Original Research Article

Indian Journal of Anesthesia and Analgesia
July – August 2020;7(4)
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.7420.21

Evaluation of Effect of Adding Dextrose to Levobupivacaine, Compared to Levobupivacaine Plain in Subarachnoid Block for Lower Limb and Lower Abdominal Surgeries

Kiran Nelamangala[1], Dinesh Krishnamurthy[2], Ravi Madhusudhana[3]

[1-3]Professor, Department of Anesthesiology, SDUMC, SDUAHER, Kolar, Karnataka, 563101, India.

How to cite this article:

Kiran Nelamangala, Dinesh Krishnamurthy, Ravi Madhusudhana. Evaluation of Effect of Adding Dextrose to Levobupivacaine, Compared to Levobupivacaine Plain in Subarachnoid Block for Lower Limb and Lower Abdominal Surgeries. Indian J Anesth Analg. 2020;7(4):999–1003.

Abstract

Context: The search of a drug which can give the perfect balance of sensory and motor block with minimal side effects has always missed researchers. We have conducted a study to study the efficacy of adding dextrose to levobupivacaine and try to find an alternate to the routinely used bupivacaine.

Aims: Evaluation of effect of adding dextrose to levobupivacaine, compared to levobupivacaine plain in terms of onset and duration of sensory and Motor blockade; Quality of analgesia.(VAS score).

Settings and Design: Open Labelled Study

Methods and Material: 140 patients admitted for elective surgeries, during the period of January 2017 to December 2017. Group L: Hyperbaric Levobupivacaine with 150 mg dextrose.(0.3 ml of 50% dextrose), volume is 3.3 ml; Group p: Plain levo Bupivacaine. (volume is 3.3 ml).

Statistical analysis used: Student t test (two tailed, independent),. Chi-square/Fisher Exact test.

Results: In Group II Time to two segmentsensory level regression was significantly more (188.89±22.32) compared to Group I (118.96±33.69); duration of analgesia and motor block was also more. VAS scores in Group II were less compared to Group I. Rescue doses required in Group II were less compared to Group I.

Conclusions: Addition of dextrose have proved to be effective in quick onset of sensory, motor blockade and longer duration of blockade and prolonged two segment regression time with no adverse side effects.

Keywords: Dextrose; Levobupivacaine; Sub arachnoid Block.

Introduction

Intrathecal medications with the perfect balance of sensory and motor block with minimal side effects is always missed by researchers.

Due to its long duration of action, racemic bupivacaine is used for the regional, intrathecal, and epidural block by most anesthetists. Myocardial depression and even cardiac arrest can occur after accidental intravascular injection, resuscitation has been found to be difficult and may be unsuccessful. This led to the search for a local anesthetic agent with lower cardiotoxicity.[1]

Ropivacaine, registered for use in 1996, introduced in India in 2009, is produced as pure

Corresponding Author: **Ravi Madhusudhana,** Professor, Department of Anesthesiology, SDUMC, SDUAHER, Kolar, Karnataka, 563101, India.

E-mail: ravijaggu@gmail.com

"S" enantiomer with lower lipid solubility, easier reversibility after inadvertent intravascular injection, significant reduction in central nervous system toxicity, lesser motor block and greater differentiation of sensory and motor block. Motor blockade of 0.75% ropivacaine was comparable to 0.5% bupivacaine.[2]

MLAD estimates for intrathecal ropivacaine, levobupivacaine, and bupivacaine in the first stage of spontaneous labor in nulliparous women is bupivacaine > levobupivacaine > ropivacaine.[3]

Therefore we have conducted a study to evaluate the efficacy of levobupivacine in the lower limb and lower abdominal surgeries and in try to find an alternate to the routinely used bupivacaine in our setup.

Objectives

Evaluation of effect of adding dextrose to levobupivacaine, compared to levobupivacaine plain in terms of time of onset of sensory blockade and Motor blockade as per Bromage scale; the height of sensory blockade, total duration of sensory blockade and motor blockade; two segment sensory regression time and Quality of analgesia. (VAS score). Number of Rescue analgesia doses for 24 hours and Incidence of adverse effects will be noted.

Materials and Methods:

Open Labelled Study

Selection of patients – Randomized table in computer

Source of Data

140 patients admitted for elective surgeries, to be done under spinal anesthesia during the period of January 2017 to December 2017.

Method of Collection of Data

Inclusion criteria: Patients belonging either gender, ASA grade I and II; Age 18-60 yr; Weight- more than 45 kg; Height- more than 150cm

Exclusion criteria: Patients suffering from cardiac Arrhythmias, heart blocks, bradycardia; Patients with known allergy to test drug; Patients with gross spinal abnormality, localised skin sepsis, hemorrhagic diathesis, neurological involvement/ diseases; Patients with head injury, raised intra cranial pressure; Patients who are hemodynamically unstable.

Sampling Procedure

After obtaining informed consent, patients will be randomly divided into two groups. Randomization will be done by computer generated table.

Group L: Hyperbaric Levobupivacaine with 150 mg dextrose. (0.3 ml of 50% dextrose), volume is 3.3 ml; Group p: Plain levo Bupivacaine. (volume is 3.3 ml)

All patients were examined a day before surgery. All were kept fasting overnight after 10:00 pm and received tab. Ranitidine 150 mg orally and tab. Alprazolam 0.5 mg orally as premedication at night before surgery and at 6:00 am with sips of water on the day of surgery. All patients were preloaded with 15 ml/kg ringer lactate solution after securing IV access with 18G cannula. In the operation theatre pulse rate, blood pressure, ECG and SpO_2 were monitored.

Under all aseptic precautions, left lateral position, 25G quincke spinal needle used for spinal block at L3-L4 interspace, midline approach and patient put to supine position. Patients in group L received 3 ml of 0.5% hyperbaric Levobupivacaine with 0.3 ml of 150 mg dextrose. Patients in group P received 3.3 ml of Plain levo Bupivacaine. The time of intrathecal injection is considered as 0 and the following parameters were observed.

Parameters observed

1. Time of onset of sensory blockade.
2. The height of sensory blockade.
3. Motor blockade as per Bromage scale.
4. Total duration of sensory blockade & motor blockade.
5. Quality of analgesia.(VAS score)
6. Two segment sensory regression time.
7. Need for rescue analgesia when patient complains of pain. (if VAS is >4, rescue analgesia Inj Tramadol; 50 mg was given and Number of doses given within 24 hrs was noted.
8. Incidence of adverse effects was noted.

Vitals recorded every 2 min for 10 min and then every 10 min throughout the intra operative period and also at the completion of surgery. The vital signs recorded at time 0, 2 min, 5 min and then every 10 min for first hour and half hourly till the end of surgery.

Rescue analgesia: is defined as analgesia given when patient complains of pain (VAS >4).

Quality of analgesia was assessed by visual analogue scale.

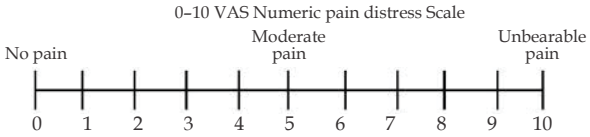
Visual analogue scale for pain:

0 No pain

1-3 Mild pain

4-6 Moderate pain

7-10 Severe pain



Motor blockade will be assessed using Bromage scale

Bromage scale: Grade Definition

0 Full flexion of knee and feet.

1 Inability to raise extended leg; able to move knee and feet.

2 Inability to raise extended leg and move knee; able to move feet.

3 Complete block of lower limb

Statistical Methods: Statistical analysis

Results on continuous measurements are presented on Mean ±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value: 0.01<P £ 0.05)

** Strongly significant (P value : P£0.01)

Statistical software: The Statistical software namely SPSS 22.0, and R environment ver. 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

Samples are age matched with P=0.505 and gender matched with P=0.567. Onset of sensory block was significantly fast in group II, less than 2 minutes in 33.3% compared to group I, 18.1%. maximum level of sensory block achieved, T6 was 45.8% in group II compared to 30.6% in Group I patients. After 6 minutes there was a significant drop in heart rate in Group II compared to Group I. Hemodynamics was stable in both groups.

In Group II Time to two segment regression of sensory level was significantly more (188.89±22.32) compared to Group I (118.96±33.69); total duration of analgesia and motor block was also more.

Table 2: VAS score when patient complaints of pain distribution in two groups of patients studied

VAS score when patient complaints of pain	Group I	Group II	Total
1	6(8.3%)	10(13.9%)	16(11.1%)
2	24(33.3%)	30(41.7%)	54(37.5%)
3	34(47.2%)	22(30.6%)	56(38.9%)
4	8(11.1%)	10(13.9%)	18(12.5%)
Total	72(100%)	72(100%)	144(100%)
Mean ± SD	2.61±0.80	2.44±0.90	2.53±0.85

P=0.242

VAS scores in Group II were less compared to Group I.

Table 3: Number of rescue analgesia doses given during 24 hours

Number of rescue analgesia doses given during 24 hours	Group I	Group II	Total
0	0(0%)	32(44.4%)	32(22.2%)
1	14(19.4%)	15(20.8%)	29(20.1%)
2	44(61.1%)	25(34.7%)	69(47.9%)
3	14(19.4%)	0(0%)	14(9.7%)
Total	72(100%)	72(100%)	144(100%)
Mean ± SD	2.00±0.63	0.90±0.89	1.45±0.94

P<0.001**

Table 1: Comparison of study variables according to two groups of patients studied

Variables	Group I	Group II	Total	P value
Time to two segment regression of sensory level (mins)	118.96±33.69	188.89±22.32	153.92±45.19	<0.001**
Total duration of analgesia (mins)	191.88±40.86	261.67±31.31	226.77±50.42	<0.001**
Time for complete motor recovery (mins)	175.14±39.79	302.65±32.72	238.9±73.56	<0.001**

Rescue doses required in Group II were less compared to Group I.

Discussion

Levobupivacaine is the S(–) enantiomer of racemic bupivacaine. The cardiotoxicity of levobupivacaine is less than that of racemic bupivacaine, due to the lower affinity of the S(–) isomer than the R(+) isomer for the inactivated state of the cardiac sodium channel. In view of this potential decrease in cardiotoxicity, levobupivacaine appears to be an attractive alternative to racemic bupivacaine.[1]

The volume of distribution and overall clearance of levobupivacaine was significantly lower than that of dextrobupivacaine (Burm et al. 1994).[4] Pharmacokinetics of the unbound fraction of levobupivacaine accounts for its less toxicity. Because of its increased protein-binding affinity, unbound fraction of levobupivacaine was significantly lower than that of unbound dextrobupivacaine.[5] The higher clearance of the unbound levobupivacaine explains the shorter elimination half-life of levobupivacaine. An increase in postoperative levels of alpha-1-glycoprotein (Dauphin et al. 1997) binds large amounts of levobupivacaine. [6]

Levobupivacaine has a safety margin of 1.3, which means toxic effects are not seen until the concentration rises by 30%. The concentration necessary to produce cardiac and neurotoxicity is higher for levobupivacaine than for racemic bupivacaine.[7]

Subarachnoid block with Levobupivacaine has similar sensory and motor characteristics and recovery like bupivacaine. Onset of sensory and motor block is hastened with hyperbaric levobupivacaine as compared to isobaric levobupivacaine. 15 mg of levobupivacaine provides an adequate sensory and motor block lasting for approximately 6.5h. Minimum effective local anesthetic dose of levobupivacaine as recommended by an up- and-down sequential design study is 11.7 mg.[7]

The quality of anesthesia, sensory and motor block characteristics and hemodynamics in patients requiring a higher level of spinal block for lower abdominal approach after either hyperbaric or isobaric levobupivacaine are of particular interest. Generally we use the hyperbaric form of local anesthetics for intra-abdominal surgery but the manufactured hyperbaric form of levobupivacaine is not available so it was interesting to know whether it is worth making it hyperbaric.[8]

According to Sananslip V et al., hyperbaric solution had a faster onset of sensory and motor block and reached T4 sensory levels, sufficient for the planned surgical procedures, faster, and more reliably than with isobaric. Nine patients (90%) in the hyperbaric group underwent surgery completely without additional anesthesia compared with four (40%) in the isobaric group.[8]

Sen et al. study says hyperbaric levobupivacaine had a faster onset of sensory and motor block and had a shorter duration of sensory and motor block than did the isobaric form, except for 2-segment regression time, which were similar in both groups.[9]

According to Mcloed GA et al., the density of local Anesthetics decreases with increasing temperature and increases in a linear fashion with the addition of dextrose. Levobupivacaine 5 mg ml±1 has a significantly higher density compared with bupivacaine 5 mg ml±1 and ropivacaine 5 mg ml±1 at 23 and 37°C both with and without dextrose. Levobupivacaine 7.5 mg ml±1 is an isobaric solution within all patient groups at 37°C.[10]

Glucose was usually used to increase the density of anesthetic solution, which can be great benefit to cycle fluctuations inhibition in clinical anesthesia. Hyperbaric local anesthetics made with glucose produce effectiveness in controlling the level of anesthesia.[11]

Difference in density between cerebrospinal fluid (CSF) and local Anesthetic is an important factor in determining the distribution of the solution. Local anesthesia density reduces with increased temperature and increases with an increase in glucose concentration.

But some studies that have reported that neurotoxicity occurred after intrathecal administration of local anesthetic mixed with glucose compared with intrathecal injection 5% lidocaine alone, the rats with 5% lidocaine with 10% glucose had induced more severe sensory impairment and morphologic damage.[11]

In our study we have compared the effects of plain levobupivacaine (0.5% 3.3 ml, 5 mg per ml) and addition of dextrose (0.3 ml 150 mg) to levobupivacaine (0.5% 3 ml 5 mg per ml). When compared to above studies, addition of dextrose have proved to be effective in faster onset of sensory and motor blockade and longer duration of blockade and prolonged two segment regression time with no adverse side effects.

In view of reducing the side effects caused by the use of dextrose, we use lesser dose that is 0.3 ml 50 mg per 0.1 ml when compared to Hyperbaric

Bupivacaine which we use daily has 80 mg per ml dextrose in it.

Conclusion

Addition of dextrose have proved to be effective in faster onset of sensory and motor blockade and longer duration of blockade and prolonged two segment regression time with no adverse side effects.

Key Messages

Levobupivacaine has less toxicity effects compared to bupivacaine and is available in plain form which is used in short surgeries and the block may not be extended with changing the position of patient as with Heavy bupivacaine. We have added dextrose to make it heavy and the beneficial effects are studied here.

Prior publication: Nil

Support: SDUAHER

Conflicts of interest: Nil

Permissions: Nil

References

1. Glaser C, Marhofer P, Zimper G, et al. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesth Analg 2002;94:194–98.
2. Khan A, Nanda HS, Chandra R. Levobupivacaine versus Ropivacaine: A Comparative Study of the Analgesic and Hemodynamic Spectrum. International Journal of Scientific Study 2016;16:190–95.
3. Camorcia M, Capogna G, Columb M. Minimum Local Analgesic Doses of Ropivacaine, Levobupivacaine, and Bupivacaine for Intrathecal Labor Analgesia. Anesthesiology 2005;102:646 –50.
4. Burm AG, Van der Meer AD, Van Kleef JW. Pharmacokinetics of the enantiomers of bupivacaine following intravenous administration of the racemate. Br J Clin Pharmacol 1994;38:125–9.
5. Burlacu CL, Buggy DJ. Update on local anesthetics: focus on levobupivacaine. Therapeutics and Clinical Risk Management 2008;4:381–92.
6. Dauphin A, Gupta RN, Young JE. Serum bupivacaine concentrations during continuous extrapleural infusion. Can J Anesth 1997;44:367–70.
7. Bajwa SJS, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. JOACP 2013;29:530–39.
8. Sanansilp V, Trivate T, Chompubai P, et al. Clinical Characteristics of Spinal Levobupivacaine: Hyperbaric Compared with Isobaric Solution. The Scientific World Journal 2012;12:1–7.
9. Sen H, Purtuloglu T, Sizlan Z. Comparison of intrathecal hyperbaric and isobaric levobupivacaine in urological surgery. Minerva Anestesiologica 2010;76:24–28.
10. McLeod GA. Density of spinal Anesthetic solutions of bupi–vacaine, levobupivacaine, and ropivacaine with and without dextrose. Br J Anesth. 2004;92:547–51.
11. Ma H, Xu T, Xiong X, et al. Effects of glucose administered with lidocaine solution on spinal neurotoxicity in rats. Int J Clin Exp Med 2015;8:20638–44.