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ORIGINAL ARTICLE

COMPARISON OF 0.5% ROPIVACAINE & 0.5% BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR PATIENTS UNDERGOING ABDOMINAL HYSTERECTOMY

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ABSTRACT: Ropivacaine is a new intermediate-acting amide local anesthetic which is structurally closely related to a chemical group of amino amides in present clinical use e.g. bupivacaine and mepivacaine. Ropivacaine has pharmacodynamic and pharmacokinetic properties in animals resembling those of bupivacaine.[1-3] In human volunteers, ropivacaine has been shown to be less prone than bupivacaine to produce mild central nervous system and cardiovascular changes after intravenous infusion Hence we designed a study to compare ropivacaine 0.5% with bupivacaine 0.5% for epidural anesthesia for abdominal hysterectomy. Healthy women, scheduled for elective abdominal hysterectomy were enrolled into this randomized, double- blind, parallel-group study. Epidural block was obtained with 20 ml of ropivacaine (group R) or bupivacaine (group B) and surgery started when anesthesia reached T6. Heart rate and blood pressure were assessed before the test dose and at five minute intervals for initial 30mins and then every 10mins until the full recovery. At the same intervals, sensory and motor block characteristics were determined. Adverse events were recorded. Sixty patients were enrolled and data available for analysis was 30 ropivacaine and 30 bupivacaine. Mean duration for total sensory blockade was 323.50±39.33mins for R group as compared to 312.0±30.36mins for B group ($p>0.05$). Motor onset time in group R was 17.26±1.78, 25.44±1.79 and 28.28±1.79mins for grade 1, 2 and 3 motor block respectively, compared to 16.73± 1.99, 25.14±2.05 and 28.66± 2.82mins for group B ($p>0.05$). Duration of motor block in group R was 211.66± 32.91mins as compared to 288.66± 36.99mins in group B. (P value < 0.0001). Analgesia was excellent in 83.33% cases and satisfactory in 10 % cases in group R as compared to 86.66% and 3.33% in group B respectively. 6.66% patients in group R and 10% patients in group B required intravenous fentanyl supplement and were considered as unsatisfactory. The most common adverse events were hypotension (13.33% gp. R and 20% in gp. B) and nausea (13.33% and 20% in group R and B, respectively). Ropivacaine 0.5% and bupivacaine 0.5% produced a similar duration of sensory anesthesia and both agents produced equally satisfactory block for abdominal hysterectomy. Ropivacaine 0.5% can be used as a safe and better alternative to bupivacaine due to its proved lesser cardio toxicity and more rapid recovery from motor blockade.

KEYWORDS: Ropivacaine, bupivacaine, epidural anesthesia, abdominal hysterectomy.

INTRODUCTION: Ropivacaine is a new intermediate-acting amide local anesthetic. It is structurally closely related to a chemical group of amino amides in present clinical use, e.g. bupivacaine and mepivacaine. The latter are racemic mixtures, whereas ropivacaine is the pure (S)-enantiomer. It is available as the monohydrate of the hydrochloride salt of 1-propyl- 2,6-pipecoloxylidide.Ropivacaine has pharmacodynamic and pharmacokinetic properties in animals resembling those of bupivacaine.[1-3]

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However, in animals, ropivacaine has a lower central nervous system and cardio toxic potential than bupivacaine.[4] In human volunteers, ropivacaine has been shown to be less prone than bupivacaine to produce mild central nervous system and cardiovascular changes after intravenous infusion.[5] Initial clinical studies in epidural anesthesia have indicated that pharmacodynamic and pharmacokinetic properties for ropivacaine are comparable to those seen with bupivacaine.[6-8] The onset and duration of sensory block and the overall clinical efficacy of anesthesia have been reported to be comparable for the two drugs. The frequency and degree of motor block was similar for both the groups. The anesthetic characteristics of ropivacaine have also been tested in animals and humans, and compared with bupivacaine. In equi-potent concentrations the degree of motor blockade is less pronounced with ropivacaine than bupivacaine and there is a greater propensity for blocking A^{δ} and C fibres.[7] If true, this may prove to be advantageous in obstetric patients in labour and in others suffering from acute and chronic pain.

The present study was designed to evaluate the quality and nature of epidural block achieved with ropivacaine 0.5% versus bupivacaine 0.5% in patients undergoing abdominal hysterectomy.

Patients and Methods: The study was randomized double-blind and with two parallel treatment groups. Inclusion criteria were ASA I-II patient scheduled for elective abdominal hysterectomy under epidural anesthesia, age group 30-60yrs, Weight between 50 and 100kg, Height at least 145cms. Patients were not eligible if there was a history of allergy or sensitivity to amide-type local anesthetics, diabetes, a psychiatric history which could lead to unreliability in the clinical assessment, alcohol, drug or medication abuse as judged by the investigator or a contraindication for epidural procedures. The patients were randomized in two groups, Group R (Ropivacaine) and Group B (Bupivacaine). Double-blindness was maintained by means of the identical appearance of the ropivacaine and bupivacaine solutions and ampoules.

Anesthetic Protocol: One liter of crystalloid solution was administered before initiation of the epidural block. The epidural catheter was placed with a 16-18G Tuohy needle in the L_{2-3} or L_{3-4} interspaces, using the midline approach, with the patient in the sitting or lateral position. A test dose of 3 ml lidocaine 1.5% with 15µgm epinephrine was used to assess catheter placement. Following this, 20 ml of the study drug (100mg) was injected through the epidural catheter at a rate of 4 ml/min. Surgery was started when analgesia was achieved at the T6 dermatome level, assessed with pin prick using a short beveled 23G needle, and adequate surgical anesthesia was obtained. Adequate surgical anesthesia in this context signified no pain after using a clamp to pinch the skin within the area of incision.

If block did not reach dermatome level T_6 or if surgical anesthesia was not obtained within 30 min, an additional 5ml (25mg) of the study drug were given. If the block did not reach T 6 or if surgical anesthesia was not obtained after a further 15 min (45 rain after injection of the main dose), another 5ml (25mg) were given. If the block did not reach T 6 or if surgical anesthesia was still not achieved after another 15min (60min after main dose), the patient was withdrawn from further efficacy assessment. Assessments of sensory block were performed at 5, 10, 15, 20, 25, 30, 45 and 60 min after the main dose and then every 30 min until the return of normal sensation. The onset and end of analgesia was determined bilaterally, using a short beveled 23G needle. Analgesia was recorded at dermatome levels S_3, S_1, Ls, L_5, L_4, T_{12}, $T_{10,}$ T_8 and T_6; together with the maximal spread of analgesia (Upper and lower spread).

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Assessments of motor block were performed immediately after the assessments of sensory block until the return of normal motor function. The onset and end of all degrees of motor block were assessed bilaterally according to the modified Bromage scale:[8]

0= No motor block (Ability to move hips, knees and ankles).

1= inability to raise extended leg (Able to flex knee).

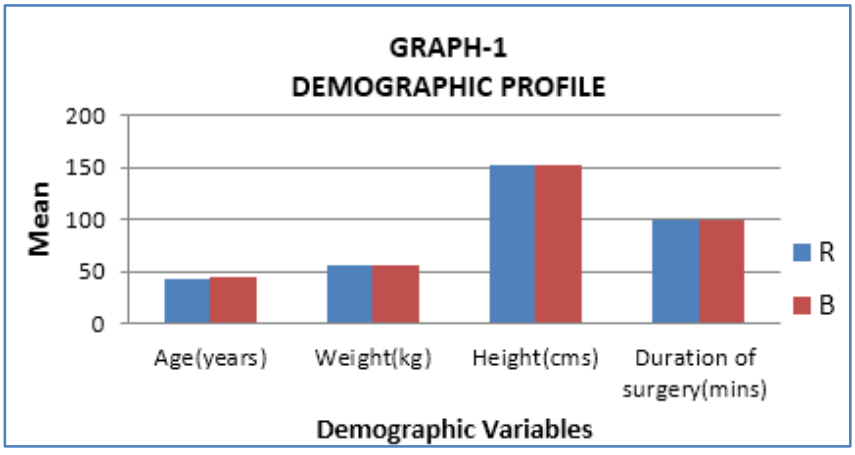
2 = inability to flex knee (Able to flex foot only).

3= inability to flex ankle joint (Unable to flex foot or knee).

Heart rate and systolic and diastolic blood pressure were measured with an automated non-invasive blood pressure cuff. Values were recorded before the test dose and initially at 5 minutes intervals for 30 minutes and after that at 10 minutes intervals till the return of normal sensations. A systolic blood pressure of <90mmHg or >180mm Hg was considered to be hypotension or hypertension, respectively. A heart rate of< 50bpm or >140 bpm was considered to be bradycardia or tachycardia, respectively. A systolic blood pressure <90mmHg was treated with 5-10mg ephedrine iv and a heart rate <50bpm was treated with 0.6mg atropine iv. Pain on incision was recorded as being present or absent and, if present, its intensity was assessed using a ten point visual analogue scale. At any time after delivery, the patient could be given 50µgm fentanyl iv if she experienced pain or discomfort. The quality of anesthesia (i.e. quality of analgesia and abdominal wall muscle relaxation) was assessed by the investigator and surgeon after the end of the operation as excellent, satisfactory and unsatisfactory.

Adverse Events: Patients were assessed for adverse events. An adverse event was defined as any unfavorable, unintended event, temporally associated with administration of the study drug, whether or not considered to be drug related. A serious adverse event was one which constituted a definite hazard or handicap to the patient. Adverse events were recorded during anesthesia and surgery, in the recovery room and daily during hospitalization, after surgery.

Sample Size Determination: The sample size for the study was calculated with the aim of showing a difference between treatments in duration of motor block, with a mean difference of at least one hour. Based on the published literature, the standard deviation of Bromage 1 motor block was assumed to be approximately 1.1 hr. With 30 patients in each group and using a significance level of 0.05, the power of the study was 93%. The calculation was made using the t test, based on the assumptions of normally distributed data, and equal variances.



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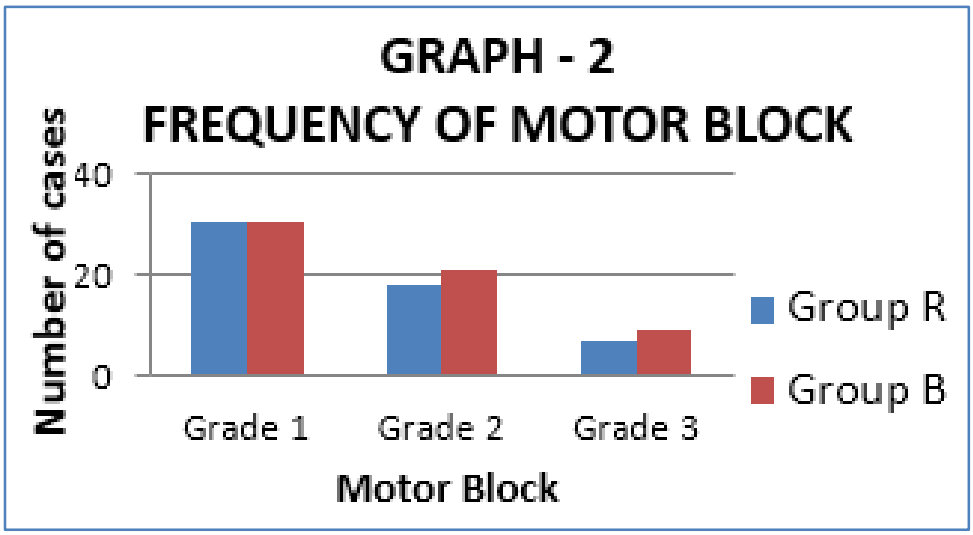
Analysis of Results: Proportions were analyzed by the use of the chi square test or if the expected frequency in any cell was less than 5, Fisher's exact test. All tests were two tailed and performed at a significance level of 0.05. Missing values are assumed to be missing at random. They have not been included in the analysis and have been taken into consideration only by the reduced sample sizes.

Results: Patient Description: Patients were divided randomly in two groups with 30 patients in each group. Group R (Ropivacaine) received 20 ml of 0.5% Ropivacaine and Group B (Bupivacaine) received 20 ml of 0.5% Bupivacaine by lumbar epidural catheter. The two groups were comparable with respect to age, height, weight and surgical time.

Anesthetic and Block Characteristics: The mean volume of study drug administered was 20ml ropivacaine and 20ml bupivacaine. Two patients in the ropivacaine group received supplemental opioid intraoperatively compared with three in the bupivacaine group (P > 0.05).

Highest level of sensory anesthesia achieved was T_4 in both the groups. The mean time to achieve highest sensory level in group R was 15.66±1.82mins as compared to 16.0±1.74mins in group B. (p>0.05). The mean duration for 2 segment sensory regression was 166.0±29.19mins for group R as compared to 171.0±32.62mins for group B. (p>0.05). Mean duration for total sensory blockade was 323.50±39.33mins for ropivacaine as compared to 312.0±30.36mins for bupivacaine. (p> 0.05). Incidence of motor block (grade 1-100% and 100%, grade 2-60% and 77%, grade 3–21% and 30% in group R and B respectively) was similar in both the groups. (p >0.05). Motor onset time in group R was 17.26±1.78, 25.44±1.79 and 28.28±1.79 mins for grade 1, 2 and 3 motor block respectively, compared to 16.73±1.99, 25.14±2.05 and 28.66±2.82mins for group B (p>0.05). Mean duration of motor block in group R was 211.66±32.91mins as compared to 288.66±36.99mins in group B. (p<0.0001).

Adverse Effect: The most common adverse effects were Hypotension and nausea. The occurrence of hypotension was 13.33% and 20.66% (Group B). For nausea it was 13.33% in Group R and 20% in group B.



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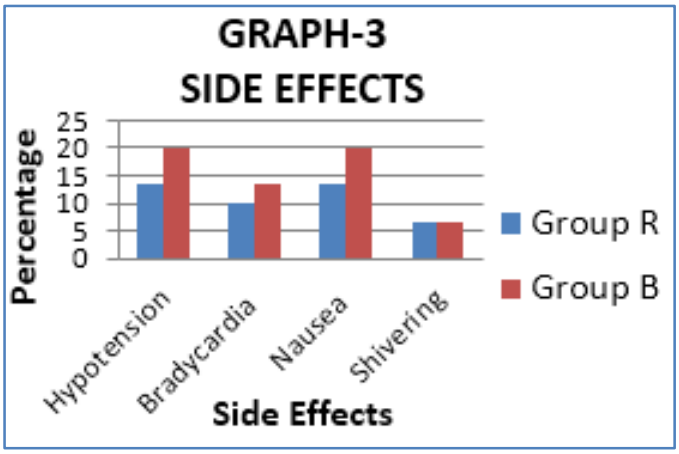

DISCUSSION: Pharmacological and laboratory investigations continue to attempt to develop a new long acting local anesthetic that is efficacious and safe. The development of long acting amide local anesthetic has traditionally focused on ever increasing duration of local anesthetic. Ropivacaine's development diverges from this tradition because its duration of sensory anaesthesia is similar to that of currently available local anesthetic. Additionally, it is different from other local anesthetic because it is prepared as a single enantiomer (The S form), rather than a racemic mixture. The clinical importance of this difference may be related to a separation of local anesthetic potency and the potential for cardio toxicity

In this study, both ropivacaine 0.5% and bupivacaine 0.5% produced effective and well-tolerated epidural anesthesia in patients undergoing hysterectomy although there was a need for supplementation of the block with intravenous opioid in about a third of the patients in each group(6.66% in gp. R and 10% in gp. B). The onset of sensory and motor block and duration of sensory block did not differ between the groups. The duration of motor block, in was shorter in patients who received ropivacaine. Several studies have demonstrated a longer duration of sensory block with bupivacaine than with ropivacaine.[9,10]

Our study, however, confirmed the results of other workers; in equal doses and concentrations, the profile of sensory block with time is the same for ropivacaine and bupivacaine.[11-13] Our data also showed that the both Bromage score and time to onset of motor block were similar in patients who received ropivacaine and bupivacaine. Others have also found no difference in onset time and a shorter duration of motor block.[9,11,13] although one study found that motor block was not only of shorter duration in patients who received ropivacaine, it was also later in onset,[12] is Others have reported that ropivacaine produced a less intense motor block motor,[10,13]

The quality of anesthesia was considered to be excellent in 83.33% of patients who had ropivacaine and 86.66% of those who had bupivacaine. This is comparable to the finding of Griffin and Reynolds who concluded that extradural block was inadequate for surgery in 10% of patients in each treatment group[11] Previous studies of under extradural anaesthesia using plain bupivacaine 0.5% also had a high incidence of inadequate block with 20-30% of patients requiring supplemental analgesia. Adverse events were evenly distributed across treatment groups, the most common adverse events were hypotension and nausea. Our incidence of adverse effects is similar to that reported by others. These events are expected in association with epidural administration of local anesthetics.

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SUMMARY: We found that ropivacaine 0.5% and bupivacaine 0.5% produced a similar duration of sensory analgesia and both agents produced equally satisfactory block for Hysterectomy. A more rapid recovery from motor block with ropivacaine 0.5% may be advantageous but it has not been a consistent finding in all studies. Adverse effects were similar in their incidence and likely more technique than drug-related. Ropivacaine 0.5% can be used as a safe and better alternative to bupivacaine due to its proved lesser cardio toxicity and more rapid recovery from motor blockade.

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