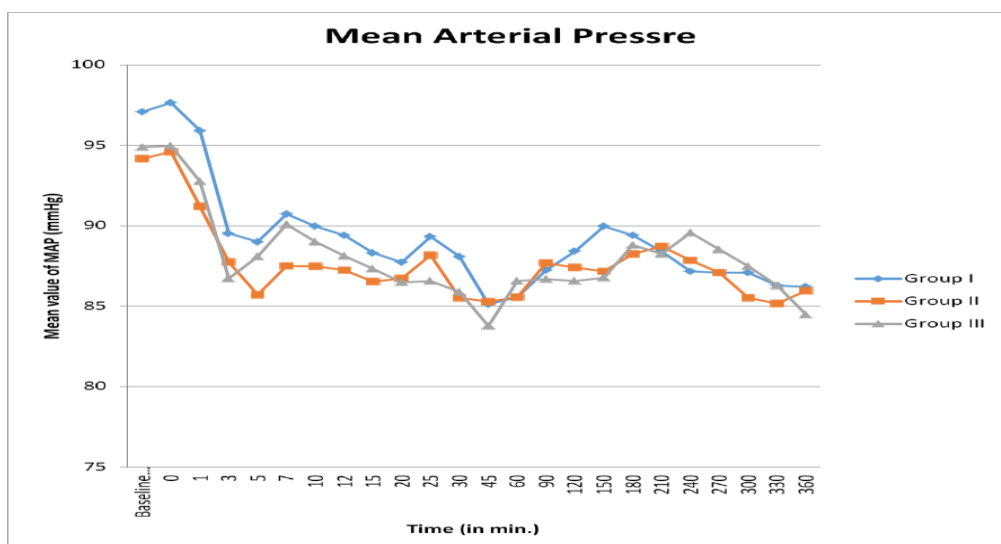


Figure2b: Trend of mean blood pressure

## DISCUSSION

In present study levobupivacaine with higher baricity had significantly faster onset of sensory and motor block, reached a higher dermatome level and also prolong the duration of sensory and motor block in comparison to isobaric levobupivacaine.

The effect of isobaric local anaesthetic agents was unpredictable. The Literature showed that clinical efficacy of hyperbaric levobupivacaine was superior to isobaric form when injected intrathecally. [14] As hyperbaric levobupivacaine is not available in market. [2] We prepared different baricity of levobupivacaine by adding different amount of dextrose to isobaric levobupivacaine solution. The

measured density of levobupivacaine at 37°C with 25 mg/ml, 37.5 mg/ml and 50 mg/ml dextrose were 1.0074, 1.0125 and 1.0186 gm/litre respectively.

The baricity of local anaesthetic agent in relation to cerebrospinal fluid is an important factor for predicting the spread of the solution in the subarachnoid area. The baricity defined as the ratio of density (mass/volume) of local anaesthesia solution and density of CSF at particular temperature. The rise of temperature, decreases the density and addition of glucose, increases the density of local anaesthetic agent. At 37°C the mean density of CSF is 1.0003 g/l, ranging from 1.0000 to 1.0006 ( $\pm 2SD$ ). Solutions at a density below

0.9990 is considered as hypobaric and those above 1.0010 as hyperbaric.

Naithani U et al [15] compared hyperbaric bupivacaine with isobaric levobupivacaine in lower limb orthopaedic surgeries, and concluded that although sensory, motor onset was significantly rapid and duration of sensory block was significantly longer in bupivacaine group as compared to levobupivacaine group. They proved that isobaric levobupivacaine offering effective sensory, motor blockage and stable hemodynamic profile with significantly decreased cardiovascular and central nervous system toxicity, is a suitable alternative to hyperbaric bupivacaine in spinal anaesthesia.

Bannister et al [6] compared 0.5% bupivacaine solutions containing different concentrations of glucose and determined longer sensory block duration in the group with the solution containing 8% glucose. Sen et al [14] also performed a similar study and proved that hyperbaric levobupivacaine had a faster onset of sensory and motor block, reaching maximum sensory block and Bromage score 3 faster, and had a shorter duration of sensory and motor block than did the isobaric form. Similarly, in our study the onset was faster and duration of block was longer with more hyperbaric than isobaric but duration of analgesia was not statistically significant. Gulen G. et al [16] compared isobaric levobupivacaine with hyperbaric bupivacaine in caesarean section, time to reach maximum motor block in isobaric levobupivacaine  $11.36 \pm 2.35$  min and in hyperbaric levobupivacaine was  $6.13 \pm 1.56$  min. These results were similar to our study.

Solakovic [17] investigated isobaric and hyperbaric bupivacaine (15 mg, 0.5%) in patients with orthopedic, urologic, and gynecologic surgery. The hyperbaric agent had a higher peak sensory block level [T5 (T1–T7)] compared with the isobaric group [T10(T5–L2)] but led to a high block with consecutive hemodynamic instability in some patients.

In our study that there was more cephalad block with hyperbaric levobupivacaine than isobaric solution similar to other studies. [18,19] While results of other studies contrast to our study. [20] This differential effect was explained by the different properties of drugs, relation to gravity and the mass movement of CSF as a result of the postural changes. [21] Gravity will tend to keep the hyperbaric solution near the lowest point of the thoracic curve (T4/T5) in the supine position and to resist attempts to move it further in a cranial direction. [17] This tendency to spread could be further increased with the viscosity of the hyperbaric solution, and prevent it mixing with the CSF. [17] The plain solution, mixed freely with CSF, has neither gravitational nor viscous effect to restrict its movement within the displaced CSF. In our study maximum cephalad spread (dermatome) in group I was T12 (in 80% patients), at T11 (in 60 % patients) in group II and at T10 (in 52% patients) in group III.

Yağana O et al [2] and Sen H et al [14] found statistically insignificant difference in two segment sensory regression in all the groups. In our study there was a statistically significant difference in two segment sensory regression and time for full recovery sensory block in all three groups.

Sen H et al [14] and Guler G et al [16] compared intrathecal hyperbaric levobupivacaine with isobaric levobupivacaine. Patients in the hyperbaric group underwent surgery completely without additional anaesthesia in most of cases compared with the isobaric group, who required additional anaesthesia in one third cases. However, in both groups the anaesthetic effect started fading away gradually at one hour after spinal injection. Although surgery could be finished in all of these patients with the help of additional sedatives or analgesics, the outcome was not satisfying. Maximum sensory cephalad spread was highest in group III followed by group II and group I respectively. It was statistically significant in all three groups.

The time of first urination and time to mobilisation are important in day case surgical procedures, in respect of hospital discharge. Postoperative mobilisation time was also affected by surgical characteristics. The most frequently encountered factor restricting the meeting of discharge criteria has been reported to be the return to spontaneous urination. [22] Therefore, in the current study, the time to return of spontaneous urination was taken as a criteria rather than time of discharge. In Group I this time was 128 min, which was significantly shorter than the times of both Group II and Group III. In a study by Cappelleri et al [22] in which hyperbaric forms of levobupivacaine and ropivacaine were compared in unilateral spinal anaesthesia for knee arthroscopy, this period was reported as 238 min in the group with 7.5 mg levobupivacaine including 8.2% glucose. The time to discharge of this group was defined as the time of first urination.

Post-operative nausea and vomiting were the most frequent adverse effect in groups. Hypotension was easily treated by incremental dose of mephentermine without any sequels. The incidence of hypotension was similar in all three groups which was not statistically significant ( $p > 0.05$ ).

## CONCLUSION

Our study concluded that levobupivacaine with higher baricity had a faster sensory and motor onset, reached a higher dermatome level. Duration of sensory and motor block was more with hyperbaric levobupivacaine. Clinical efficacy of intrathecal 7.5mg hyperbaric levobupivacaine with 5% dextrose was better than 2.5% and 3,75% dextrose for short surgical procedures of lower limb orthopaedic surgeries, although not much difference were noted between 3.75% and 5% dextrose containing levobupivacaine.

The limitations of our study was all patients ASA physical status I or II, so results cannot be generalized to ASA physical status III and IV patients. There was no comparison was made of the times

to mobilization and actual discharge. Hence, further studies that compare the effect of various concentration of intrathecal hyperbaric levobupivacaine with large sample size are needed.

**Conflict of interest statement:** Nil

**Declaration:** This study was conducted as MD thesis in our institute.

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How to cite this article: Verma A, Singariya G, Kamal M et al. Comparison of different concentration of dextrose as an adjuvant to levobupivacaine in lower limb surgeries: A randomised double-blinded controlled trial. *Int J Health Sci Res.* 2018; 8(3):11-18.

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