Original Article

A prospective comparison of the efficacy of 0.5% bupivacaine vs 0.75% ropivacaine in peribulbar anesthesia for vitreoretinal surgery

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Purpose: To date, there is no information on the comparison of the effect of 0.5% bupivacaine with 0.75% ropivacaine solution for vitreoretinal surgery. The aim of the study was to compare the efficacy of 0.5% bupivacaine with 0.75% ropivacaine in peribulbar anesthesia for vitreoretinal surgery. This was a prospective randomized double-blinded observational study in a hospital setting. Sixty patients planned for vitreoretinal surgery were randomized into two groups based on the peribulbar injection administered either with 0.5% bupivacaine or 0.75% ropivacaine solution, as Group B (n = 30) and Group R (n = 30), respectively. Time of onset of analgesia, akinesia, and the need for supplemental anesthesia were noted. Student's t-test or Mann-Whitney U test were used for comparing continuous variables and Chi-square or a Fischer exact test were used as appropriate for comparing two proportions. **Results:** The patients in Group R showed an earlier onset of both, analgesia (1.97 min vs. 2.10 min, P = 0.002) and akinesia (2.77 min vs. 4.20 min, $P < 0.001$) compared with the patients in Group B. The efficacy of the block attained was Grade 5 (adequate anesthesia and akinesia without supplementation) in about 97% of the patients in Group R while only 90% in Group B. However, the differences between the groups for the efficacy of the block were not statistically significant (P = 0.301) neither for Grades 5 nor for Grade 4 and 3 (P = 1.00 for both). The onset of postoperative pain was similar for both groups (P = 1.00). **Conclusion:** We concluded that 0.75% ropivacaine is a better choice of local anesthetic solution for patients undergoing primary vitreoretinal surgery compared with 0.5% bupivacaine.

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An ideal local anesthetic agent used for intraocular surgery must have a rapid onset with an adequate duration of action, to permit a painless and movement-less surgery, while not prolonging the akinesia. Ropivacaine is a newer amino-amide local anesthetic which is synthesized as a pure levo-enantiomer, and is reported to provide good anesthesia with motor block and also has lesser cardiovascular effects compared with bupivacaine.[1] Perello *et al*.[2] studied the efficacy of ropivacaine alone and as a mixture with lidocaine and with lidocaine-bupivacaine as a peribulbar injection for cataract surgery. They further recommended the use of 0.5% ropivacaine as a single drug for peribulbar anesthesia for cataract surgery. Ozcan *et al*.[3] also showed that ropivacaine used in the peribulbar block was better than bupivacaine-lidocaine mixture under the same standard conditions in terms of reducing intraocular pressure and postoperative pain in intraocular surgery. Similarly, Gioia *et al*.[4] compared the efficacy of ropivacaine and a lidocaine-bupivacaine mixture in peribulbar anesthesia for vitreoretinal (VR) surgery.

We have previously reported that mixing lidocaine and bupivacaine has no advantage over 0.5% bupivacaine solution in peribulbar anesthesia for VR surgery. Plain bupivacaine solution alone provides a better quality of anesthesia for VR surgeries.[5] However, to date, there is no information on the comparison of the effect of 0.5% bupivacaine with 0.75% ropivacaine solution in vitreoretinal surgery under peribulbar anesthesia. Therefore, the primary aim of the study was to compare the efficacy of 0.5% bupivacaine with 0.75% ropivacaine solution for patients undergoing vitreoretinal surgery under peribulbar anesthesia.

Methods

This was a prospective, randomized, double-blinded study done at a tertiary eye care center in South India. After obtaining ethical approval from the institutional review board of the Vision Research Foundation in Chennai, India (Study code: 579-2016-P. Date of approval: 04 January 2017), sixty patients gave written informed consent to participate in the study. The study adhered to the tenets of the Declaration of Helsinki. Both men and women 40 years of age or older, who were scheduled for vitreoretinal surgery (scleral buckle alone or vitrectomy plus belt buckle [240 bands] with or without additional procedure) under peribulbar

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anesthesia, were enrolled in the study. Intellectually disabled patients, patients receiving preoperative sedation, those with a history of previous intraocular surgery, orbital surgery, or ocular trauma, and those with a history of allergies to local anesthetics were excluded.

All eligible patients were randomized into two groups as Group B and Group R and received 0.5% bupivacaine and 0.75% ropivacaine solution, respectively for peribulbar anesthesia. In both the groups, injection hyaluronidase 7.5 IU/ml was used. Randomization was done based on computer-generated random numbers. The anesthetic solution bupivacaine (sensorcaine 0.5%; AstraZenica), ropivacaine (ropin, Neon Laboratories Ltd), and hyaluronidase (hynidase; Shreya Life sciences, Aurangabad, India) were prepared by an anesthetist. Baseline heart rate and blood pressure were noted. The patients underwent routine monitoring which included electrocardiograph (ECG), noninvasive blood pressure (NIBP), and pulse oximetry. The peribulbar block involving two injections in the extraconal space—one in the lower temporal quadrant and the other in the medial peribulbar space was given at a rate of 5 ml in 10 s, by a second blinded anesthesiologist. A 23G, 1" steel needle was used for the peribulbar block.

The globe was massaged with the help of three middle fingers placed over a sterile gauze pad, with the middle finger applying gentle pressure directly over the eyeball for a time interval of 2 min. For every 30 s, the pressure was released for 5 s for the vascular pulsations to occur. At the end of the second min, injection into the medial peribulbar quadrant was given, followed by a digital ocular massage of the globe as mentioned above for a time interval of 2 min. The time of onset of the effective blockade was noted by the onset of analgesia and akinesia in the eye, every 30 s by the second blinded anesthesiologist. Adequacy of analgesia was assessed by holding the bulbar conjunctiva with toothed forceps while adequacy of akinesia was assessed using the scoring system of Brahma and colleagues[6] as 3-full movement, 2-moderate movement, 1-flicker, and 0-no movement.

Ocular movements were scored for each direction of gaze in the superior, inferior, medial, and lateral directions, with a possible total maximum score of 12 points. After 5 min following medial injection, if there was a full movement in any direction or a total ocular movement score of 6 or greater, supplementary anesthesia was provided with an inferolateral injection of 3–5 ml of the test solution. A further inferolateral injection was performed if the block was still inadequate after 10 min. The need for supplementary regional anesthesia and the total volume of local anesthetic solution required was recorded. Vital signs were monitored throughout the surgery every 15 min. Patients were encouraged to communicate with the surgeon regarding pain during the surgery and if necessary, intraoperative parabulbar (sub-Tenon's block) supplementation with the same test solution was given.

The operating surgeon who was also masked to the solution used, finally graded the efficacy of anesthesia as shown in Table 1.

Throughout the study, the block was administered by the same blinded anesthesiologist and surgery was performed by a single surgeon. Postoperative symptoms such as nausea, vomiting, and the time of onset of pain (tolerable/intolerable pain, requiring analgesics) if any, were noted by an assisting doctor who was masked to the study details. Oral paracetamol tablet was given in the immediate postoperative period for all patients. If pain was tolerable (mild), then patients were given tablet paracetamol. If it was intolerable (moderate to severe), then, 30 mg of intramuscular injection Ketorolac was administered and the same was recorded.

Table 1: Efficacy of regional anesthesia

Grade	Anesthesia (adequate or not)	Akinesia (adequate or not)	Supplementation (required or not)
5	+	+	-
4	+	-	-
3	-	+	+
2	+	-	+
1	-	-	+
0	-	-	+*

*or other complication and surgery terminated

Statistical analysis

Data were examined for normality of distribution. To compare the clinical characteristics between the two groups, a student's *t*-test was utilized for normally distributed variables. Variables, namely, the onset of analgesia, akinesia, and the onset of pain did not follow a normal distribution; therefore, these variables were compared using a Mann-Whitney U test. Proportions were compared using a Chi-square or a Fischer exact test as appropriate. SPSS software version 14.0 (SPSS, Inc./IBM, Chicago, IL) was used for statistical analysis. Results were considered significant if the *P* value was less than 0.05.

Results

Table 2 shows the patient characteristics and the type of surgery performed.

Patients in the two groups did not differ in terms of age ($P=0.723$), weight ($P=0.974$), heart rate ($P=0.990$), systolic ($P=0.462$) or diastolic blood pressure ($P = 0.845$) The two groups did not differ in terms of duration of surgery ($P=0.861$) or the distribution of patients who underwent scleral buckle (SB) only ($P = 1.000$), SB + vitrectomy (V), ($P = 0.585$), phacoemulsification (PE) with intraocular lens (IOL) or scleral fixated (SF) IOL + V, ($P = 0.248$), or V plus lens aspiration ($P = 0.593$).

The mean volume of local anesthetic solution needed for achieving effective block was higher in the bupivacaine group compared to the ropivacaine group, (10.9 ml vs. 9.3 ml, $P = 0.031$) [Fig. 1a]. Fig. 1b shows a bar graph showing the distribution of time of onset of akinesia and analgesia in both the groups. In Group R, patients had an earlier onset of analgesia (1.97 min vs. 2.10 min, $P = 0.002$) and akinesia (2.77 min vs. 4.20 min, $P < 0.001$) compared with patients in Group B. The onset of postoperative pain was similar in both groups. ($P = 1.00$), Fig. 1c shows a bar graph showing the distribution of patients during surgery who required parabulbar supplementation once, twice, and those who needed intramuscular ketorolac during the postoperative period. The proportion of subjects who required intraoperative parabulbar supplementation once (43% in Gr B Vs. 6.6% in Gr R, $P=0.057$), twice (6.6% in Gr B vs. 0.0% in Gr R $P = 0.491$) and those who required postoperative intramuscular ketorolac (6.6% in Gr B

Table 2: Patient characteristics in Bupivacaine (Group B) Vs Ropivacaine (Group R)

	Bupivacaine (*n*=30)					Ropivacaine (*n*=30)					*P*
	n	Mean or %	SD	Min	Max	*n*	Mean or %	SD	Min	Max	
Age (mean in years)	30	57	8.7	40	75	30	57.9	10.8	41	85	0.723
Weight (in Kg)	30	67	12.9	40	90	30	66.9	10.8	47	83	0.974
Heart rate (per min)	30	77	10	50	100	30	77	11	50	105	0.990
Systolic BP (mmHg)	30	151	22	113	190	30	155	22	110	188	0.462
Diastolic BP (mmHg)	30	87	6	78	104	30	87	6	75	100	0.845
Duration of surgery (min)	30	137.7	32.7	60	210	30	136.2	33.1	80	200	0.861
Type of surgery (%)											
SB	1	3.3				1	3.3				1.000
SB and V	11	36.7				9	30				0.585
PE/SF IOL+V	6	20				10	33.3				0.248
V only (plus L)	12	40				10	33.3				0.593

BP=Blood pressure, Kg, Kilogram, min=Minute, ml=Milliliter, SB=Scleral buckling/encirclage, V=Vitrectomy, PE/SFIOL=Phacoemulsification/scleral fixated IOL, L=Lensectomy/lens aspiration

vs. 3.3% in Gr R, *P* = 1.00) was all higher in Group B than in Group R but the differences were not statistically significant, Fig. 2a shows the distribution of various grades of the efficacy of regional anesthesia in Gr B and Fig. 2b shows efficacy in Gr R. Efficacy of the anesthesia attained was Grade 5 in 97% of the patients in Group R while in Group B only 90% of the patients attained it. However, the difference in the proportion who achieved various grades of the block was not statistically significant (*P* = 0.301) for any grade of anesthesia.

We also assessed the onset of analgesia and akinesia vitrectomy alone versus vitrectomy combined with other procedures. In the Group B, the mean time of onset of akinesia in vitrectomy alone was 161.2 (91.9) and in combined surgeries it was 312.7 (167.8), (*P* = 0.068); the mean time of onset of analgesia in vitrectomy alone was 122.0 (11.3) and it was 128.3 (10.8) for vitrectomy combined surgeries (*P* = 0.356). In the Group R, the mean time of onset of akinesia in vitrectomy alone was 187.0 (133.5) and in combined surgeries was 155.5 (104.2), (*P* = 0.368); the mean time of onset of analgesia was 121.0 (3.1) and in combined surgeries it was 117.0 (14.5), (*P* = 0.431).

There were no adverse events in the study.

Discussion

We compared the efficacy of 0.5% bupivacaine with 0.75% ropivacaine solution for patients undergoing vitreoretinal surgery under peribulbar anesthesia. The study found that 0.75% ropivacaine had a quicker onset of akinesia and analgesia with a similar duration of action. The need for supplementation for analgesia was also less with ropivacaine solution.

The time of onset of akinesia is significantly prolonged in Gr B compared to Gr R patients. This could probably be a likely explanation for the higher mean + SD volume of bupivacaine solution (10.9 + 3.2 ml) compared to the mean + SD volume of ropivacaine (9.3 + 2.5 ml) solution needed for achieving effective regional blockade.

With just a single inferolateral injection, total akinesia and complete lid block cannot be achieved. However, with a second medial peribulbar injection, both can be attained. Therefore, we used two injections.[7,8]

Similar to our study, Giola *et al*.[4] reported better postoperative anesthesia with ropivacaine as compared to combined lignocaine and bupivacaine. However, this study was limited only to macular surgeries, where the globe manipulation was minimal. Similar to our study, Seidenari *et al*.[9] in their series of 919 vitreoretinal surgeries, found total akinesia in 87.5% and analgesia (no pain) in 93% of the operated cases. However, they assessed these parameters 15 min after the block. Since we assessed the parameters after 5 min, we could comment on the onset of akinesia and analgesia.

Perello *et al*.[2] in their randomized control trial compared the efficacy of plain ropivacaine with bupivacaine-lidocaine and ropivacaine-lidocaine mixtures for peribulbar blocks in cataract surgery. Unlike our study, they did not find an early onset of akinesia and analgesia with ropivacaine. However, they had used lower concentration, 0.5% ropivacaine. Similar differences in onset, based on the concentration of the drug used has been shown by Casati *et al*.[10] in the interscalene brachial plexus block.

The rate of onset of anesthesia is determined by its pKa value (the pH at which 50% of the drug exists in its active nonionized form). However, the pKa values are similar for bupivacaine and ropivacaine. The earlier onset of akinesia and analgesia with ropivacaine could probably be related to the differential lipid solubility of the two drugs.

As the cataract surgery is done before the vitreoretinal surgery in a combined procedure, the benefit of earlier onset of both analgesia and akinesia with ropivacaine can be utilized based on the type of procedure. Previous studies have reported the use of topical ropivacaine for vitreoretinal surgeries,[11,12] along with sedatives for short-duration procedures. However, for more lengthy procedures and those requiring globe manipulation, this approach may not be ideal. Therefore, we did not use topical anesthesia for our study participants.

One of our study limitations is that we did not assess postoperative discomfort at the injection site. Another potential

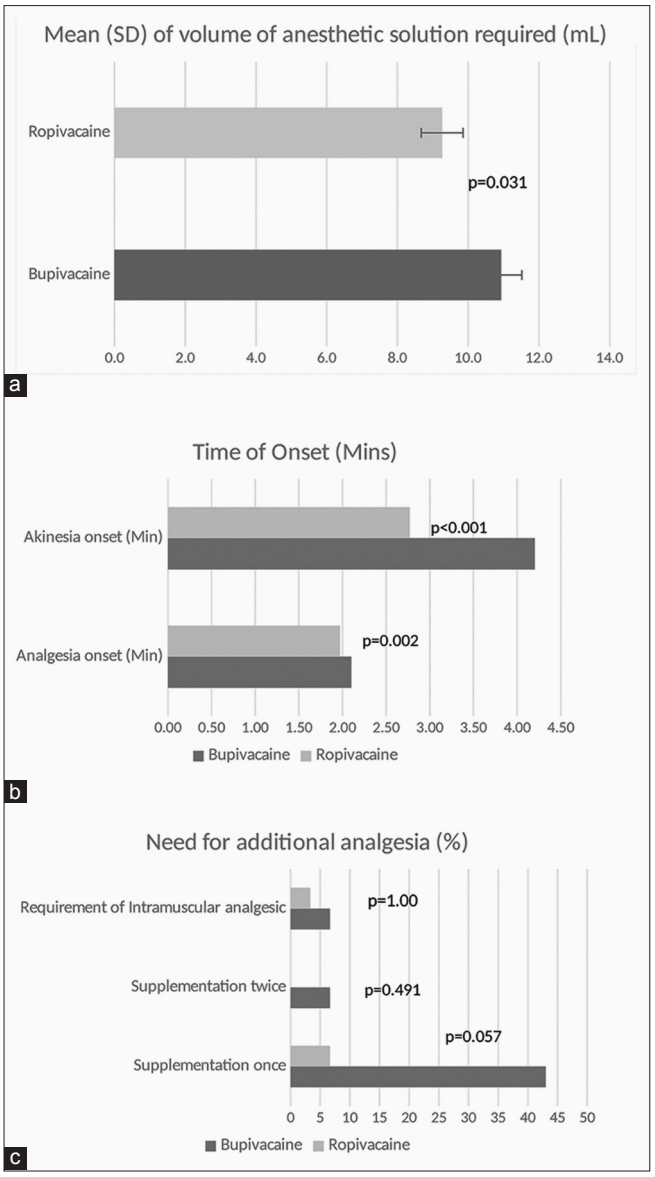

Figure 1: (a) Mean (SD) of the volume of anesthetic solution required (mL) (b) Time of onset of analgesia and akinesia (c) Need for additional analgesia

limitation is that we did not use any postoperative pain assessment scale.

Conclusion

Our study emphasizes more about the noninferiority of the drugs in comparison and we conclude that 0.75% ropivacaine is a better choice of local anesthetic solution for patients undergoing primary vitreoretinal surgery than 0.5% bupivacaine.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) have given their consent for their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

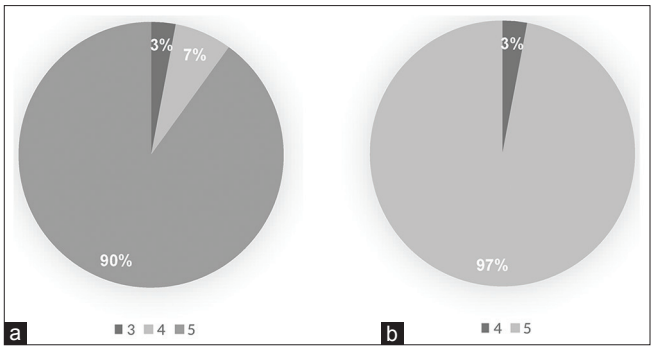

Figure 2: Proportion of subjects according to grading of efficacy (a) Bupivacaine (b) Ropivacaine

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Conflicts of interest

There are no conflicts of interest.

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