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A comparative study of intrathecal levobupivacaine-clonidine and bupivacaine in the quality of anesthesia for patients undergoing hernioplasty

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ABSTRACT

Background: Bupivacaine is most commonly used amino-amide drug for subarachnoid block in hernioplasty. Levobupivacaine has similar pharmacological activity to that of bupivacaine with minimal cardiotoxicity. Clonidine, an α^2 adrenergic agonist, potentiates the action of local anesthetics when used intrathecally and enhances post-operative analgesia. **Aims and Objectives:** This prospective, comparative, observational study was aimed to compare the effects of 0.5% levobupivacaine with clonidine and 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty for the quality of surgical anesthesia and hemodynamic changes with any significant intraoperative complications. **Materials and Methods:** After receiving approval from the institutional ethics committee and written informed consent, 80 male patients aged between 18 and 60 years, BMI <30 kg/m^2, height >150 cm, and American society of anesthesiologists physical status1 and 2 posted for elective hernioplasty were enrolled into two equal groups of 40 patients, group LC and group B. Patients in group LC received 15 mg 0.5% isobaric levobupivacaine with 30 μg clonidine and patients in group B received 15 mg hyperbaric bupivacaine intrathecally. SPSS version 20 was used for analysis, and $P<0.05$ was considered statistically significant. **Results:** In group LC, onsets of both sensory and motor blocks were delayed, whereas durations of motor and sensory block with analgesia were longer. Tachycardia, hypotension, nausea, vomiting, and shivering were observed greater in numbers in group B, whereas incidence of bradycardia was more in group LC. **Conclusion:** Prolonged duration of sensory and motor block, prolonged analgesic effect, and hemodynamic stability without any significant adverse effects may make this combination a better alternative to hyperbaric bupivacaine for hernioplasty.

Key words: Levobupivacaine; Clonidine; Bupivacaine; Hernioplasty

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INTRODUCTION

Subarachnoid block is the most widely used anesthetic technique employed for patients undergoing hernioplasty providing fast onset and effective sensory and motor blockade.[1] Hyperbaric bupivacaine is widely used amino-amide drug for subarachnoid block due to its long duration of action and combined sensory and motor blockade.[2] However, bupivacaine has profound systemic toxicity. It is more cardiotoxic, can precipitate ventricular arrhythmias by its sodium channel blockade in the conduction system.[3] Levobupivacaine, the pure S(-) enantiomer of bupivacaine, has emerged as a useful alternative for subarachnoid block to hyperbaric bupivacaine.[4,5] Clinically, levobupivacaine is better tolerated, and reports of cardiotoxicity and neurotoxicity are minimal.[6] Occasional adverse effects are usually reversible with minimal treatment without any fatal outcome.

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Clonidine is an alpha 2 adrenergic receptor agonist potentiating the action of local anesthetics when applied intrathecally, thus enhancing post-operative analgesia.[7] It has been used as alternative to neuraxial opioids reducing chances of respiratory depression.[8]

Aims and objectives

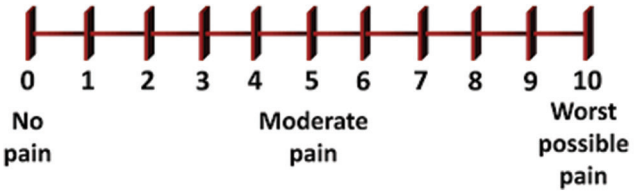
This study was aimed to compare the effects of 0.5% isobaric levobupivacaine with clonidine and 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty for the quality of surgical anesthesia with respect to onset of desired sensory block, onset of desired motor block, duration of sensory block, duration of motor block, duration of spinal analgesic effect, hemodynamic changes, and any significant complications (nausea, vomiting, shivering, bradycardia, and tachycardia) during intraoperative period.

MATERIALS AND METHODS

After receiving approval from the institutional ethics committee (Memo No: BMC/Ethics/061 dated January 28, 2020) and written informed consent from the patient, a prospective, comparative, observational study was conducted for a period starting from February 2020 to July 2020. A study conducted to compare same drugs in vaginal hysterectomy enrolled thirty patients in three groups.[9] Taking a cue from the study, we decided to enroll 40 patients in two groups.

Eighty male patients aged between 18 and 60 years, BMI <30 kg/m^2, height >150 cm American society of anesthesiologists physical status 1 and 2 posted for elective hernioplasty had been selected, whereas patients with severe systemic disorder, difficult airway, emergency surgery, and any contraindications to central neuraxial blockade had been excluded. Eighty patients were enrolled into 2 equal groups of 40 patients. The investigators were not involved in formulating any treatment plans at any stage of the study. All patients received premedication with diazepam 5 mg orally at 10 pm on day before surgery and patients were not allowed to take solid food 6 h before surgery and clear fluid 2 h before surgery. Pantoprazole 40 mg and metoclopramide 10 mg 2 h before surgery were given to all patients orally.

Intravenous cannulation (i.v.) was done inside operation theater using 18 gauze cannula and co-loaded with 10 mL/kg Ringer's lactate and patients were briefed about the methods used for assessing sensory and motor blockade along with 11-point visual analog scale (VAS).[10]



Visual analog scale

Multichannel monitor including electrocardiogram, pulse oximeter, and non-invasive blood pressure was attached, and baseline parameters were noted.

Then patients were kept in sitting position. After antiseptic dressing and draping, subarachnoid block was given at L3-L4 intervertebral space using 25 gauze Quincke's needle. Patients who received 15 mg 0.5% isobaric levobupivacaine with 30 μg clonidine were enrolled in group LC and patients enrolled in group B received 15 mg hyperbaric bupivacaine intrathecally. Patients were then shifted to supine position.

Intraoperative heart rate (HR), mean arterial pressure (MAP), and oxygen saturation (SpO_2) were monitored continuously and recorded immediately after the block, then every 5 min for next 15 min and then every 15 min till the end of the surgery. Sensory levels were checked bilaterally at midclavicular line by loss of cold sensation to rectified spirit every minute until desired level till 10th thoracic vertebrae (T10) was achieved. Motor block assessment was done according to modified Bromage scale as given below, until Bromage 3 was achieved.

MODIFIED BROMAGE SCALE[11]

0 – No paralysis, able to flex hips/knees/ankles
1 – Able to move knees, unable to raise extended legs
2 – Able to flex ankles, unable to flex knees
3 - Unable to move any part of the lower limb.

Surgery was started once desired level of sensory block up to T10 was achieved. Onset of Sensory Block was defined as the interval between intrathecal administrations of drug to desired level of sensory block up to T10 dermatome. Onset of motor block was defined as the interval between intrathecal administration of drug to Bromage scale score 3.

Status of pain was assessed by VAS,[9] ranging from 0 (no pain) to 10 (maximal pain). Duration of sensory block was defined as interval between onset of sensory block to VAS score 3. Duration of motor block was defined as interval between onset of motor block to the point at which Bromage score was back to zero. Duration of spinal analgesic effect was defined as interval between intrathecal

administration of drug to requirement of first dose of rescue analgesia (t).

After establishment of sensory block, midazolam 1 mg i.v. was given for sedation, and oxygen was delivered at 4lit/min through facemask.

Hemodynamic parameters such as HR, MAP, and SpO_2 were monitored in postoperative period and recorded at1 h intervals till the requirement of first dose of rescue analgesia.

Hypotension was defined as decrease in MAP by >20% of the baseline value. Bradycardia was defined as HR <60 beats/min, and tachycardia was defined as HR more than 100 beats/min.

Bradycardia was treated by atropine 0.6 mg i.v. Hypotension was corrected by phenylephrine i.v. in titrated dose. Nausea and vomiting were treated by the correction of hypotension and ondansetron 4 mg i.v., and shivering was treated by warm fluids, warm blanket, and tramadol 50 mg i.v.

There was no patient loss in the study period.

Continuous variables were expressed as mean, median, and standard deviation and compared across the groups using Mann–Whitney U-test. Categorical variables were expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi-Square test for Independence of Attributes/Fisher's Exact Test as appropriate. The statistical software SPSS version 20 had been used for the analysis. An alpha level of 5% had been taken, i.e., if any $P<0.05$, it had been considered statistically significant.

RESULTS

All demographic variables are comparable in both the study groups (Table 1).

Patients in group LC (as shown in Table 2) took longer average time (9.50±0.94 min) to reach desired height of sensory block up to T10 than patients in group B with average time (2.56±0.51 min). Patients in group LC took longer average time (10.89±1.07 min) to reach Bromage 3 than patients in group B with average time (3.34±0.36 min). Duration of sensory block was longer for group LC with average time (337.65±10.64 min) than in group B with average time (171.73±6.09 min). Duration of motor block was longer for group LC with average time (304.25±13.36 min) than in group B with average time (159.15±5.44 min). Duration of spinal analgesic effect was longer in group LC with average time (345.13±9.37 min) than group B with average time (179.25±5.13 min).

Table 3 shows hypotension was not observed in 92.5% (n=37) participants in group LC, whereas 7.5% (n=3) participants had one episode. In Group B, 50% (n=20), 12.5% (n=5), and 2.5% (n=1) of participants had one, two, and three episodes, respectively. Eighty seven and percentage (n=35) of participants in group LC had no episode of bradycardia, whereas 12.5% (n=5) of participants had single episode of bradycardia as compared to 92.5% (n=37) of participants in group B with no episodes of bradycardia, whereas 7.5% (n=3) of participants had 1 episode of bradycardia. Ninety-two and half percent (n=37) of participants in group LC did not report any episode of tachycardia, whereas 7.5% (n=3) showed single episode of tachycardia, whereas 50% (n=20) of participants in group B showed no tachycardia and rest 50% showed 1 episode of tachycardia which was statistically significant. Two and a half percent participants (n=1) in group LC and 27.5% (n=11) in group B showed 1 episode of nausea and vomiting. Two and a half percent participants (n=1) in group LC and 40% (n=16) in group B showed 1 episode of shivering.

DISCUSSION

Hyperbaric bupivacaine is most commonly used intrathecal local anesthetic drug for infra-umbilical surgeries such as hernioplasty, but unfavorable cardiac profile along with short duration of sensory and motor block makes its uses tricky. Levobupivacaine has stable hemodynamic profile, as compared to bupivacaine. Addition of clonidine as an adjuvant to levobupivacaine has not been extensively studied yet in hernioplasty surgeries. In this study, we have compared the levobupivacaine-clonidine combination to bupivacaine for the quality of surgical anesthesia and also

Table 1: Demographic variables

Demographic Variables	Group		P-value	Significance
	Group LC	Group B		
Age (years)	50.33±3.94 (50)	50.25±4.97 (1)	0.828	Not significant
Height (cm)	159.03±3.15 (159)	160.30±4.55 (160)	0.148	Not significant
Weight (kg)	67.98±2.78 (68)	67.48±4.03 (68)	0.410	Not significant
BMI (kg/m^2)	26.90±1.30 (26.69)	26.33±2.24 (26.24)	0.192	Not significant

Data has been presented as mean±standard deviation (Median)

Table 2: Quality of anaesthesia

Variables	Group		P-value	Significance
	Group LC	Group B		
Duration of surgery (min)	55.15±3.45 (55)	55.50±2.78 (56)	0.677	Not Significant
ONSET of sensory block up to T10 dermatome (min)	9.50±0.94 (9.50)	2.56±0.51 (2.50)	<0.001	Significant
Onset of motor block Bromage 3 (min)	10.89±1.07 (11)	3.34±0.36 (3.5)	<0.001	Significant
Duration of sensory block up to VAS score 3 (min)	337.65±10.64 (340)	171.73±6.09 (172)	<0.001	Significant
Duration of motor block up to Bromage 0 (min)	304.25±13.36 (301)	159.15±5.44 (160)	<0.001	Significant
Duration of analgesia (t) (min)	345.13±9.37 (350)	179.25±5.13 (180)	<0.001	Significant

Data has been presented as mean±standard deviation (median, VAS: Visual analog scale)

Table 3: Undesirable incidences

Number of episodes	Group		Total n (%)	P-value	Significance
	Group LC n (%)	Group B n (%)			
Bradycardia					
0	35 (87.5)	37 (92.5)	72 (90)	0.655	NotSignificant
1	5 (12.5)	3 (7.5)	8 (10)		
Total n (%)	40 (100)	40 (100)	80 (100)		
Hypotension					
0	37 (92.5)	14 (35)	51 (63.75)	<0.001	Significant
1	3 (7.5)	20 (50)	23 (28.75)		
2	0 (0)	5 (12.5)	5 (6.25)		
3	0 (0)	1 (2.5)	1 (1.25)		
Total n (%)	40 (100)	40 (100)	80 (100)		
Tachycardia					
0	37 (92.5)	20 (50)	57 (71.25)	<0.001	Significant
1	3 (7.5)	20 (50)	23 (28.75)		
Total n (%)	40 (100)	40 (100)	80 (100)		
Shivering					
0	39 (97.5)	24 (60)	63 (78.75)	<0.001	Significant
1	1 (2.5)	16 (40)	17 (21.25)		
Total n (%)	40 (100)	40 (100)	80 (100)		

hemodynamic profile in intraoperative period and any other significant side effects.

The onset of desired sensory block and desired motor block were found to be faster in the present study when hyperbaric bupivacaine alone was used as opposed to levobupivacaine–clonidine combination. This delay in patients who received levobupivacaine and clonidine could be explained by differences in the density of drugs and also structural differences of two agents as density of hyperbaric bupivacaine is greater than levobupivacaine – clonidine combination. Although Vanna et al.,[12] in 2006 observed in a study that there was no significant differences in onset for either sensory or motorblock between isobaric levobupivacaine and hyperbaric bupivacaine for transurethral endoscopic surgery. However, delayed onset of sensory block for levobupivacaine–clonidine combination in our study was in line with a study conducted by Jethani K et al. previous study appears to be retracted.[13]

Duration of sensory block and analgesia in levobupivacaine-clonidine combination receiving participants were found to be longer than those receiving hyperbaric bupivacaine alone. Analgesic potency ratio of levobupivacaine and bupivacaine was 0.81 and motor block potency ratio 0.71 as observed in another study.[14] Addition of clonidine to levobupivacaine enhanced the analgesic effect by spinal cord anti-nociception through post-junctional α_2 adrenergic receptor mediated nor-adrenaline release in dorsal horn. Niemi[15] observed that the addition of clonidine in dose of 3 μg/kg increased duration of sensory analgesia for knee surgeries. Other investigators observed that the duration of motor block was increased when clonidine was added to local anesthetics.[16] In this study, levobupivacaine–clonidine combination receiving participants showed longer duration of motor block than those who received bupivacaine (304 min vs. 159 min, respectively).

Hypotension occurred in 65% of participants in participants receiving bupivacaine, whereas only 7.5% participants in levobupivacaine-clonidine combination group showed some episodes of hypotension. This could be explained by more cephalic spread of hyperbaric drug in supine position. The previous study has concluded that specific gravity of isobaric levobupivacaine is very similar to cereberospinal fluid causing less effect of gravitational forces. Hence, chance of unexpected high cephalic spread is much lower in levobupivacaine-clonidine combination group.[17]

Twelve and half a percent (n=5) of participants in levobupivacaine-clonidine combination group showed episodes of bradycardia, while in bupivacaine group, it was 7.5% (n=3). Effect of clonidine on presynaptic-mediated inhibition of noradrenaline and direct action on AV node could explain increased bradycardia episodes in levobupivacaine-clonidine combination group.[18]

Percentage of participants showing tachycardia (50% vs. 7.5%), nausea and vomiting (27.5% vs. 2.5%), and shivering (40% vs. 2.5%) were greater in bupivacaine recipients than levobupivacaine – clonidine combination group, respectively.

Limitations of the study

This observational study was conducted in a small population coming from a very small geographical area. Multicentric interventional double-blinded randomized studies are needed to have a clear scientific opinion regarding the use of levobupivacaine and clonidine combination as a substitute to hyperbaric bupivacaine. Hyperbaric levobupivacaine was not available in our study setting at that point of time. Hence, we could not compare two hyperbaric drugs at the same time. Difference in baricity was an important limitation in this study.

CONCLUSION

Isobaric levobupivacaine-clonidine combination provides better hemodynamic stability among participants. The onset of desired sensory and motor blockade was delayed for this combination than hyperbaric bupivacaine. However, prolonged duration of sensory and motor block, prolonged analgesic effect without any significant adverse effects make this combination a safer and better alternative to hyperbaric bupivacaine for patients undergoing hernioplasty.

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REFERENCES

1. Casati A, Moizo E, Marchetti C and 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(5):1387-1392.
   https://doi.org/10.1213/01.ANE.0000132972.61498.F1
2. Berde CB and Strichartz GR. Local anesthetics. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP and Young WL, editors. Miller's Anaesthesia. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 1044.
3. Berde CB and Strichartz GR. Local anesthetics. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP and Young WL, editors. Miller's Anaesthesia. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 1048.
4. Sanford M and Keating GM. Levobupivacaine: A review of its use in regional anaesthesia and pain management. Drugs. 2010;70(6):761-791.
   https://doi.org/10.2165/11203250-000000000-00000
5. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, et al. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesth Analg. 2002:94(1):194-198.
   https://doi.org/10.1097/00000539-200201000-00037
6. Foster RH and Markham A. Levobupivacaine: A review of its pharmacology and use as a local anaesthetic. Drugs. 2000;59(3):551-579.
   https://doi.org/10.2165/00003495-200059030-00013
7. Van TuijlI, van Klei WA, van der Werff DB and Kalkman CJ. The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after Caesarean section: A randomized controlled trial. Br J Anaesth. 2006;97(3):365-370.
   https://doi.org/10.1093/bja/ael182
8. Shelgaonkar VC, Manjrekar PS, Narwate S and Sonowal J. Clinical evaluation of intrathecal 0.5% isobaric levobupivacaine with and without fentanyl or clonidine in elective lower abdominal and orthopedic surgeries. Res Chron Health Sci. 2015;1(3): 156-166.
9. Bhavani V and Raajesh IJ. Comparison of intrathecal isobaric levobupivacaine, levobupivacaine-clonidine, with hyperbaric bupivacaine as a control for quality of anaesthesia intraoperative hemodynamics and duration of post-operative pain relief in patients undergoing vaginal hysterectomy. Indian J Clin Anaesth. 2016;3(2):148-154.
   https://doi.org/10.5958/2394-4994.2016.00031.7
10. Wewers ME and Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. Res Nurs Health. 1990;13(4):227-236.
   https://doi.org/10.1002/nur.4770130405
11. Brull R, Macfarlane AJ and Chan VW. Spinal, epidural, and caudal anesthesia. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP and Young WL, editors. Miller's Anaesthesia. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015. p. 1703.
12. Vanna O, Chumsang L and Thongmee S. Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery. J Med Assoc Thai. 2006;89(8):1133-1139.
13. Jethani K, Gangwani V, Rakesh DR. Comparison between hyperbaric bupivacaine, isobaric levobupivacaine and levobupivacaine with clonidine given intrathecally in patients undergoing lower limb orthopaedic surgery under spinal anaesthesia. IJMSIR 2020;5(4):95-100.
14. Camorcia M, Capogna G, Lyons G and Columb M. Epidural test dose with levobupivacaine and ropivacaine: Determination of ED(50) motor block after spinal administration. Br J Anaesth. 2004;92(6):850-853.
   https://doi.org/10.1093/bja/aeh155
15. Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamics, and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anaesthesiol Scand. 1994;38(7):724-728.
   https://doi.org/10.1111/j.1399-6576.1994.tb03985.x

16. Burlacu CL, Frizelle HP, Moriarty DC and Buggy DJ. Fentanyl and clonidine as adjunctive analgesics with levobupivacaine in paravertebral analgesia for breast surgery. Anaesthesia. 2006;61(10):932-937.
https://doi.org/10.1111/j.1365-2044.2006.04793.x
17. Gori F, Corradetti F, Cerotto V and Peduto VA. Influence of positioning on plain levobupivacaine spinal anesthesia in cesarean section. Anesthesiol Res Pract. 2010;2010:212696.
https://doi.org/10.1155/2010/212696
18. Baker A, Klimscha W, Eisenach JC, Li XH, Wildling E, Menth-Chiari WA, et al. Intrathecal clonidine for postoperative analgesia in elderly patients: The influence of baricity on hemodynamic and analgesic effects. Anesth Analg. 2004;99(1):128-134.
https://doi.org/10.1213/01.ANE.0000114549.17864.36

Authors Contribution:
SDu- Literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation; **SDa-** Clinical protocol, manuscript preparation, editing; **DS-** Definition of intellectual content, concept, design, coordination, and manuscript revision; **JN-** Design of study, statistical analysis and interpretation, review manuscript, and submission of article.

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