ORIGINAL ARTICLE

# The efficacy of 0.75% levobupivacaine versus 0.75% ropivacaine for peribulbar anesthesia in vitreoretinal surgery

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## ABSTRACT

**Background:** We evaluated the anesthetic efficacy and the postoperative analgesic effects of 0.75% levobupivacaine versus 0.75% ropivacaine for peribulbar anesthesia in patients undergoing primary vitreoretinal surgery. **Methods:** We investigated 120 patients subjected to vitreoretinal surgery under peribulbar anesthesia. They were randomized into two equal groups according to the local anesthetic (LA) used, namely, 0.75% levobupivacaine or 0.75% ropivacaine, both with the addition of hyaluronidase. Nerve block was carried out by injection of 5–7 mL of the LA using single injection percutaneous peribulbar anesthesia with a short needle. **Results:** When compared with 0.75% ropivacaine, 0.75% levobupivacaine provided more successful akinesia at 10 min after block ($P=0.026$), fewer supplementary injections ($P=0.026$), and less volume (mL) was used ($P=0.031$). Also, levobupivacaine provided significantly longer motor block duration (342 ± 27 min versus 206 ± 40 min, $P=0.001$) and significantly longer sensory block duration (513 ± 24 min versus 394 ± 11 min, $P=0.001$) when compared with ropivacaine. In the postoperative period, the patients in the levobupivacaine group achieved lower values of verbal numeric rating scale of pain compared with patients in the ropivacaine group among the period from 4 to 12 h. Also, there were significantly ($P=0.001$) lower diclofenac consumption (mg) and the percentage of patients who required tramadol rescue medication were significantly less ($P=0.034$) in the levobupivacaine group compared with the ropivacaine group. **Conclusion:** We are concluding that, at equipotent doses and concentrations, 0.75% levobupivacaine provides more effective peribulbar anesthesia and more effective postoperative analgesia for vitreoretinal surgery compared with 0.75% ropivacaine.

**Key words:** *Levobupivacaine, peribulbar anesthesia, ropivacaine*

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## INTRODUCTION

The well-known toxic effects of bupivacaine on the central nervous system and the cardiovascular system were a base for the development of new long-acting local anesthetics (LAs), such as ropivacaine and levobupivacaine, to present a safer alternative to bupivacaine. These toxic effects seem to be less severe when comparable plasma levels of these pure levorotatory agents are reached. These LAs are practical alternatives to bupivacaine, and may present some advantages where a greater differentiation between motor and sensory block is evident.[1]

The characteristics of patients for vitreoretinal surgery, most of them elderly and with associated diseases, such as diabetes mellitus and cardiac problems, make LA advisable to reduce risks and morbidity. LAs with long duration, rapid onset, and minimal side effects, especially on cardiac and central nervous system, have been popular in regional ophthalmic anesthesia.[2] Vitreoretinal surgery is frequently associated with a high incidence of postoperative pain, probably as a result of traction on the ocular muscles and sclera and/or to increased intraocular pressure due to expansion of the gas bubble or tight buckling or encirclement.[3] For many ophthalmic surgeons, LA has become more preferred over general anesthesia (GA) owing to quicker patient rehabilitation, the avoidance of probable

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complications from GA, and better analgesic properties postoperatively.[4]

The aim of this study was to evaluate the anesthetic efficacy (as a primary end-point) and the postoperative analgesic effects (as a secondary end-point) of 0.75% levobupivacaine versus 0.75% ropivacaine for peribulbar anesthesia in patients undergoing primary vitreoretinal surgery.

## METHODS

After obtaining approval from the Institutional Ethics Committee and written informed consent from all the patients, 120 adult patients American Society of Anesthesiologists (ASA) I-III, scheduled for elective primary retinal detachment surgery without scleral buckle or encircling procedures under peribulbar anesthesia, were included in this prospective, double-blind, randomized study. Adequate akinesia and expected surgical time to be less than 3 h were inclusion criteria for this study. Exclusion criteria included age bracket younger than 18 years, patients refusing LA, patients with a single eye, allergy to LA solutions, clotting abnormalities, history of sleep apnea, impaired mental status, and drug abuse. This study was conducted in the Magrabi Eye and Ear Hospital in Oman between the period of January 2010 and June 2011. All operations were carried out by the same surgeon.

Patients admitted to the operating room fasted for 8 h and unpremedicated. A peripheral i.v. catheter was inserted and standard monitoring was conducted and recorded, including heart rate (HR), noninvasive arterial blood pressure, electrocardiogram (5 leads), and peripheral oxygen saturation ($SpaO_2$). A nasal cannula was applied and supplemental oxygen was given throughout the procedure at 4 L/min. The patients were randomly divided (using the block randomization method, with a block size of 6) to 1 of 2 groups according to the LA solution used to receive either 0.75% levobupivacaine (Chirocaine, Abbott Laboratories, Elverum, Norway) plus hyaluronidase 15 IU/mL (levobupivacaine group, $n$=60) or 0.75% ropivacaine (Naropin, Astra-Zeneca, Zug, Switzerland) plus hyaluronidase 15 IU/mL (ropivacaine group, $n$=60). The studied LA solutions were prepared at the bedside before the injection and provided in patient specific, sealed packaging by a member of staff not otherwise involved in the study. All peribulbar blocks were performed by a senior anesthetist experienced in the technique who was blinded to the kind of LA solution used. The patients who were blinded to the LA solution used, received single percutaneous injection percutaneous peribulbar anesthesia using a 25-G 16-mm short-bevel needle. The position of the injection site was in the inferior orbital margin and in the same line with the inferior lacrimal canaliculus. The needle was advanced in an anteroposterior direction for half of its length and then obliquely in the direction of the optical foramen as described by Rizzo and colleagues.[5] After negative aspiration, 5–7 mL of the LA solution was slowly injected until the presence of a complete drop and fullness of the upper eyelid. Mechanical orbital compression was then applied for 10 min in both groups, using a Honan balloon adjusted to 30 mmHg.

All measures were assessed by the senior anesthetist who performed the peribulbar block. Motor block was evaluated by the assessment of the akinesia in the 4 quadrants using a 3-point scoring system, which was categorized as follows: 0=akinesia, 1=partial akinesia, and 2=normal movement, with a maximal score of 8 for the 4 muscles. The block can only be considered successful, if the akinesia score was 3 or less.[6] In such event, if one or more of the components of ocular movement showed inadequate motor blockade (akinesia score >3) 15 min after block, supplementary anesthesia (3 mL) was injected into the involved quadrant using the same length needle as for the primary block. After that, an additional assessment was performed 5 min later. The incidence of any complications was routinely recorded. Sensory block was considered along with abolition of the corneal reflex next to instillation of drops of physiological solution on the conjunctiva and cornea. The total volume of LA solution injected (mL) was calculated. The motor block and sensory block durations (min) were then evaluated frequently in the postoperative period every hour as there was no surgical contraindication to remove the eye cover. The degree of postoperative pain was assessed by using the verbal numeric rating scale (VNRS) of pain (VNRS) where 0=no pain and 10=the worst pain imaginable at 1, 2, 4, 6, 8, 12, and 24 h postoperatively. If the VNRS for pain was >4, diclofenac 1 mg/kg was given intramuscularly. If the patient complained of severe pain (VNRS was >7), as well as the diclofenac, tramadol 100 mg was given intravenously by infusion over 15 min as rescue analgesia medication. Both analgesics were given in a maximum frequency of 6 h, and 3 doses maximally per 24 h. The total diclofenac consumption (mg) and the number of patients (%) requiring tramadol as rescue analgesia medication was recorded.

We have chosen the number of patients who developed successful block (10 min after block) to calculate the required sample size for this study. The required sample size was calculated to be 60 patients per group with $a$=0.05 and a power of 90% to detect a difference of at least 25% in the successful block. The statistical analysis of our results was conducted using the computer program SPSS version 15.0 for Windows (SPSS, Chicago, IL, USA). Data

were expressed as mean±SD or number (percentages). The 2-way repeated measures analysis of variance was used to compare the interval data, and Student's *t* test was used as the post hoc test to determine differences between and within groups. Fisher's exact test was used to compare nominal data or percentages. Bonferroni correction for repeated comparisons was applied if necessary. $P<0.05$ was considered significant.

## RESULTS

This study demonstrated comparable results regarding age (49.7 vs 52.4 years, $P=0.139$), sex, weight (70.8 vs 68.7 kg, $P=0.108$), and duration of surgery (161.8 vs 158.9 min, $P=0.065$) in the levobupivacaine group compared with the ropivacaine group, respectively. The percentage of patients who developed successful akinesia (10 min after block) were significantly higher ($P=0.026$) in the levobupivacaine group (91.6%) compared with the patients in the ropivacaine group (75%). The percentage of patients who required supplementary injection were significantly lower ($P=0.026$) in the levobupivacaine group (8.3%) compared with the patients in the ropivacaine group (25%). In the levobupivacaine group, the mean volume of levobupivacaine administered was 6.3 mL, which was significantly less ($P=0.031$) than the volume of ropivacaine (6.7 mL) administered in the ropivacaine group. As well, the motor block duration (min) was significantly longer ($P=0.001$) in the levobupivacaine group (342±27) compared with the patients in the ropivacaine group (206±40). The sensory block duration (min) was significantly longer ($P=0.001$) in the levobupivacaine group (513±24) compared with the patients in the ropivacaine group (394±11) [Table 1].

In the postoperative period, the patients in the levobupivacaine group achieved lower values of verbal numeric rating scale of pain compared with the patients in the ropivacaine group among the period from 4 to 12 h postoperatively [Figure 1]. The diclofenac consumption (mg) was significantly less ($P=0.001$) in the levobupivacaine group (86.9±11.7) compared with the patients in the ropivacaine group (182.2±36.1). Furthermore, the percentage of patients who required tramadol rescue medication were significantly less ($P=0.034$) in the levobupivacaine group (6.6%) compared with the ropivacaine group (21.6%) [Table 1].

## DISCUSSION

Levobupivacaine and ropivacaine are pure S (_) isomers of the family of *n*-alkyl–substituted pipecholyl xylidines. Their physicochemical properties are relatively similar, but the issue of their clinical profile is to some extent controversial. Levobupivacaine is known to be more lipophilic and theoretically more potent than ropivacaine, but clinical investigations show conflicting findings in terms of anesthetic and analgesic characteristics.[7,8] We hypothesized that the pure S-enantiomer of bupivacaine provides more effective peribulbar anesthesia and longer-lasting analgesia than ropivacaine for vitreoretinal surgery where adequate akinesia was a surgical requisite and a high incidence of postoperative pain is frequently associated.

This study has demonstrated that the use of levobupivacaine for peribulbar block in vitreoretinal surgery provided more effective peribulbar anesthesia with more patients who developed successful block (10 min after block), fewer patients who required supplementary injection, and less volume of LA solution was used compared with

**Table 1: Descriptive statistics for the quality of peribulbar block and the postoperative analgesia**

| | Levobupivacaine group (*n*=60) (%) | Ropivacaine group (*n*=60) (%) | *P* value |
|---|---|---|---|
| Number of patients (%) developed successful block (10 min after block) | 55 (91.6) | 45 (75)* | 0.026 |
| Number of patients (%) required supplementary injections | 5 (8.3) | 15 (25)* | 0.026 |
| Total volume of LA solution injected (mL) | 6.30±0.90 | 6.75±1.30* | 0.031 |
| Motor block duration (min) | 342.35±27.26 | 206.38±40.12* | 0.001 |
| Sensory block duration (min) | 513.16±23.77 | 393.88±11.19* | 0.001 |
| Total diclofenac consumption (mg) | 86.90±11.79 | 182.23±36.10* | 0.001 |
| Number of patients (%) requiring tramadol as rescue analgesia medication | 4 (6.6) | 13 (21.6)* | 0.034 |

Data are displayed as mean (SD) or number (%). *Statistically significant compared with the levobupivacaine group

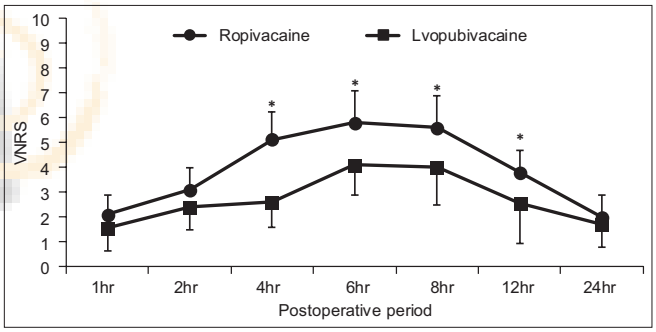


**Figure 1:** The verbal numeric rating scale of pain 24 h postoperatively

ropivacaine. Furthermore, the motor block duration and the sensory block duration (min) was significantly longer in the patients of levobupivacaine group compared with the patients in the ropivacaine group. In terms of efficacy of postoperative analgesia, levobupivacaine provided more effective postoperative analgesia with lower diclofenac consumption and fewer patients requiring tramadol as a rescue analgesia medication.

To our knowledge, this is the foremost study to evaluate the efficacy of equipotent doses and concentrations of 0.75% levobupivacaine versus 0.75% ropivacaine for peribulbar block in vitreoretinal surgery. However, comparing unequipotent doses or concentrations of these LAs or their usage in different surgeries have been described in previous studies.[7-14] Similar results have been described by Di Donato and colleagues[9] who compared 0.5% levobupivacaine with 0.75% ropivacaine for peribulbar anesthesia in cataract surgery and found that the sensory and motor block offset times and akinesia scores (6 min after block) were higher in the levobupivacaine-treated group than in the ropivacaine-treated group. Also, Borazan and colleagues[10] evaluated the efficacy of 0.75% levobupivacaine and 1% ropivacaine in peribulbar anesthesia for cataract surgery with phacoemulsification. They reported that the akinesia score was similar in both groups at 10 min after block, which could be attributed to the higher concentration of ropivacaine used, while the verbal pain score at 4 h postoperatively was significantly less in the patients received 0.75% levobupivacaine compared with the patients received 1% ropivacaine. It is worthy to note that this study was not a masked study as the same person served as surgeon and observer.

In previous studies designed for different clinical applications, Fournier and colleagues[11] compared equipotent concentrations and dosage of levobupivacaine 0.5% and ropivacaine 0.5% to provide analgesia after sciatic nerve block. They reported that 0.5% levobupivacaine provided longer-lasting analgesia after foot and ankle surgery compared with the same dose of ropivacaine. The time for the first request of pain medication with levobupivacaine 0.5% was significantly longer than with ropivacaine. The call for postoperative rescue analgesia was higher in the ropivacaine group. Furthermore, Casati and colleagues[12] reported that the patients receiving 0.5% ropivacaine for lumbar epidural anesthesia may have a higher incidence of inadequate intraoperative motor block compared with 0.5% levobupivacaine.

On the other hand, previous studies designed for ocular blocks using different LA drugs, Aksu and colleagues[13] compared 0.5% levobupivacaine, with 0.5% bupivacaine, and 2% lidocaine for retrobulbar anesthesia in vitreoretinal surgery. They reported that levobupivacaine provides longer motor and sensory block duration and higher surgeon and patient satisfaction than lidocaine. Also, Birt and Cummings[14] evaluated the efficacy and safety of 0.75% levobupivacaine vs 0.75% bupivacaine for peribulbar anesthesia. They reported that levobupivacaine and bupivacaine are equally successful in achieving clinically satisfactory peribulbar anesthesia with few adverse effects.

When comparing levobupivacaine and ropivacaine, the differences in molarity must be taken into consideration due to differences in the molecular weight. Thus, taking molecular weights into account, levobupivacaine has 7%–8% more active molecules than ropivacaine.[15] Pertaining to this study, it was proven that the motor block duration and the sensory block duration (min) were significantly longer in the patients of levobupivacaine group than in the patients in the ropivacaine group. This is clearly not only explained by the difference in molarity but also potentially by the difference in protein binding between levobupivacaine (95%) and ropivacaine (90%–92%). However, our results cannot be concluded to a generalized concept in clinical practice because there is a contention in the literature about the controversial results, with different results according to the site of deposition of LAs.[7,8] The type of block may also have an influence on the potency ratio between these 2 drugs, because clinical equipotency has mainly been demonstrated in patients undergoing sciatic nerve block and epidural analgesia.[11,12] We are concluding that, at equipotent doses and concentrations, 0.75% levobupivacaine provides more effective peribulbar anesthesia and more effective postoperative analgesia for vitreoretinal surgery compared with 0.75% ropivacaine.

### Declaration of interests

- This work was carried out in Magrabi Eye and Ear Hospital, Muscat, Sultanate of Oman.
- The author indicates that no source(s) of funding, including foundations, institutions, pharmaceutical and device manufacturers, private companies, or intramural departmental sources.

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