Comparison of Levobupivacaine 0.5% or Bupivacaine 0.5% Both in a Mixture with Lidocaine 2% for Superficial Extraconal Blockade

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ABSTRACT

Purpose: To evaluate the quality and efficacy of Peribulbar blockade for superficial extraconal anesthesia with levobupivacaine 0.5% versus bupivacaine 0.5%, both combined with lidocaine 2% for patients undergoing phacoemulsification.

Materials and Methods: In this prospective, double blind study, 150 patients were randomly divided into two groups: group-1 received a Peribulbar block (PB) with a mixture of levobupivacaine 0.5% and lidocaine 2% while group-2 received a PB with a mixture of bupivacaine 0.5% and lidocaine 2%. The block was performed by insertion of a short needle (15 mm) in infra-temporal space just above inferior orbital notch. An initial volume of 6-9 ml of either mixture was injected until total upper eyelid drop. Akinesia score was assessed at 2, 5, and 10 min after the block. The degree of pain was assessed by a verbal rating scale immediately after block, at the end of surgery and 4 h postoperatively. The patients and surgeons were asked to rate their satisfaction level of the quality of block postoperatively. Data were analyzed with the unpaired, two-tailed t-test and the Chi-square test as appropriate. P < 0.05 was considered statistically significant.

Results: There were no significant differences between groups with respect to the akinesia score (P = 0.2) at 2, 5, and 10 min, the number of supplementary injections (P = 0.84) and initial and total required volume of local anesthetics (P = 0.80 and 0.81, respectively). There was no significant difference between the groups regarding surgeon and patient satisfaction (P = 0.53 and P = 0.74, respectively). Similarly the verbal rating scales assessed at three different occasions were not significantly different between the groups (P > 0.05 all cases). The need for additional intra-operative topical anesthetic was also similar between the groups. (P = 0.69).

Conclusions: Superficial extraconal block with a mixture of levobupivacaine 0.5% and lidocaine 2% or bupivacaine 0.5% and lidocaine 2% provides similar block quality and efficacy.

Key words: Levobupivacaine vs. Bupivacaine, Local Anesthesia, Superficial Extraconal Block

INTRODUCTION

Superficial extraconal block for cataract surgery is an effective method for intraoperative and postoperative analgesia. Use of a short acting amide, lidocaine, mixed with a longer acting bupivacaine is a popular combination to produce optimal effects for cataract surgery. Bupivacaine is highly lipidsoluble, and contains a chiral center on the piperidine ring, resulting in two optically active stereoisomers, dextrobupivacaine, or levobupivacaine S (-) bupivacaine. It is well known that racemic bupivacaine has a narrow therapeutic index and carries a higher risk for cardiotoxicity. Levobupivacaine has high pKa value and low lipid solubility with a clinical profile very similar to bupivacaine in providing effective anesthesia and analgesia.
Investigators have reported that racemic bupivacaine markedly reduced the stroke index, ejection fraction, acceleration index, and produced greater prolongation of the QT interval compared to levobupivacaine.\textsuperscript{2-5} Other studies have reported that levobupivacaine has a better profile compared to racemic bupivacaine in terms of neurotoxicity.\textsuperscript{6} The reduced toxic profile of levobupivacaine is beneficial for achieving higher plasma concentrations and dose without signs of cardiovascular or systemic toxicity. Furthermore, the success rate of cardiopulmonary resuscitation after toxic doses of levobupivacine is higher compared to bupivacaine intoxication.\textsuperscript{7}

There is a relative paucity of studies describing the use of levobupivacaine 0.5% for the standard peribulbar block (PB) or for superficial extraconal anesthesia.\textsuperscript{8-10} The majority of patients undergoing cataract surgery are elderly and have several co-morbidities. Hence the use of anesthetics with the potential for reduced cardiovascular and neurologic toxicity is strongly desirable in these patients.

In this study we examined the efficacy and blocking quality of 0.5% levobupivacaine versus 0.5% bupivacaine for superficial extraconal anesthesia in combination with lidocaine 2% and hyaluronidase 5 IU/ml for patients undergoing phacoemulsification.

**MATERIALS AND METHODS**

Approval for this randomized, double blind study was granted from the local Institutional Research and Human Ethics committees. All patients signed a written informed consent. All patients were American Society of Anesthesiologist (ASA I-III). Exclusion criteria included patients with history of allergy to amide anesthetic or hyaluronidase, with local sepsis, serious impairment of coagulation, orbital abnormalities, monocular patients, history of previous surgery in the study eye, and nystagmus. Patients with a history of long term use of benzodiazepines and/or opiates, presence of neurological disorders which might have affected their level of anxiety or pain threshold, uncooperative or extremely anxious patients and those with communication problems (language barrier, impaired hearing) were also excluded from the study.

On the day of the surgery, patients were asked to fast for 6 h and were premedicated with 1 to 2 tablets of Revacid (Paracetamol 500 mg + Codeine 10 mg) (The Arab Pharmaceuticals Manufac. Co, Jordan) and hydroxyzine one and half hour before the procedure. In the preoperative holding area, standard monitoring (pulse oximetry, electrocardiography, and non-invasive blood pressure) was performed, an intravenous cannula was placed and ocular motility in the major directions of gaze was assessed. Patients were randomly divided into two equal groups (75 patients each) by random numbers picked by induction room nurse who was blind to the study.

Superficial extraconal anesthesia was performed by insertion of 15 mm long needle (Becton Dickinson, BD Microlance 3, Benelux, Belgium) through the lower eyelid, as far laterally as possible in the inferotemporal quadrant just above the inferior orbital notch. The needle was inserted until its hub reached the orbital rim. Digital pressure was applied with the thumb and index fingers around the needle hub during injection. The purpose was to obliterate the lower eyelid space and promote the posterior spread of the anesthetic. After negative aspiration, patients received local anesthetics of either levobupivacaine 0.5% (group 1) or bupivacaine 0.5% (group 2), both in a mixture of lidocaine 2% in 3:2 volume ratio (Astra Sodertalje, Sweden) with hyaluronidase 5 units/ml (CP Pharmaceutical Ltd, Wrexham, United Kingdom) as an adjuvant to increase the absorption and spread of the mixture. An initial volume of 6 to 9 ml was injected until total drop of the upper eyelid, which was used as an endpoint mark.\textsuperscript{1} This was immediately followed by application of a Honan's balloon at a cuff pressure of 30 mm Hg.

Simple akinesia score was used to assess eyeball movement at 2, 5, and 10 min by an anesthesiologist who was masked to the kind of medications delivered to the eye. The score involved the assessment of eye movement in four major directions of gaze (superior, inferior, medial, and lateral). Normal movement in each direction was graded 2, reduced movement graded 1, and flickering or total akinesia, graded zero. Thus, the score ranged from 0−8.\textsuperscript{11} If the akinesia score was 3 or higher, a supplementary injection of 3 to 5 ml was delivered using the same mixture of medication either medially or supero-nasally depending on the site of residual movement.

If a patient experienced pain intraoperatively, supplementary topical anesthetic (tetracaine HCL 1%) (Laboratoire Chauvin, Z.I. Riptotier Haut, Aubenas-France) was instilled by the surgeon. At the end of the procedure, surgeons who were masked to the medications used for superficial extraconal anesthesia were requested to rate their satisfaction with the block quality (0 = absolutely not satisfied to 10 = totally satisfied). Patients who were also masked to the type of medication used, were requested to rate the degree of pain on verbal pain scale (VPS) (0 = no pain to 10 = most severe pain) immediately after the block, at the end of the procedures and before discharge (4 h postoperatively).

**Statistical Analysis**

The results were analyzed using SPSS version 14 (SPSS Inc., Chicago, IL, USA). Sample size calculation using G*Power 3.1.2 software (Heinrich-Heine-University, Dusseldorf, Germany) indicated that 75 patients in each group were required based on 0.5 differences in the mean final akinesia score between groups. The type-I error was set at 0.05 and type-II error was set at 0.20. Numerical data such as means and standard deviations were analyzed using unpaired, two-tailed t-test. Categorical data
were expressed as number and percentages using the Chi-square test for comparison. A P value less than 0.05 was considered statistically significant.

**RESULTS**

The study cohort was comprised of 150 patients between 40 to 75 years of age. Demographic and descriptive data are presented in Table 1. Age, body mass index, sex, operated eye, ASA classification, axial length of the studies eye globe, and duration of surgery were not significantly different between groups (P > 0.05, all cases).

The primary volume of inferotemporal injection and the total volume of local anesthetic were not significantly different between groups (P = 0.80 and P = 0.81, respectively). The mean akinesia score at 2, 5, and 10 min did not differ between groups (P = 0.24, P = 0.27, P = 0.22, respectively). The number of patients requiring supplementary injection and supplementary topical anesthetic intraoperatively, were comparable between groups (P = 0.84, P = 0.56, respectively) [Table 2]. No major block related complications occurred for the duration of this study.

Verbal pain score (VPS) at various times and patient and surgeon satisfaction are presented in Table 3. There was no significant difference in VPS between groups immediately after the block, at the end of the surgery and 4 h postoperatively (P = 0.59, P = 0.56, P = 0.31, respectively). There was no significant difference in surgeon’s (P = 0.53) and patient’s (P = 0.73) satisfaction between groups.

**DISCUSSION**

The outcome of this study indicates that the use of 0.5% levobupivacaine for phacoemulsification produced comparable results to a racemic mixture of 0.5% bupivacaine, both with 2% lidocaine and hyaluronidase 5 IU/ml. There were no statistically significant differences in akinesia score, anesthetic supplementation, pain, and surgeon’s or patient’s satisfaction between the groups.

The outcome of our study concurs with other similar studies. Birt and Cummings reported similar efficacy of 0.75% levobupivacaine and 0.75% bupivacaine, both mixed with hyaluronidase or peribulbar anesthesia. They did not use the study drug in a mixture with lidocaine as we did and they used a longer needle (31 mm) with 5 ml primary volume. We rather used a relatively diluted drug concentration of 0.5% with a shorter needle (15 mm). However, Lai et al. found that a mixture of bupivacaine 0.75% and lidocaine 2% provided better akinesia than a mixture of levobupivacaine 0.75% and lidocaine 2% but in our study akinesia at 10 min did not differ from previous studies that used longer needles for injection.

Hence anterior injection of anesthetics improves safety without decreasing the block quality.

In this study, the need for supplemental injection to achieve adequate anesthesia was similar between the two groups. Similar results were reported for retrobulbar and PBs when comparing different concentrations of levobupivacaine to bupivacaine.
Some patients experienced mild pain during the injection of local anesthetic but trivial pain was reported at the end of the procedure and before discharge. There was no difference in subjective pain between groups. These outcomes are similar to a study by Borazan et al. 9 who reported no difference in verbal pain scale between patients using a mixture of bupivacaine 0.5% and lidocaine 2% or levo-bupivacaine 0.75% perioperatively. Additionally, Birt and Cummings 12 demonstrated no differences in pain between 0.75% levo-bupivacaine and 0.75% bupivacaine on injection, postoperative pain and time required for the first postoperative analgesia. 12 However, Aksu et al. 13 reported that pain during injection and after the surgical procedure was lower with 0.5% levo-bupivacaine compared to 0.5% bupivacaine and 2% lidocaine. This difference could be attributed to differences in the study population. In our study, 24% of patients required supplementary injections. The incidence of PBs requiring supplementary anesthesia has been reported to be as high as 54%. 14 This may lead to the possibility of administering higher volume of local anesthetic solution with increase risk of toxicity. Blocking with levo-bupivacaine will have theoretical advantage in this situation, especially in patients having cardiovascular disease.

We found a good level of surgeon’s and patient’s satisfaction that did not differ between groups. Di Donato et al. 10 found no difference in patient’s/surgeon’s satisfaction between 0.5% levo-bupivacaine and 0.75% ropivacaine when peribulbar anesthesia was performed with 19 mm long needle. Alternately, Aksu et al. 13 reported better surgeon’s/patient’s satisfaction in a levo-bupivacaine-treated group compared to a bupivacaine-treated group. 15

Clinically, it seems that both bupivacaine and levo-bupivacaine are being providing satisfactory conditions to perform surgery, with a similar clinical profile in dosages used to produce surgical anesthesia. The outcome of this study indicates that levo-bupivacaine has a clinical profile similar to racemic bupivacaine, and that the minimal differences observed between the two agents could be related to the slightly different anesthetic potency.

In conclusion superficial extraconal block with a mixture of levo-bupivacaine 0.5% and lidocaine 2% or bupivacaine 0.5% and lidocaine 2% provides similar block quality and efficacy for phacoemulsification. As levo-bupivacaine has a theoretical advantage of having better safety profile, it is better to be given preference over bupivacaine to improve patient safety, especially in elderly patients with co-existing cardiovascular disease.

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Cite this article as: Ahmad N, Zahoor A, Al Assiri A, Al Jastaneiah S, Riad W. Comparison of levo-bupivacaine 0.5% or bupivacaine 0.5% both in a mixture with lidocaine 2% for superficial extraconal blockade. Middle East Afr J Ophthalmol 2012;19:330-3.

Source of Support: Nil, Conflict of Interest: None declared.