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A comparative study of intrathecal low dose bupivacaine with fentanyl and low dose levobupivacaine with fentanyl in transurethral resection of prostate: Randomized, double blind, prospective study

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Abstract

Objective: Isobaric levobupivacaine has been recently introduced for intrathecal use and there are very few studies comparing it with widely used hyperbaric bupivacaine. So this randomized trial was planned to study the effectiveness of intrathecal low dose isobaric levobupivacaine with fentanyl and compare it with low dose hyperbaric bupivacaine with fentanyl in transurethral resection of prostate.

Materials and Methods: This prospective, randomized, double blinded study was conducted in 60 ASA physical status I and II patients, aged between 50-80 years and posted for transurethral resection of prostate under subarachnoid block. Enrolled patients were divided into two groups of 30 each. Patients in Group B received 7.5mg, 0.5% hyperbaric bupivacaine with 25mcg fentanyl intrathecally while patients in Group L received 7.5mg, 0.5% isobaric levobupivacaine with 25mcg fentanyl intrathecally. Time to achieve sensory block to T10 level, max spread of sensory block, time to two-segment regression and time to S1 regression were recorded. Motor blockade was assessed at every 2 minute for 20 minute, at the end of the surgery and in recovery room. Onset time of motor block, maximum motor block and duration of motor block were also recorded.

Results: A total of 60 subjects were enrolled. Baseline parameters were comparable. Onset of sensory block was significantly faster in group B compared to group L. The mean time of onset in Group B was 4.75±0.79 min. and in Group L was 6.60±0.61 min. Both group had statistically significant difference in onset and duration of motor block. The mean time of onset of motor block in Group B was 6.4±1.6 min and in Group L was 9.9±2.3 min. The mean duration of motor block in Group B was 164.17±22.8min and in Group L was 138.27±23.5min. Group B had statistically significant dense block compared to group L. The median MBS in Group B was 1(95% C.I. 1.18-1.68) and in Group L was 2 (95% CI 2.13-2.86). In group B, 20 patients had complete motor block while in group L number of patient with complete motor block was only 4.

Conclusion: Our results, suggest that subarachnoid low-dose isobaric levobupivacaine fentanyl provides lesser degree of motor block & for short duration when compared with heavy bupivacaine.

Keywords: Levo bupivacaine, Bupivacaine, TURP, Spinal anaesthesia

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Introduction

Now a day increasing numbers of elderly patients are coming for surgery due to longer life expectancy. Benign hypertrophy of prostate (BPH) is common in this age group for which transurethral resection of prostate (TURP) is required in symptomatic patients.(1) This patient population has a greater anesthetic risk because of the prevalence of coexisting cardiovascular and pulmonary diseases.(2) Spinal anesthesia (SA) is technique of choice for TURP which besides providing surgical anesthesia and postoperative analgesia, has added advantage of preserving cerebral function which in turn allows earliest recognition of unique complication related to TURP.(3)

Racemic hyperbaric bupivacaine has been considered as local anesthetic of choice for SA. Recently levobupivacaine, a pure S-enantiomer of racemic bupivacaine is introduced as an attractive alternative to bupivacaine. Its cardiovascular (CVS) and central nervous systems (CNS) toxicity is reported to be lower as compared to bupivacaine.(4) In view of very few studies(7,8,9) about clinical use of levobupivacaine in SA this randomized, double blind, prospective study was planned. In this study clinical effectiveness, hemodynamic effect, sensory & motor block characteristic of intrathecally administrated isobaric 0.5% levobupivacaine was compared with hyperbaric 0.5% bupivacaine in patient posted for TURP.

Methodology

This prospective, randomized, double blinded study was conducted at a tertiary care center in western Rajasthan, India. After approval of Institutional Ethics Committee and written informed consent from patients, 60 ASA physical status I and II patients, aged between 50-80 years posted for elective TURP were enrolled. Patients having known hypersensitivity to amide local anesthetics, abnormal coagulation profile, spinal anomalies, skin infections and unwilling to accept regional anesthesia were excluded from study.

Simple randomization was done with computer generated random number sequence. Subjects were randomized with a 1:1 allocation ratio as consecutive eligible subjects got enrolled and divided into 2 groups of 30 each. The allocated interventions were written on paper slips, placed in serial-numbered, opaque envelopes and sealed. The envelopes were serially opened and the allocated intervention was implemented. Patients in Group B received 7.5mg, 0.5% hyperbaric bupivacaine with 25µg fentanyl intrathecally while patients in Group L received 7.5mg, 0.5% isobaric levobupivacaine with 25µg fentanyl intrathecally. An anesthesiologist prepared the intrathecal drugs just prior to positioning the patient for SA. Patient and the anesthesiologist who attended patient intraoperatively and collected data in the postoperative period were blinded to the study drug.

Preanesthetic evaluation and necessary routine investigations were done. In operating room, routine monitoring including continuous electrocardiography for heart rate (HR), non-invasive blood pressure for mean blood pressure (MBP) and plethysmography for peripheral oxygen saturation (Spo2) were attached and baseline vital parameters were recorded. Intravenous access was secured with 20 G and ringer lactate solution was started. After aseptic precautions, lumbar puncture was performed at L3–L4 using a 25 G spinal needle with the patient in sitting position and the study drug solution was injected as per the groups allocated. Immediately after performing intrathecal injection, patients were placed in the supine position and time (T_0) was noted. Block characteristic (sensory and motor block) was assessed every 2 minute for 20 minute. Sensory blockade was assessed by pinprick in the mid-clavicular line in each dermatome on both sides with a blunt 27 G needle at three point scale, 0- Sharp pain; 1- Dull pain (analgesia); 2- No pain (anesthesia). Maximum height of the block and time taken to achieve maximum height was also recorded. Motor blockade was assessed based on a modified Bromage scale (MBS)[5] at six point scale, 1- Complete motor block, 2-Able to move feet only, 3- Just able to move knee, 4- Weakness on hip flexon on supine position, 5- No weakness on hip flexon on hip flexon in supine position, 6-Able to perform knee band.

Onset of sensory blockade was defined as the time taken from the completion of the injection of study drug till the patient did not feel the pin prick at T10 level. The onset time of motor blockade was defined as the interval between intrathecal administration of drug and impairment in motor power on movement.

ECG, SpO2, and NIBP were monitored and recorded at every 2 minute for 20 minute and then every 5 minute till the end of the surgery. Supplementary 5 $L.min^{-1}$ O_2 was given to all patients via a facemask. No additional analgesics were administered during the surgery. At the end of the surgery patient was shifted to post-anesthesia care unit (PACU).

In PACU monitoring of the vitals and block characteristic was done at every hour till complete motor recovery. For sensory block, time to two-segment regression and time to regression to S1 dermatome was recorded. Duration of sensory block was taken as the time from the onset of sensory block to regression of sensory block upto S1 dermetome. The duration of motor blockade was defined as the interval from intrathecal administration to the point at which patient was able to move his limbs.

Side effects such as nausea, vomiting, bradycardia, hypotension, respiratory depression (RR <8/min) and pruritus were noted and treated accordingly. A decrease in MBP more than 20% from baseline level or to < 60 mmHg was defined as hypotension and treated with IV ephedrine 5mg bolus. HR ≤ 50 beats/min was defined as bradycardia and treated with IV atropine 0.5mg bolus.

Sample size of minimum 28 was derived based on the assumption of α (type 1 error) of 5%, β (type 2 error) 0.2, and power of the study 80% to detect a 35% difference in duration of motor block. The data obtained was tabulated and analyzed using the computer software (SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). Results of continuous measurements were presented as mean (standard deviation [SD]) if not specified, and results of categorical measurements were presented in numbers or ratio. Student's *t*-test was used for numerical values and chi-square test was used for categorical values. The value $P < 0.05$ was considered statistically significant.

Result

Demographical characteristics and duration of surgery were comparable in both groups (Table 1). Intraoperative hemodynamics were comparable and there was no significant difference between both groups (Fig. 1).

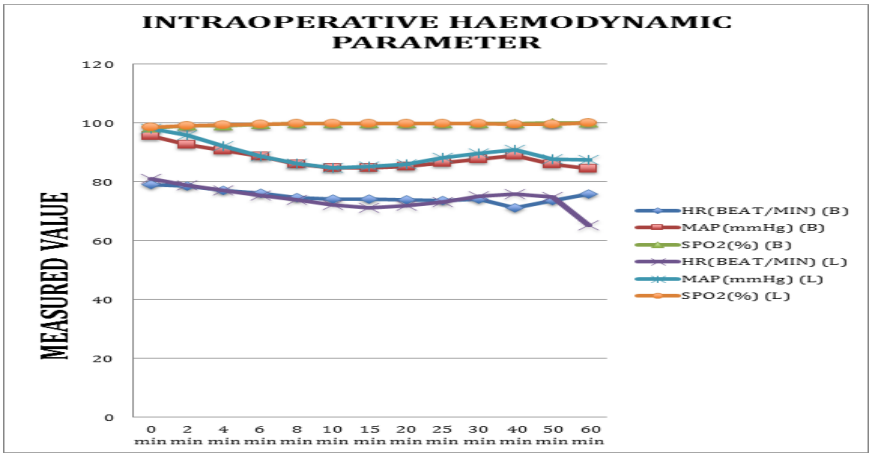

Fig. 1: Intraoperative Haemodynamics in both group

Onset of sensory block was significantly faster in group B compared to group L. The mean time of onset of sensory block in Group B was 4.75±0.79 min and in Group L was6.60±0.61 min (p value <0.05). Both group had statistically significant difference in onset and duration of motor block. The mean time of onset of motor block in Group B was 6.4±1.6 min and in Group L was 9.9±2.3 min (p value < 0.05). The mean duration of motor block in Group B was 164.17±22.8min and in Group L was 138.27±23.5min (p value <0.05). (Table 2). Group B had statistically significant dense block compared to group L. The median MBS in Group B was 1(95% C.I. 1.18-1.68) and in Group L was 2 (95% CI 2.13-2.86) p value was <0.0001. In group B, 20 patients had complete motor block while in group L number of patient with complete motor block was only 4 (Table 3).

Maximum spread of sensory block was limited to T6 dermatome in both groups. Two segment regression time, regression time of sensory block to S1 dermatome, duration of sensory block was comparable in both group and there was no statistically significant difference.

Patient in both group had minor side effects related to opioid use as nausea vomiting and pruritis but none of them showed statistically significant difference. None of the patient had incidence of hypotension, bradycardia or respiratory depression (Table 4)

Table 1: Patients demographics

Variable	Group B (Mean ± SD)	Group L (Mean ± SD)	P value
Age (Years)	65.20±6.7	66.63±6.5	> 0.05
Height (cm)	160.27±6.4	160.63±6.2	> 0.05
Weight (kg)	62.10±7.0	62.86±6.1	> 0.05
ASA (1:2)	23:7	20:10	> 0.05
Duration of surgery(Min)	43.06±7.8	43.16±8.0	> 0.05

Table 2: Block characteristics

Variable	Group B (Mean ± SD)	Group L (Mean ± SD)	P value
Time of onset of sensory block (Min)	4.75±0.7	6.60±0.6	< 0.05
Time of onset of motor block (Min)	6.40±1.6	9.96±2.3	< 0.05
Maximum sensory level achieved (Thoracic dermatome)	6.33±1.5	6.13±1.1	> 0.05
Time to Two segmental regression (min)	78.80±12.9	80.13±12.0	> 0.05
Time to S1 segment Regression (min)	182.40±18.2	174.90±15.8	> 0.05

Duration of motor block (min)	164.17±22.8	138.27±23.51	< 0.05
Duration of sensory block (min)	217.97±26.8	210.33±30.6	> 0.05

Table 3: Distribution of MBS

MBS	Group B (no. of patients)	Group L (no. of patients)
1	20	4
2	7	12
3	3	10
4	0	3
5	0	1
6	0	0
Total	30	30

Table 4: Distribution of adverse effect

Side Effect	Group B(No. of patients)	Group L (No. of patients)
Nausea & Vomiting	3	2
Bradycardia	0	0
Hypotension	0	0
Pruritis	7	6
Shivering	3	3
Respiratory Depression	0	0

Discussion

Geriatric patients are always challenging for anesthesia as Advancing age, co-morbidities, altered pharmacokinetics and pharmacodynamics of drugs increase the morbidity and mortality in these patients.[2,3] Bibulet et al[6] reported that intrathecal administration of bupivacaine was associated with 40% increase in incidence of hypotension in elderly population compared to young population. No ideal anesthetic technique has been described in elderly population but if a thorough understanding of changes that occurs in physiology and pharmacology is there, an optimal anesthetic technique can be designed.

SA is the most commonly used anesthetic technique for TURP surgery. Levobupivacaine, the pure S-enantiomer of racemic bupivacaine, is a new long-acting local anesthetic that has recently been introduced in the clinical routine. Levobupivacaine is proving increasingly popular to replace bupivacaine given its similar efficacy and fewer cardiovascular and CNS side effects.[4] Its pharmacokinetic properties are similar to those of racemic bupivacaine. In most of the studies where the same doses of levobupivacaine and bupivacaine were used, sensory and motor block characteristics were found to be similar.[7-9]

Various studies suggested that intrathecal hyperbaric bupivacaine is associated with higher incidence of hypotension and bradycardia intraoperatively. Rosa Herrera et al[10] studied hemodynamic impact of isobaric levobupivacaine versus hyperbaric bupivacaine for subarachnoid anesthesia in patients aged 65 and older undergoing hip surgery and found that levobupivacaine group had lower incidence of intraoperative hypotension. Fattorini et al[9] reported better cardiovascular stability in the levobupivacaine group compared to bupivacaine in orthopedic surgery. Our study didn't found any significant difference in hemodynamic stability. It was possible probably because dose of local anesthetic (LA) used was too small to produce any significant cardiovascular effect. Addition of fentanyl further helped in reducing the dose of LA. Ben David et al[11] compared bupivacaine alone and fentanyl added as adjuvant to bupivacaine and found that bupivacaine alone is associated with higher incident of hypotension.

Our results showed that intrathecal hyperbaric bupivacaine is associated with early onset of sensory & motor block as compared to isobaric levobupivacaine. Hyperbaricity of bupivacaine may be attributed to it as it helped in early cephalic spread of LA. Our results are in line of other studies where both agents were compared intrathecally.[12] D'Souza et al[13] compared intrathecal hyperbaric 0.5% bupivacaine and isobaric 0.5% levobupivacaine for lower abdominal surgeries and proved that hyperbaric bupivacaine produces clinically and statistically significant earlier onset of sensory and motor block as compared to isobaric levobupivacaine. Sari et al,[14] Erdil et al[15] and Erbay et al[16] found that onset of motor block & progression of block to T4 was significantly fast in bupivacaine group when compared with levobupivacaine in spinal anesthesia.

Our study results show that hyperbaric bupivacaine produces dense motor block for prolonged duration compared to isobaric levobupivacaine. This result is well supported by various previous studies.[16] The mean Maximum MBS achieved in Group B was significantly higher compared to levobupivacaine. In bupivacaine group 20 patients had complete block while in levobupivacaine group only 4 patients had complete motor block. Acboy et al[17] compared intrathecal administration of bupivacaine with fentanyl and levobupivacaine with fentanyl and found that bupivacaine produces higher degree of motor block compared to levobupivacaine. Gulen Guler et al[18] compared levobupivacaine and hyperbaric bupivacaine for cesarean sections in spinal anesthesia and concluded that the combination of levobupivacaine with fentanyl can be a good alternative in cesarean sections as duration of motor block is short compared to bupivacaine. Gautier et al[19] compared the same doses of levobupivacaine and bupivacaine during spinal anesthesia for caesarean

delivery, and reported that duration of motor block and analgesia was shorter in the levobupivacaine. Addition of opiods further decreases duration of motor block. Kararmaz et al[20] studied that addition of fentanyl to levobupivaine significantly shortens duration of motor block.

The max sensory level achieved, two segment regression time and regression time to S1 dermatome didn't had significant difference among both group. There was no significant difference regarding adverse reaction among both groups.

Conclusion

We conclude from this study that subarachnoid administration of low-dose 0.5% levobupivacaine (7.5mg) plus fentanyl in elderly patients undergoing TURP was as safe as the administration of low-dose hyperbaric bupivacaine (7.5mg) plus fentanyl. Our results, suggest that subarachnoid low-dose isobaric levobupivacaine fentanyl provides lesser degree of motor block & for short duration when compared with heavy bupivacaine. Although onset is delayed with isobaric levobupivacaine, it can be considered as suitable alternative of bupivacaine for short duration surgeries which requires less motor blockage.

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