ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 03 | March - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF TRAMADOL AS AN ADJUVANT TO INTRATHECAL ISOBARIC LEVOBUPIVACAINE FOR ELECTIVE LOWER LIMB SURGERIES UNDER SPINAL ANESTHESIA

Anesthesiology

Dr. Shiv Shankar Jangid (P.G. Resident) Department of anaesthesia, Jhalawar Medial college, jhalawar, Rajasthan, India.

Dr. S. P. Chittora (H.O.D.), Department of anaesthesia, Jhalawar Medial college, jhalawar, Rajasthan, India.

Dr. Mohammed Mishal* (P.G. Resident) Department of anaesthesia, Jhalawar Medial college, jhalawar, Rajasthan, India. *Corresponding Author

Dr. Akil Hussain Associate Professor, Department of anaesthesia, Jhalawar Medial college, jhalawar, Rajasthan, India.

ABSTRACT

Background: Long acting local anesthetics are used in subarachnoid block to increase the duration of anesthesia. Adjuvants are added to improve the duration of analgesia. The objective of this study was to evaluate the efficacy of tramadol as an intrathecal adjuvant to levobupivacaine in terms of duration of analgesia, onset of sensory blockade, onset of motor blockade, and duration of motor blockade.

Methodology: After obtaining the Institutional Ethical Committee approval and informed consent, sixty patients posted for infraumbilical surgeries were recruited. Randomization was done using a sealed envelope technique. Patients were divided into two groups: LT received 2.5 ml of 0.5% isobaric levobupivacaine with tramadol 25 mg (0.5 ml) and LS received 2.5 ml of 0.5% isobaric levobupivacaine with 0.5 ml of normal saline. Duration of analgesia, onset of sensory blockade, and onset and duration of motor blockade were recorded.

Results: There was no statistical difference in demographic data between the two groups. The mean onset time of sensory blockade in Group LS was 7.17±3.07 min and for Group LT was 8.53 ± 2.47 min, which was not statistically significant between two groups (P = 0.064). The mean onset time of motor blockade in Group LS was 9.76 ± 3.18 min and for Group LT was 11.23 ± 2.47 min, which was statistically significant between the two groups (P = 0.050). The mean time duration of analgesia in Group LS was 265.60± 39.18 min and for LT was 304.30 ± 24.88 min. There was mild prolongation of analgesia in Group LT, but it was statistically significant (P <0.001). The mean duration of motor blockade in Group LS was 197.93 ± 4.41 min and Group LT was 236.20 ± 33.89 min, which was statistically significant between the two groups (P <0.001). **Conclusion:** Tramadol as an adjuvant to isobaric intrathecal levobupivacaine does prolong analgesia significantly.

KEYWORDS

Analgesia, intrathecal adjuvants, levobupivacaine, tramadol

INTRODUCTION

Spinal anesthesia is a safe, reliable, and inexpensive technique with the advantage of providing surgical anesthesia and postoperative pain relief. It is also an effective treatment for operative pain and blunts autonomic, somatic, and endocrine responses. Till recently, bupivacaine 0.5% heavy was the only drug used for spinal anesthesia after the discontinuation of Lidocaine's intrathecal use. Bupivacaine is available as a racemic mixture of its enantiomers, dextrobupivacaine and levobupivacaine. Levobupivacaine, the pure S ( ) enantiomer of racemic bupivacaine, is a new long acting local anesthetic that has recently been introduced in India because of its significantly decreased cardiovascular and central nervous system toxicity;[1 3] levobupivacaine seems to be an attractive alternative to bupivacaine. Conventionally, the dose of levobupivacaine used for spinal anesthesia is 15 mg.[4 6] Although 15 mg isobaric levobupivacaine dose provides an adequate sensory and motor block for most surgical procedures, the duration of sensory blockade and motor blockade is shorter and is more hemodynamic stable when compared to hyperbaric bupivacaine.[7,8] Intrathecal adjuvants are added primarily to increase the duration of analgesia. It would be very advantageous to have early ambulation, hemodynamic stability, and prolonged analgesia in most clinical settings, particularly in day care surgery. We did the study to assess the feasibility of achieving this using tramadol as an intrathecal adjuvant to isobaric levobupivacaine. Fentanyl is the most common opioid which has been studied as an adjuvant to spinal anesthesia. We chose tramadol as we wanted to find out if it would be a good alternative in situations where fentanyl is not freely available due to licensing issues with fentanyl and also because fentanyl is a short acting opioid.

This study was aimed to evaluate the efficacy of low dose tramadol as an intrathecal adjuvant to isobaric levobupivacaine in terms of onset of sensory blockade, duration of analgesia, onset of motor blockade, duration of motor blockade.

METHODS-

This was a prospective randomized study conducted in Department of Anaesthesiology at a tertiary care hospital after the approval by the Institutional Research and Human Medical Ethics Committee. Sixty patients of American Society of Anesthesiologists (ASA) physical status Class 1 and 2, in the age group of 18–60 years who were posted for elective infraumbilical surgeries under spinal anesthesia were included for the study. Pregnant patients, patients posted for emergency surgeries, patients shorter than 150 cm, and patients having any absolute contraindication for spinal anesthesia such as raised intracranial pressure, severe hypovolemia, bleeding diathesis, local infection, and patients allergic to any of the study drugs were excluded from the study. Sixty patients were divided into two groups: Group LS (levobupivacaine + normal saline) of thirty patients and Group LT (levobupivacaine + tramadol) having 30 patients.

All patients were evaluated in the preanesthesia clinic and also underwent thorough preanesthetic checkup the night before surgery. Informed consent was obtained from each patient after explaining about the anesthetic procedure and details of the study. All patients were premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg on the night before surgery and on the morning of surgery and a fasting status of 8h was ensured. Intravenous (IV) line was secured with 18 G IV cannula and preloading was done with normal saline 10 ml/kg 15 min before spinal anesthesia. Baseline oxygen saturation, heart rate, systolic, diastolic, and mean arterial pressure (MAP) were recorded. Patients were randomized by sealed envelope technique into one of the two groups – Group LS and Group LT.

Group LS: Received 2.5 ml (12.5 mg) of 0.5% intrathecal isobaric levobupivacaine with 0.5 ml with normal saline. Group LT: Received 2.5 ml (12.5mg) of 0.5% intrathecal isobaric levobupivacaine with tramadol 25 mg (0.5 ml tramadol). The test drugs were loaded in a 5 ml syringe by an anesthesiologist who was not involved in the study, just before spinal anesthesia. Thus, both the observer and the subjects were blinded to the study drugs. Patients were placed in left lateral position. Under strict aseptic precautions, lumbar puncture was performed at the level of L3–L4 through a midline approach using 25 G or 26 G Quincke spinal needle and study drug was injected after the confirmation of needle tip in the subarachnoid space by free flow of cerebrospinal fluid. The onset of sensory blockade was assessed using ether soaked gauze for every 2 min till complete loss of sensation at T8. Motor block was assessed every 2 min till a modified Bromage score of 3 was achieved.

Hemodynamic parameters were recorded at the baseline, 5th min, and then for every 10 min till the end of surgery. Hypotension was defined as MAP <65 mm Hg and was treated with IV mephentermine 6 mg boluses. Bradycardia was defined as heart rate <50 beats/min and was treated with IV atropine 0.6 mg. Patients in whom there was inadequate spinal blockade or spinal anesthesia failed or in cases where spinal anesthesia wears off before completion of surgery general anesthesia was to be administered and such cases were to be excluded. In our study, we did not have to administer general anesthesia to any of the patients as rescue anesthetic plan. Patients were monitored in the postoperative period for hemodynamic changes. Verbal numerical rating score was recorded every 15 min postoperatively; the time when the patient first complained of pain and if the verbal numerical rating scale score was ≥4, injection diclofenac sodium 75 mg was administered in 100 ml normal saline as rescue analgesia.

Time interval from onset of sensory block to requirement of first rescue analgesia was recorded as the duration of analgesia. Further analgesia was given as per the institutional acute postoperative pain service protocol. Duration of motor blockade was assessed by monitoring modified Bromage scale every 15 min postoperatively till the patient was able to completely move both the lower limbs (Bromage score 0).

Complications such as nausea or vomiting and shivering were recorded. Shivering was treated by covering the patient and using a patient warmer.

The study parameters were defined as follows-

1. **Onset of Sensory Block:** Time interval from spinal injection time to achieve T10 blockade
2. **Duration of analgesia:** Time interval from onset of sensory block to requirement of first rescue analgesia.
3. **Onset of Motor Block:** Time interval from spinal injection time to Bromage scale 3.
4. **Duration of motor block:** Time interval from onset of motor block to attainment of complete movements (Bromage 0) in both lower limbs.

STATISTICALANALYSIS-

Statistical analysis was done with an alpha error of 0.05 and power of 80% to achieve a difference of 60 min in the duration of analgesia, sample size was calculated as 30 in each group. Statistical analysis was carried out using IBM SPSS Statistics for Windows, (Version 19.0. Armonk, NY: IBM Corp.). Descriptive analysis was reported as mean and standard deviation, median, and range of continuous variables and $P < 0.05$ was considered statistically significant. Parametric data were analyzed using unpaired *t*-test.

RESULTS

The mean age of patients in Group LS was 38.56 ± 11.17 years and in Group LT was 41.33 ± 14.51 years. There was no statistical difference in age distribution between the two groups (P = 0.532). The mean weight of patients in Group LS was 66.70 ± 6.80 kg and in Group LT was 63.23 ± 9.20 kg. There was no statistical difference in weight distribution between the two groups (P = 0.224).

Table-01: Comparison of onset and duration of sensory and motor blockade

	Group LS (Mean±SD)	Group LT (Mean±SD)	P value
Onset of sensory blockade (min)	7.17 ± 3.07	8.53 ± 2.47	0.064
Duration of sensory blockade (2SRT) (min)	98.77±12.30	104.60±12.51	0.074
Onset of motor blockade (min)	9.76 ± 3.18	11.23 ± 2.47	0.050
Duration of motor blockade (min)	197.93±4.41	236.20±33.89	<0.001
Total duration of analgesia (min)	265.60±39.18	304.30±24.88	<0.001

In Group LS, 23 patients had no complications, 3 patients had hypotension, 3 patients had shivering, and 1 patient had bradycardia. In Group LT, 24 patients had no complications, 4 patients had hypotension, 1 patient had shivering, and 1 patient had bradycardia [Table 2].

Table 2: Complications

Complication	Group LS	Group LT
Nil	23	24
Hypotension	3	4
Shivering	3	1
Bradycardia	1	1
Vomiting	0	0

DISCUSSION

In this study, we have evaluated the efficacy of tramadol as an adjuvant to levobupivacaine for intrathecal administration in infraumbilical surgeries. We studied the onset of sensory and motor blockade and duration of sensory and motor blockade. To the best of our knowledge, there are no studies evaluating the efficacy of tramadol as an adjuvant to intrathecal isobaric levobupivacaine for elective infraumbilical surgeries.

Longacting local anesthetics are used in subarachnoid block to increase the duration of anesthesia. Adjuvants increase the duration of analgesia. Levobupivacaine has been recently introduced in India. Levobupivacaine has been introduced into clinical practice because of its lower cardiac and central nervous system toxic effects. Bardsley *et al*., Morrison *et al.*, and Huang *et al*.[13] concluded that levobupivacaine, the pure S (−) enantiomer of racemic bupivacaine, a new long acting local anesthetic, has significantly decreased cardiovascular and central nervous system toxicity compared to racemic bupivacaine. We have used tramadol as intrathecal adjuvant in our study. Tramadol exists as the racemic (1:1) mixture of the (+) and (−) enantiomer. It has dual mechanism of action. The (+) enantiomer of tramadol contributes to analgesia by inhibiting the reuptake of serotonin, the (−) enantiomer by inhibiting the reuptake of noradrenaline, and the Odesmethyl metabolite by binding with relative high affinity (compared to tramadol) to the μ opioid receptor. The monoaminergic activity of tramadol increases the inhibitory activity of the descending pain pathways thus resulting in a suppression of nociceptive transmission at the spinal level.[10,13] In our study, isobaric levobupivacaine 0.5% 2.5 ml with tramadol 25 mg as an adjuvant (3 ml) Group LT and levobupivacaine 0.5% 2.5 ml with 0.5 ml (3ml) Group LS was administered intrathecally. The mean onset time of sensory blockade following spinal anesthesia in Group LS was 7.17 ± 3.07 min and for Group LT was 8.53 ± 2.47 min. There was no statistical significance in onset of sensory blockade between two groups (P = 0.064) [Table-1]. The mean duration of sensory blockade using 2 segment regression time following spinal anesthesia for Group LS was 98.77 ± 12.30 min and Group LT was 104.60 ± 12.51 min. This was of no statistical significance difference in the duration of sensory blockade between the two groups (P =0.074) [Table-1]. The mean onset time of motor blockade following a spinal anesthesia in Group LS was 9.76 ± 3.18 min and for Group LT was 11.23 ± 2.47 min. This was of statistical significance in onset of motor blockade between the two groups (P = 0.05) [Table-1]. The mean duration of motor blockade following spinal anesthesia for Group LS was 197.93 ± 34.41 min and Group LT was 236.20 ± 33.89 min. This was of statistical significance difference in the duration of motor blockade between the two groups (P <0.001) [Table-1]. The total duration of analgesia in Group LS was 265.60± 39.18 min and for LT was 304.30 ± 24.88 min. There was prolongation of analgesia in Group LT and it was statistically significant (P <0.001) [Table-1].

Sezen *et al.* have done the comparison of levobupivacaine Group L and levobupivacaine with fentanyl as an intrathecal adjuvant, Group LF in infraumbilical surgeries under spinal anesthesia.[14] Onset of maximum sensory block in Group LF (levobupivacaine fentanyl) was 8.46 ± 1.87 min and for Group L (levobupivacaine) was 15.80 ± 2.43 min and maximum Bromage score was 2 in both groups but was achieved earlier in Group LF ($P < 0.000$). Duration of motor blockade for Group LF (levobupivacaine + fentanyl) was 188.52 ± 9.81 min and for Group L (levobupivacaine) was 152.76 ± 9.79 min. Total duration of analgesia was also prolonged in Group LF 265.16 ± 26.18 min as compared to Group L 168.16 ± 11.08 min.

Chattopadhyay *et al*. compared the anesthetic efficacy and safety of two concentrations of local anesthetic agent levobupivacaine in patients undergoing vaginal hysterectomy.[15] Forty four patients of ASA physical status Classes I and II were randomized to receive an intrathecal injection of one of two local anesthetic solutions. Each patient in Group A (n = 22) received 2 ml of isobaric levobupivacaine 5 mg/ml (10 mg) with 25 μg of fentanyl, while each patient in Group B (n

= 22) received 4 ml of isobaric levobupivacaine 2.5 mg/ml (10 mg) with 25 µg of fentanyl, onset of sensory block till T10 for Group A (2 ml isobaric levobupivacaine 5 mg/ml with 25 µg of fentanyl) was 6.9 ± 1.7 min and for Group B (4 ml isobaric levobupivacaine 2.5 mg/ml with 25 µg of fentanyl) was 6.4 ± 1.5 min ($P > 0.05$). The onset of motor block was significantly faster in Group A compared with that in Group B. Onset of Grade 3 motor block for Group A was 8.9 ± 5 min and for Group B was 12.8 ± 7 min ($P < 0.05$). Duration of sensory block for Group A was150.6 ± 14 min and for Group B was 121.4 ± 10 min ($P < 0.05$). Duration of motor block for Group A was 130.6 ± 12 min and for Group B was 108.8 ± 11 min ($P < 0.05$).

Chakraborty *et al*. studied the role of intrathecal tramadol added as an adjuvant to bupivacaine for spinal anesthesia in patients undergoing major gynecological surgery, two groups, that is, Group A and Group B.[9] Group A ($n = 25$) received 3 ml of 0.5% hyperbaric bupivacaine (15 mg) with 0.2 ml of normal saline and Group B ($n = 25$) received 3 ml 0.5% hyperbaric bupivacaine and 0.2 ml (20 mg) tramadol by intrathecal route at L3–L4 interspace. Standard monitoring of the vital parameters was done. Levels of sensory block and sedation score were recorded. Assessment of pain was done using visual analog scale (VAS). In Group B patients, the VAS score was significantly lower as compared to Group A patients. The duration of analgesia was 210 ± 10.12 min in Group A; whereas in Group B, it was 380 ± 11.82 min, which was found to be statistically significant ($P < 0.05$). The mean duration of motor blockade following spinal anesthesia for Group LS (Normal saline) was 170.23 min and Group LT (tramadol) was 190.76 min. There was no statistically significant difference in the duration of motor blockade between the two groups ($P = 0.14$).

Parthasarathy and Ravishankar compared postoperative analgesia using intrathecal hyperbaric lignocaine 5% with 10 mg tramadol Group T and hyperbaric lignocaine alone Group C.[16] Duration of postoperative analgesia was significantly longer in Group T (lignocaine 5% with 10 mg tramadol) 310 ± 127.49 min than Group C (hyperbaric lignocaine) 131 ± 40.51 min ($P < 0.01$), there was no significant adverse effects recorded. Parthasarathy and Ravishankar concluded that lignocaine with tramadol provided effective postoperative pain relief in the initial 12 h in comparison to lignocaine alone.

We have observed that the mean time duration of analgesia in Group LS (normal saline) was 265.60 ± 39.18 min and for LT (Tramadol) was 304.30 ± 24.88 min. There was mild prolongation of duration of analgesia in Group LT, but it was statistically significant ($P < 0.001$); these findings are similar to the study done by Parthasarathy and Ravishankar comparing postoperative analgesia using intrathecal hyperbaric lignocaine 5% with 10 mg tramadol - Group T and hyperbaric lignocaine alone - Group C.[16] Duration of postoperative analgesia was significantly longer in Group T (310 ± 127.49 min) than Group C (131 ± 40.51 min) ($P < 0.01$). They have found significant prolongation of analgesia in spite of using a short-acting local anesthetic, i.e., lignocaine. In our study, the onset of sensory blockade in Group LT (levobupivacaine 0.5% 2.5 ml with tramadol 25 mg) was 8.53 ± 02.47 min, contrary to the findings of the study done by Chattopadhyay et al. in which they found a faster onset of sensory blockage of 6.9 ± 1.7 min when fentanyl 25 µg was used as an adjuvant to 3 ml 0.5% isobaric levobupivacaine.[15] In our study, the onset of motor blockade in Group LT was 11.23 ± 2.47 min contrary to the findings of the study done by Chattopadhyay et al. in which they found a faster onset of motor blockade of 8.9 ± 5 min when fentanyl 25 µg was used as an adjuvant to 3 ml 0.5% isobaric levobupivacaine.[15] Isobaric levobupivacaine has unpredictable onset of spinal anesthesia, contrary to previous studies. We have to give spinal anesthesia well in advance before the start of surgery. Tramadol in low doses prolongs analgesia without much adverse effects, moderate prolongation of analgesia of 30 min which is not clinically significant.

CONCLUSION-

twenty five milligram tramadol as an adjuvant to isobaric intrathecal levobupivacaine prolong analgesia significantly. Tramadol is an effective adjuvant to intrathecal isobaric levobupivacaine.

REFERENCES-

1. Bardsley H, Gristwood R, Baker H, Watson N, Nimmo W. A comparison of the cardiovascular effects of levobupivacaine and rac bupivacaine following intravenous administration to healthy volunteers. Br J Clin Pharmacol 1998;46:245 9.
2. Morrison SG, Dominguez JJ, Frascarolo P, Reiz S. A comparison of the electrocardio graphic cardiotoxic effects of racemic bupivacaine, levobupivacaine, and ropivacaine in anesthetized swine. Anesth Analg 2000;90:1308 14.
3. Huang YF, Pryor ME, Mather LE, Veering BT. Cardiovascular and central nervous system effects of intravenous levobupivacaine and bupivacaine in sheep. Anesth Analg 1998;86:797 804.
4. Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, ropivacaine and levobupivacaine. Acta Biomed 2008;79:92 105.
5. Burlacu CL, Buggy DJ. Update on local anesthetics: Focus on levobupivacaine. Ther Clin Risk Manag 2008;4:381 92.
6. Foster RH, Markham A. Levobupivacaine: A review of its pharmacology and use as a local anaesthetic. Drugs 2000;59:551 79.
7. Casati A, Moizo E, Marchetti C, Vinciguerra F. A prospective, randomized, double blind comparison of unilateral spinal anesthesia with hyperbaric bupivacaine, ropivacaine, or levobupivacaine for inguinal herniorrhaphy. Anesth Analg 2004;99:1387 92.
8. Guler G, Cakir G, Ulgey A. A comparison of spinal anesthesia with levobupivacaine and hyperbaric bupivacaine for cesarean sections: A randomized trial. Open J Anesthesiol 2012;2:84 9.
9. Chakraborty S, Chakrabarti J, Bhattacharya D. Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries. Indian J Pharmacol 2008;40:180 2.
10. Alemanno F, Ghisi D, Fanelli A, Faliva A, Pergolotti B, Bizzarri F, *et al.* Tramadol and 0.5% levobupivacaine for single shot interscalene block: Effects on postoperative analgesia in patients undergoing shoulder arthroplasty. Minerva Anestesiol 2012;78:291 6.
11. Raffa RB, Friderichs E, Reimann W, Shank RP, Codd EE, Vaught JL. Opioid and nonopioid components independently contribute to the mechanism of action of tramadol, an 'atypical' opioid analgesic. J Pharmacol Exp Ther 1992;260:275-85.
12. Budd K, Langford R. Tramadol revisited. Br J Anaesth 1999;82:493 5.
13. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clin Pharmacokinet 2004;43:879 923.
14. Sezen G, Demiraran Y, Karagoz I, Kucuk A. The assessment of bupivacaine tramadol and levobupivacaine tramadol combinations for preemptive caudal anaesthesia in children: A randomized, double blind, prospective study. Int J Clin Exp Med 2014;7:1391 6.
15. Chattopadhyay S, Halder B, Saha GC, Karmakar S, Pahari S. Comparison of two concentrations of isobaric intrathecal levobupivacaine for vaginal hysterectomy. Indian J Pain 2013;27:154 8.
16. Parthasarathy S, Ravishankar M. Single dose intrathecal tramadol in the management of post appendicectomy pain. J Anaesth Clin Pharmacol 2002;18:419 22.