



A comparative study between levobupivacaine 0.5% plus lignocaine 2% or bupivacaine 0.5% plus lignocaine 2% for peribulbar block in cataract surgery

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ABSTRACT

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Background and Aim: Local anesthetic techniques are increasingly popular for ophthalmic surgery. Levobupivacaine, the pure S (-) enantiomer of bupivacaine, has strongly emerged as a safer alternative for regional anesthesia than its racemic sibling, bupivacaine. The present Study was performed with an aim to compare between levobupivacaine 0.5% or bupivacaine 0.5% both in a mixture with lignocaine 2% for peribulbar block in cataract surgery.

Methodology: In this prospective double blind study, all the patients were randomly divided in two groups, Group B patients received inj bupivacaine 0.5% (5 ml) + lignocaine 2% (5 ml) + hyaluronidase (5 IU/ml), and Group L patients received inj levobupivacaine 0.5% (5 ml) + lignocaine 2% (5 ml) + hyaluronidase (5 IU/ml) for peribulbar block by akinetic technique to provide anesthesia for cataract surgery. The study was conducted for the period of one year. After routine pre anesthetic assessment, a peripheral intravenous (i.v.) line was inserted in 6 hours fasted patient and standard monitoring was conducted and recorded, including heart rate (HR), noninvasive arterial blood pressure (BP), electrocardiogram (5 leads), and peripheral oxygen saturation (SpO₂). Motor block was evaluated by assessment of akinesia in four quadrants using general akinesia scoring system.

Results: There were no significant difference between groups with respect to the akinesia score (p = 0.24) at 2, 5 and 10 min, the number of supplementary injections (p = 0.83) and initial and total required volume of local anesthetics (p = 0.78 and p = 0.79). There was no significant difference between the groups regarding surgeon and patient satisfaction (p > 0.52). Similarly the verbal rating scales assessed at three different occasions were not significantly different between the groups (p > 0.05). The need for additional intra-operative topical anesthetic was similar between the groups (p = 0.64).

Conclusion: Peribulbar block with a mixture of levobupivacaine 0.5% and lignocaine 2% or bupivacaine 0.5% and lignocaine 2% provides similar block quality and efficacy.

Key words: Peribulbar block; Akinesia; Cataract surgery; Elderly; Levobupivacaine

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INTRODUCTION

Local anesthetic techniques are preferred for

ophthalmic surgery, and vary from a non-invasive topical anesthesia to an akinetic (needle or cannula based) anesthesia.¹ Each technique has its own risk

or benefit profile, and proven to be highly successful if performed correctly. The non-akinetic methods include topical, subconjunctival, deep fornix anesthesia and lignocaine gel, whereas the akinetic methods include intraconal (retrobulbar), extraconal (peribulbar) and subtenon's anesthesia. The quest for searching newer and safer anesthetic agents for regional anesthesia has always been one of the primary needs in anesthesiology practice.

Levobupivacaine¹, the pure S (-) enantiomer of bupivacaine, has strongly emerged as a safer alternative² for regional anesthesia than its racemic sibling, bupivacaine. Levobupivacaine has been found to be equally efficacious as bupivacaine, but with a superior pharmacokinetic profile. Clinically, levobupivacaine has been observed to be well-tolerated in regional anesthesia techniques.^{3,4} The incidences of adverse drug reactions are related to faulty administration technique (resulting in systemic exposure); however, allergic reactions can also occur rarely.^{5,6} The available literary evidence in anesthesia practice indicated that levobupivacaine and bupivacaine produce comparable surgical sensory block, similar adverse side effects and provision of similar analgesia with good comparable patient outcome. As majority of patients undergoing cataract surgery are elderly and having several co morbidities safe local anesthetic drugs are better to be used.

Bupivacaine is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (-) isomer and dextrobupivacaine, R (+) isomer.⁷ Several central nervous system (CNS) and cardiovascular adverse reactions have been reported in the literature after inadvertent intravascular injection or intravenous regional anesthesia have been linked to the R (+) isomer of bupivacaine. The levorotatory isomers were shown to have a safer pharmacological profile, with less cardiac and neurotoxic adverse effects. The decreased toxicity of levobupivacaine is attributed to its faster protein binding rate. The pure S (-) enantiomers of bupivacaine, i.e., ropivacaine and levobupivacaine were thus introduced into the clinical anesthesia practice.^{7,8} As majority of patients undergoing cataract surgery are elderly and having several comorbidities, safer local anesthetic drugs need to be used.⁹

METHODOLOGY

A total of 100 American Society of Anesthesiologist physical status 1-3 scheduled for cataract surgery were included in the study. After obtaining institutional ethics committee approval for randomized double blind study, written informed consent was obtained from of all the study participants of both genders. Participants were evaluated for analgesia and effectiveness of levobupivacaine 0.5 % or bupivacaine

0.5 %, both in a mixture with lignocaine 2% for peribulbar block for cataract surgery. The study was conducted for the period of one year.

Patients allergic to local anesthetic solution, with any signs of local infection, congenital or acquired coagulation deficits or orbital anomalies, which had neurologic or psychiatric disorders who refused to anesthesia technique were excluded from the study.

After routine pre anesthetic assessment (history, physical examination, routine investigation, grading), a peripheral intravenous line was inserted in 6 hours fasted patient and standard monitoring was conducted and recorded, including HR, noninvasive arterial blood pressure (BP), electrocardiogram (5 leads), and peripheral oxygen saturation (SpO₂). Patients did not receive any sedation. Premedication was given with inj glycopyrrolate 0.2 mg and inj ondansetron 4 mg i.v. 10 min before surgery. All the patients were randomly divided in two groups, Group B patients received inj bupivacaine 0.5% (5 ml) + lignocaine 2% (5 ml) + hyaluronidase (5 IU/ml), and Group L patients received inj levobupivacaine 0.5% (5 ml) + lignocaine 2% (5 ml) + hyaluronidase (5 IU/ml) for peribulbar block to provide anesthesia for cataract surgery.

Under all aseptic conditions, preparation of drug mixture was done according to group. The same anesthesiologist performed all peribulbar block and all surgery was performed by same surgeon who was blinded to the anesthetic used. Percutaneous peribulbar injection was given at the junction of the outer one third and inner two third of the lower orbital rim by using a 15 mm long, 23-G hypodermic needle (Becton Dickinson, BD Microlance 3). The needle was advanced in an anteroposterior direction for half of its length and then obliquely in the direction of the optical foramen. After negative aspiration, 6 to 9 ml of the study drug solution was slowly (over 30-40 sec) injected in both the groups until total drop of upper eyelid, which was used as an end point. This was followed by application of Honan's balloon at a cuff pressure of 30 mmHg.

Motor block in all four quadrants was evaluated by using simple akinesia scoring system at 2,5 and 10 min by an anesthesiologist who was blind to the kind of medication used. All four recti muscles were individually assessed in terms of movements after injection of local anesthetic and categorized as per following scoring system; full movement = 2; partial movement = 1; no movement = 0.

Sum total of all four muscle scores was done and then the effectiveness of the block was evaluated. Maximum score was 8 for the four muscles (superior, inferior, medial, lateral rectus) and the minimum score was 0. Block was evaluated after 8 to 10 min of first injection, if akinesia score was 4 or higher

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supplementary injection on the superior aspect of the orbital margin was given. Superior (supplementary) injection of 3 to 5 ml was delivered using same mixture of drugs either medially or superonasally depending upon the residual movement of the muscle. Mechanical orbital compression by Honan's balloon was then applied for 5 min in both groups. The block

was considered successful, if the akinesia score was 3 or less after second injection. Sensory block was considered along with abolition of the corneal reflex next to instillation of drops of physiological solution (normal saline) on the conjunctiva and cornea.

The incidence of any complication like conjunctival edema, increase in orbital pressure (higher than 20 mmHg measured by tonometer), and high systemic toxicity were routinely recorded. Systemic complications may be caused by local anesthetic toxicity associated with overdose or intravascular injection, and allergic or vasovagal reactions.

After giving the study drug, intra-operative vital signs, akinesia score, supplementary injection required and duration of surgery were recorded. After completion of surgery, the surgeons were requested to rate their satisfaction with block quality (0 = not satisfied to 10 = fully satisfied). Patients were also requested to rate their degree of pain on verbal pain scale (0 = no pain to 10 = severe pain) immediately after the block, at the end of procedure and before discharge (6 hours postoperatively). Postoperative rescue analgesia (tablet ibuprofen 500 mg) was given when the patients complained of pain.

Table 1: Demographic data of the participants

Variable	Group-B N = 50	Group-L N = 50	p-value	Significance
Age (y)	59.48 ± 9.696	57.52 ± 9.329	0.306	N.S.
Weight (kg)	61.25 ± 9.601	61.74 ± 8.521	0.784	N.S.
Mean duration of surgery	13.5 ± 4.54	13.4 ± 2.54	0.54	N.S.
M : F	21 : 29	24 : 26		

p > 0.05 is non-significant (N.S.)

Table 2: Local anesthesia volume, akinesia and supplementation

Variables	Group B (n = 50) (Mean ± SD)	Group L (n = 50) (Mean ± SD)	p-value
Primary volume injected,	7.2	7.62	0.78
Total volume injected,	10.2 ± 3.3	10.3 ± 3.1	0.79
Akinesia score; 2 min 5 min 10 min	1.1 ± 1.6 0.84 ± 1.3 0.68 ± 1.3	0.98 ± 0.4 0.50 ± 0.88 0.42 ± 0.8	0.2
Number of patients who required supplementary injection	18 ± 22.8	19 ± 24.1	0.8
Number of patients who required supplementary topical anesthesia intraoperatively	3 ± 2.8	2 ± 1.8%	0.64

P value denotes statistically significant difference between groups.

P < 0.05 is statistically significant

Table 3: Pain scale and the surgeons and patients satisfaction level

Variables	Group(B) (n = 50) (Mean ± SD)	Group(L) (n = 50) (Mean ± SD)	p-value
Verbal pain scale			
1. During block	2.1 ± 1.5	2.4 ± 1.6	0.59
2. At the end of the surgery	0.31 ± 1.0	0.45 ± 1.2	0.54
3. 4 h postoperative	0.70 ± 1.1	0.30 ± .04	0.54
Surgeon's satisfaction	9.40 ± 1	9.31 ± 1.1	0.52
Patient's satisfaction	8.35 ± 1.2	8.30 ± 1.2	0.73

P value denotes statistically significant difference between groups. *p* < 0.05 is statistically significant

Statistical analysis:

The results were analyzed using SPSS version 15. The required sample size was calculated to be 50 patients per group with a = 0.05 and a power of 90% to detect a difference of at least 25% in the successful block. Numerical data such as means and standard deviations were analyzed using unpaired, two tailed t-test. Categorical data were expressed as numbers and percentages using the chi-square test for comparison. *P* < 0.05 was considered statistically significant.

RESULTS

Demographic and descriptive data are presented in Table 1. There were 21 male patients and 29 female patients whose age ranged between 18 to 60 years (59.48 ± 9.696 y) Group B, whereas in group L, there were 24 male and 26 female patients with age

57.52 ± 9.329 y. The average weights, age, sex, ASA physical status, and duration of surgery were not different between two groups significantly ($p > 0.05$).

The primary volume injected in inferotemporal region and the total volume of local anesthetic were not significantly different between groups ($p = 0.78$ and $p = 0.79$ respectively). The mean akinesia score at 2, 5 and 10 min did not differ between groups ($p = 0.24$, $p = 0.26$, $p = 0.23$ respectively).

The number of patients requiring supplementary injection and supplementary topical anesthetic intra-operatively, were comparable between groups. ($p = 0.83$ and $p = 0.54$ respectively (Table 2). No major block related complications like redness, conjunctival edema or local anesthetic toxicity reaction were noted during the study.

Verbal pain scores at various times and patient and surgeon satisfaction scores are presented in Table 3. No significant difference noted in verbal pain scale between both the group immediately after the block, at the end of surgery and 4 h postoperatively ($p = 0.59$, $p = 0.54$, $p = 0.32$ respectively). There was no significant difference in surgeons' ($p = 0.53$) or patients' satisfaction between groups.

Hemodynamic values such as non-invasive systolic and diastolic arterial blood pressures, heart rate and SpO_2 did not show any statistically significant intra-group differences during entire study period.

DISCUSSION

Ophthalmic surgery is most frequent surgical procedure requiring anesthesia in developing country. Nearly 2 million patients undergo cataract surgery each year in United States. Most of the procedures are performed under regional anesthesia like retrobulbar or peribulbar block or topical anesthesia. Regional anesthesia is more preferable because it is economical, easy to perform and lower risks involved. Local anesthesia has rapid onset of action and provides favorable surgical condition like dilated pupils with low intraocular pressure.

Eye blocks have long been limited to blocks performed by the surgeons with only monitored anesthesia care or no anesthesiologist assistance at all. Continuous hunt for newer and safer anesthetic agents has always been one of the primary needs in anesthesiology practice.

Our study has demonstrated that levobupivacaine and bupivacaine are equally successful in achieving clinically satisfactory peribulbar anesthesia with few adverse effects. Animal studies have shown a longer duration of action for levobupivacaine compared with racemic bupivacaine, probably reflecting the vasoconstrictive effect of levobupivacaine at lower

doses, while time to onset may be related to its vasodilatory effect at higher doses.⁹ Studies in humans have reported a similar potency for levobupivacaine compared with racemic bupivacaine,¹⁰ but with less motor blockade and more minor cardiotoxicity using levobupivacaine than racemic bupivacaine.^{11,12} The peribulbar technique we used has a reputation to be safe, being distant from the vessel-rich medial compartment and easy to perform along with minimal needle related risks of retrobulbar hemorrhage and intraneural injection. Peribulbar anesthesia requires relatively large volume of local anesthetics and concerns have been expressed about potential for systemic toxicity.¹³ The incidence of peribulbar blocks requiring supplementary injection has been reported as high as 30 % and 26% with bupivacaine and levobupivacaine respectively, in other studies.¹⁴ The ideal agent for peribulbar anesthesia should have a wide therapeutic index, rapid onset of dense motor and sensory block and duration of action sufficient for surgery. The common combination of bupivacaine and lignocaine achieved many of these aims. Small differences in the block technique may explain the variability in results. The principal drawbacks is potential cardiac and neurological toxicity. Lignocaine has wider therapeutic index, but when used as a sole agent for peribulbar anesthesia, the duration of anesthesia is often too short.

In the present study, addition of hyaluronidase to the drug mixtures significantly reduced the time of onset. It causes increase in pH that is directly proportional to the amount administered and enhances the diffusion of local anesthetic into the nerves without increasing the plasma drug concentration. We have used 5 IU / ml doses of hyaluronidase instead of 15 IU/ml, as it was reported that high concentrations of this enzyme can inhibit skin viability. Also concentration-dependent hyaluronidase toxicity was mentioned to be a cause of postoperative periorbital inflammation after cataract surgery following regional anesthesia. Enzyme act on hyaluronic acid, a component of connective tissue, liquefies the interstitial barrier and increases local anesthetic spread through tissue planes.^{15,16}

In our study, both local anesthetic preparations appeared to be well tolerated and produced good surgical conditions with little adverse reaction. There were no statistical difference in akinesia scores, anesthetic supplementation, pain and surgeons' or patient satisfaction between the groups. Hemodynamic stability, and need for supplemental injection was also same in both groups.

The outcome of our study correlates with the similar other studies. We were unable to assess the duration of motor block as patient's eyes were covered with bandaged post operatively. Mclure and Rubin compared 0.75% levobupivacaine with 0.75 % racemic

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bupivacaine for peribulbar anesthesia. In their study they concluded that there was no statistically significant difference in time to satisfactory block, perioperative pain score or frequency of adverse events.¹⁷ They concluded that safer pharmacological profile of levobupivacaine may offer significant advantage in elderly population undergone cataract extractions in which concurrent disease is common.

Birt and Cummings⁹ reported similar efficacy of 0.75 % levobupivacaine and 0.75 % bupivacaine, both mixed with hyaluronidase for peribulbar block. The time for the onset of satisfactory anesthesia and akinesia were compared between these two drugs. In our study we have used (0.5%) of study drug and combined both the study drug with lignocaine. Results are similar in both studies. In addition Birt and Cummings reported similar incidence of pattern of postoperative pain and requirement of first postoperative analgesia in both groups, which also correlated with our study.

Another study¹⁸ compared two drugs for peribulbar anesthesia and found similar time to onset and duration of anesthesia. Complete akinesia was obtained more frequently when hyaluronidase was added to both groups. They concluded that levobupivacaine is longer acting local anesthetic with limited cardio toxicity and neurotoxicity and may be considered landmark for vitreoretinal surgery in elderly patient.

In a similar study, Nauman and Zahoor concluded that there were no significant differences between levobupivacaine 0.5% and bupivacaine 0.5% in terms of akinesia score, supplementary injection, surgeon and patient satisfaction, and verbal pain score.¹⁹ However in our study addition of hyaluronidase significantly shortened the time to onset for racemic bupivacaine. Addition of hyaluronidase did not significantly improve the time to onset for levobupivacaine, indicating that the vasoconstrictive effect of levobupivacaine is unfavorable for diffusion of local anesthetic, even in the presence of hyaluronidase.

Lai and Sutton²⁰ compared levobupivacaine 0.75% and bupivacaine 0.75% with lignocaine 2% and hyaluronidase for peribulbar anesthesia and concluded that 0.75% levobupivacaine in combination with 2% lignocaine was significantly less effective in terms of speed of onset of anesthesia than bupivacaine 0.75% and lignocaine 2% for peribulbar block. This result is

in contrast to our study where levobupivacaine 0.5% and bupivacaine 0.5% both along with lignocaine 2% are equally effective in time to onset of anesthesia.

We found a good level of surgeon's and patient's satisfaction and that did not differ between groups. Similar result was found by other researchers.²¹ However, Aksu et al.²² reported better surgeon and patient satisfaction in a levobupivacaine treated group compared to bupivacaine treated group.

Clinically it seems that both bupivacaine and levobupivacaine provide satisfactory conditions to perform surgery with a similar clinical profile in dosage used to produce surgical anesthesia. The minimal differences observed between the two agents could be related to the slightly different anesthetic potency. The results do not suggest superior efficacy of levobupivacaine compared with racemic bupivacaine, because of their similar activity as regards to time to onset, duration of action, and motor block. Based on our experience of ophthalmic surgery in elderly patients, levobupivacaine is a suitable anesthetic because of its limited neurotoxicity and low cardiotoxicity, which represents a valid reason for use of levobupivacaine.

LIMITATIONS

The sample size of the present study was small, so to generalize the results, we may need a multi-center larger trial.

CONCLUSION

Peribulbar block with a mixture of levobupivacaine 0.5% and lignocaine 2% or bupivacaine 0.5% and lignocaine 2% provide similar block quality and efficacy for cataract surgery. Levobupivacaine is known to have a lower cardiotoxicity and neurotoxicity as compared to bupivacaine, so it may be preferable for cataract surgery in elderly patient having co-existing systemic diseases.

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