ORIGINAL RESEARCH PAPER
Volume-9 | Issue-3 | March-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY OF INTRATHECAL ISOBARIC BUPIVACAINE (0.5%), LEVOBUPIVACAINE (0.5%) AND ROPIVACAINE (0.5%) IN PATIENTS UNDERGOING TURP.

Anaesthesiology

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ABSTRACT

This study was done to compare the anesthetic efficacy and safety of three local anesthetic agents : racemic bupivacaine and its two isomers : ropivacaine and levobupivacaine, in patients undergoing transurethral resection of prostate. One hundred-sixty two patients, ASA I-III, were randomized to receive an intrathecal injection of one of three local anesthetic solutions. Group B (n = 54) received 2 ml of isobaric bupivacaine 5 mg/ml(10 mg). Group R (n = 54) received 2 ml of isobaric ropivacaine 5 mg/ml (10 mg). Group L (n = 54) received 2 ml of isobaric levobupivacaine 5 mg/ml (10 mg). The onset and duration of sensory block at dermatome level T10,time to achieve highest level of sensory block, regression of sensory block up to L-1 as well as the onset,and duration of motor block were recorded, as were any adverse effects, such as bradycardia , hypotension, hypoxia, tremor, nausea and/or vomiting.The onset of motor block was significantly faster in the bupivacaine group compared with that in the ropivacaine group and almost the same of that in the levobupivacaine group ($P < 0.05$). Ropivacaine presented a shorter duration of both motor and sensory block than bupivacaine and levobupivacaine ($P < 0.05$).
Bupivacaine required more often the use of a vasoactive drug (ephedrine) compared to both ropivacaine and levobupivacaine and of a sympathomimetic drug (atropine) compared to the ropivacaine group.

KEYWORDS

Anesthetic techniques, regional ; anesthetic techniques, subarachnoid ; anesthetics local, bupivacaine ; ropivacaine ; levobupivacaine ; surgery.

INTRODUCTION :

Spinal anaesthesia is the most popular technique of regional anaesthesia for short duration procedures because it is simple to perform, economical and produces rapid onset of anaesthesia and complete muscle relaxation. It carries high efficiency and involves less doses of drugs being used. Although there are some limitation and complication with the use of spinal anaesthesia (fixed duration, post dural puncture headache, hypotension, lesser control of block height, transient neurological symptoms and rarely cauda equina syndrome), yet they are preventable if the technique is performed meticulously under strict aseptic precautions with proper choice of drug to be use. Bupivacaine is available as a racemic mixture of its enantiomers, dextrobupivacaine and levo bupivacaine. The last few years, its pure S-enantiomers ropivacaine and levobupivacaine, have been introduced into clinical practice because of their lower toxic effects for heart and central nervous system.The aim of the present study was to compare the safety and efficacy of either plain ropivacaine10 mg, plain bupivacaine 10 mg or plain levobupivacaine10 mg in patients undergoing transurethral resection of prostate under spinal anesthesia.

MATERIAL AND METHODS

With the approval of the research review board and Institutional Ethical Committee and written informed consent of the patient, 162 ASA physical status I-III patients, scheduled for transurethral resection of prostste under spinal anesthesia, were prospectively enrolled. Patients who had contraindications to spinal anesthesia, allergy to amide local anesthetics and a significant history of drug or alcohol abuse were excluded. Exclusion criteria also included morbid obesity (Body Mass Index BMI > 29 kg/m2), as well as diabetic, neurological and musculoskeletal diseases that could make our technique difficult.

Following arrival in the anesthetic room, I.V.access was established and an infusion of 500 ml Ringer's lactated (L-R) commenced. For spinal anesthesia 25 GZ quincke's needle was used. Correct needle placement was identified by free flow of cerebrospinal fluid and 2 ml (10 mg) of the study drug was injected over 10 s. Using a sealed envelope technique, patients were randomly allocated to three groups : patients in group B received plain bupivacaine 10 mg (2 ml isobaric 0.5%), in group L received plain Levobupivacaine 10 mg (2 ml isobaric 0.5%) and in group R received plain ropivacaine 10 mg (2 ml isobaric 05%). All 2-ml solutions were prepared in an adjacent room by a supervisor not involved in the subsequent evaluation of the study-patient. After the injection of the drug the spinal needle was removed and the patient placed supine. Standard monitoring was used throughout the operation. ECG and pulse – oximetry were monitored continuously while arterial pressure was measured at 5-min intervals. Heart rate and arterial pressure were recorded before intrathecal injection, 5 minutes after the intrathecal drug administration, and thereafter every 10 minutes till the end of the operation and one hour after the end of the operation, at the ward. Any hypotension (mean arterial pressure lower than 60 mmHg) or bradycardia (heart rate < 50/min) incidents were treated with ephedrine 5 mg or atropine 0.5 mg increments. A decrease in SpO2 to < 93% was defined as hypoxia and treated with supplemental oxygen via a Venturi - mask 40% at 4 l/min. The level of sensory block was evaluated by loss of pinprick sensation (20-gauge hypodermic needle). The test was performed every 5 minutes till loss of discrimination to pinprick for the first 60 minutes and then every 10 minutes until its full recovery. We checked bilaterally S1, L3, T12, T10, T8, T6 or higher (T4) dermatomes by needle protrusion 2 mm through a guard and we used C5-6 as baseline point for normal sensation. Sensory block score was determined using the following scale : 1 = hypoalgesia, 2 = analgesia, 3 = analgesia and hypoaesthesia and 4 = anesthesia. Motor blockade was assessed using a modified Bromage scale (0 = no motor block, 1 = hip blocked, 2 = hip and knee blocked, 3 = hip, knee and ankle blocked). The maximum modified bromage score reached and duration of the motor block (from spinal injection until modified bromage 1 and/or 0 score) were registered every 5 minutes after drug's injection until full recovery. The onset time of sensory or motor blockade was defined as the interval between intrathecal administration and maximum pinprick score, or a modified bromage score of 3, respectively. The duration of sensory or motor blockade was defined as the interval from intrathecal administration to the point of complete resolution of the sensory block, or to the point in which the modified bromage score was back to zero. The maximum level of sensory block, the onset time, the duration of sensory and motor blockade, as well as the interval from intrathecal administration to the point of a 2-segment regression of sensory blockade and the eligibility for home discharge was recorded. The occurrence of adverse events, including bradycardia, hypotension, decrease in oxygen saturation SpO2 < 93%, tremor, as well as nausea and vomiting was also recorded.

STATISTICS:

All statistical analyses were performed using the *SPSS* Statistical Software (ver. 17.0.0). Quantitative data are presented as means and standard deviation (mean ± sd) and qualitative data as frequency and 95% confidence interval (CI). Age, weight, height and BMI as well as ASA physical status were analyzed using Frequencies test. We analysed systolic, diastolic and mean arterial pressure, as well as heart rate and surgical time, using ANOVA Repeated Measures test with correction according to Bonferroni. Onset time, spread and duration of

either motor or sensory blocks as well as use of vasoconstrictive drugs or atropine were analysed with student's t test. Side effects' incidence (nausea, vomiting, tremor, convulsions) was analysed using Fischer's exact test.

RESULTS :

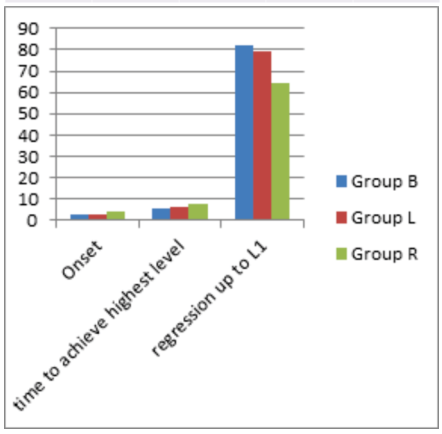
The study was confined to 162 patients of more than 55 years of age of ASA grade I-III group undergoing transurethral resection of prostate at S.M.S. hospital Jaipur. The patients were divided into 3 groups of 54 patients each.

Group B consist of (n=54) patients, received 10 mg of 0.5% isobaric Bupivacaine, total volume 2ml.

Group L consist of (n=54) patients, received 10 mg of 0.5% isobaric Levobupivacaine, total volume 2ml.**Group R** consist of (n=54) patients received, 10 mg of 0.5% isobaric Ropivacaine, total volume 2ml. Observations regarding the demographic data, pre operative vitals, sensory blockade (onset, level and duration), motor blockade (onset & duration), duration of analgesia, effects on vitals and intra operative & post operative side effects have been recorded. On statistical analysis $p<0.05$ was considered to be significant. On the basis of results obtained in the study, the following conclusions were made:-The mean time of onset of sensory block was 2.72±1.18 min in group B, 3.07±1.61 min in group L and 4.29±1.32 min in group R. Statistically there was significant difference between the groups($P<0.05$). The mean time to achieve highest level of sensory block was 5.31±1.24 min in group B, 6.01±1.60 min in group L and 7.53±1.29 min in group R more or less similar in all the groups. The mean time of sensory block to regression up to L1 dermatome 82.13±9.83 min in group B, 79.35±9.90 min in group L and 64.72±14.73 min in group R, which was earlier in group R than both L and B and significantly different but there was no significant difference between group B and group L .($P>0.05$) .

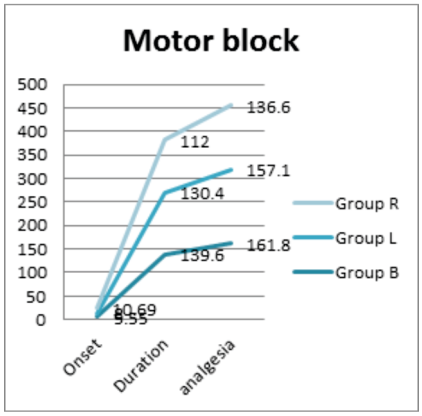
- Demographic Data

DATA	Group B	Group L	Group R	Significance
Age (Yrs.)	67.2±8.06 (56-85)	69.07 ±7.97 (58-85)	69.37±6.56 (60-87)	NS
Height(cms.)	169.83±8.29 (155-178)	169.03 ±8.02 (158-178)	168.43±7.81 (160-178)	NS
Weight (Kg.)	71.67±4.94 (60-80)	70.24 ±4.96 (64-85)	71±5.75 (62-84)	NS
ASA Grade (I/II/III)	45/6/3	44/8/2	46/5/3	NS



Sensory block

The mean time to onset of motor block was 5.55±1.32 min in group B, 8.00±1.82min in group L, 10.69±1.74 min in group R. There was significant difference between the groups. The onset of motor block was significantly faster in the bupivacaine group compared to levobupivacaine and ropivacaine group.($p<.05$).Mean duration of motor blockade was significantly more in group B (139.6±8.89) and group L(130.4±10.32) as compared to group R (112.00±9.93) min , ($P<0.05$). Mean duration of complete analgesia [161.8±12.96min in group B, 157.1±9.88 min in group L , 136.6±8.89 min in group R] and mean duration of effective analgesia [176.7±10.6min in group B, 170.5±12.18 min in group L, 147.2±9.84 min in group R] significantly more in bupivacaine group, statistically there was significant difference bet ween all the groups.($P<0.05$). No significant change in pulse rate and mean arterial pressure in all the groups.



No significant difference in the incidence of hypotension, bradycardia, nausea, and shivering in all the groups.Other adverse effect like vomiting pruritus, urinary retention headache, sedation and respiratory depression were not found in any case.

DISCUSSION

Spinal anaesthesia is the most popular and preferred technique of regional anesthesia till date for short duration transurethral resection of prostate because it is simple to perform, economical and produces rapid onset of anaesthesia. It carries high efficiency and involves less doses of drugs being used. There are some limitation and complication with the use of spinal anesthesia (fixed duration, post dural puncture headache, hypotension, lesser control of block height, transient neurological symptoms [22] and rarely cauda equina syndrome), however they are preventable if the technique is performed meticulously under strict aseptic precautions with proper choice of drug to be used.

Ropivacaine considered to be less cardiotoxic on a milligram basis.

D.A.Mc Namee et al compared plain ropivacaine with bupivacaine (17.5mg) for major orthopedic surgeries.They concluded that ropivacaine offered a reliable motor block with predictable and rapid return of motor function after surgery.

The mean age, weight, height and ASA grade were not statistically significant ($p> 0.05$) different in three groups.

Onset of sensory block was defined as the time from the intrathecal injection of the study drug to the time taken to achieve anesthesia to pin prick at T10 dermatome level. In our study mean time of onset of sensory block in group B (2.72±1.18 min.), group L (3.07±1.61 min.) and group R was (4.29±1.32min.). **Mean time to achieve highest level of sensory block** in group B (5.31±1.24 min.) and group L was (6.09±1.60 min) group R (7.53±1.29min.). In present study the mean time of onset of sensory block and mean time to achieve highest level of sensory block between the different groups were found to be comparable and statistically significant [$p < 0.05$]. Results of our study similar to **D.A. McNamee et al [2002]** study in which they concluded that intrathecal administration of either 17.5 mg plain ropivacaine or 17.5 mg plain bupivacaine was well tolerated and an adequate block for total hip arthroplasty was achieved in all patients. A more rapid postoperative recovery of sensory and motor function was seen in Group R compared with Group B.

Results of our study were also similar to ***Chung CJ et al (2004)*** *study in which they* concluded that onset time of sensory block to T10 or to peak level was later in the Ropivacaine group ($P < 0.05$). In contrast to our study **JF Luck et al.[2008]** found that there were no significant differences between the groups with regard to the mean time to onset of sensory block at T10, the extent of spread, or mean time to maximum spread. **Regression up to L1 dermatome:** In present study there was significant difference in time of sensory block regression to L1 dermatome in group B v/s R ($p<0.05$) and group L v/s R ($p < 0.05$) but there was no significant difference between group B v/s L ($p>0.05$). Results of our study coincide with ***Casati*** **A., Moizo E. et al (2004)** in which they said that the faster complete regression of spinal anesthesia observed in patients receiving ropivacaine. However, in their study, no

differences were observed in the onset time both of sensory and motor block between ropivacaine, levobupivacaine or bupivacaine. The reason for the observed differences between our results and those seen in the above-mentioned studies, is not apparent, but it could be attributed to methodological differences, such as a difference in the dosage use in the population studied or in the potency.

Onset of motor block was defined as the time taken for motor block to reach Modified Bromage score 3.The mean time of the onset of motor block in Group B (5.55±1.32minutes), in Group L (8.00±1.82minutes) and in Group R (10.69±1.74minutes). There was statistically significant difference among the study groups($p<0.05$). **Duration of motor block** mean time to achieve complete recovery of motor block and assessed by recording the time elapsed from the maximum to the Modified Bromage score 6. Duration of motor block was in group B (139.6±8.89min.) in group L (130.4±10.32min.) and in group R (112.0±9.93min). The duration of motor block was found to be significantly longer in Group B and Group L compared to Group R ($p<0.05$). Our results were similar to **Al-Abdulhadi et al.[2007] and Chung CJ et al[2004]** study in regards to time to achieve maximum motor block and duration of motor block. In these studies they concluded that there were significant differences between the groups. Duration of motor block was shorter in the ropivacaine group ($p < 0.05$). On the other hand, a more rapid postoperative recovery of sensory and motor function was seen in the ropivacaine group compared with the bupivacaine group, which is also in accordance with our findings.Moreover, **GAUTIER *et al* (2003),** compared the effects of intrathecal administration of either 8 mg isobaric bupivacaine, 8 mg isobaric levobupivacaine, or 12 mg isobaric ropivacaine, all combined with sufentanil 2.5 microg in patients undergoing caesarean section. Once more, bupivacaine provided a longer duration of analgesia and motor block than ropivacaine. It was also associated with a significant superior success rate to that observed in the levobupivacaine group.

Our results contrasts with **Cheng CR *et al* (2002)** in which they concluded that there was no significant difference between groups in the profile of sensory and motor blockade produced. Comparison of visual analogue pain scores did not show significant differences between groups at the corresponding times.

The quality of **Intraoperative analgesia** was quite good in all patients. No patient of any group complained of discomfort on skin incision.Time from the intrathecal injection to the first feeling of pain (**complete analgesia**) and to the first request of analgesic (**effective analgesia**). In our study duration of complete analgesia and duration of effective analgesia were in Group B (161.8 ± 12.96min and 176.7 ± 10.6min) and Group L (157.1 ± 9.88min and 170.5 ± 12.18min) were greater than Group R (136.6±8.89min and 147.2 ± 9.84min).

Our study in this regard coincide with **Kallio H et al[2004], Gautier et al [2003], JF Luck et al[2008] and Chung CJ et al. [Anesthesia & Analgesia 2001]** in which they concluded that ropivacaine provided significantly ($p<0.05$) shorter duration of complete analgesia (136.6±8.89 vs 161.8±12.96) and effective analgesia (147.2±9.84 vs 176.6±10.46) and faster motor recovery in comparison to bupivacaine.
Haemodynamic changes In present study hypotension defined as systolic blood pressure below 90mmhg and bradycardia defined as fall in heart rate below 60 beats per min. In our study, in group B hypotension in 3 cases and bradycardia in 1 case, in group L hypotension in 2 cases and bradycardia in 1 case and in group R hypotension in 2 cases were observed. But there were no statistically significant differences in systolic BP, MAP and pulse rate in Group B and Group L and group R.

Various studies have been performed to evaluate the effects of bupivacaine and ropivacaine administration on blood pressure. The results of the our study in this regards are also similar to study done by **Gonul Sagiroglu et al, Gautier et al, Mc Namee et al Boztug et al, Malinovskyet al. and Griffin et al.**

In our study, in group B nausea in 2 cases and shivering in 2 cases, bradycardia in 1 case and hypotension in 3 cases and in group L nausea in 1 case, shivering in 1 case, hypotension in 2 cases and bradycardia in 1 case whereas in group R shivering in 1 case and hypotension in 2 cases were observed.Hypotension was the most frequent adverse effect in groups. This hypotension was easily treated by incremental dose of mephentermine without any sequelae. Hypotension was observed in little higher no. of patients in group B as compared to group L and group R. But this difference was not statistically significant ($p > 0.05$). Other adverse effect like shivering, nausea, bradycardia were also observed in few patients but statistically there was no significant difference between the groups.The results of our study were similar to study done by **Gentili et al, Griffin et al (1995), Kleef et al (1994), Cheng CR et al [2002], JB Whiteside et al [2003]**

There was no respiratory depression observed in any of the case in our study. In another recent study, in patients undergoing transurethral resection of the bladder or prostate, patients were randomized to receive either 5 ml of 0.2% isobaric bupivacaine (10 mg) or 5 ml of 0.3% isobaric ropivacaine (15 mg) for spinal anesthesia. Despite the fact that a lower dose of bupivacaine was used in comparison with ropivacaine, there was a significant increase in the cephalad spread of the sensory block in the bupivacaine group. The degree of motor block was similar which is in accordance with our study, where a lower intensity of motor block was seen with ropivacaine than with bupivacaine with the same dose. In terms of safety, either intrathecal ropivacaine, levobupivacaine or bupivacaine provide a high degree of cardiovascular stability in low doses. The most commonly reported adverse events, nausea, vomiting, shivering, and decrease in oxygen saturation $SpO2 < 93\%$, were equally distributed between the groups.

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