Original Article

Comparative clinical trial of intracameral ropivacaine vs. lignocaine in subjects undergoing phacoemulsification under augmented topical anesthesia

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Purpose: To compare intracameral Ropivacaine to Lignocaine during phacoemulsification under augmented topical anesthesia, in terms of efficacy and safety. **Methods:** This prospective, randomized, double-masked clinical trial included subjects planned for phacoemulsification with posterior chamber intraocular lens implantation for visually significant uncomplicated senile cataract, under augmented topical anesthesia. Cases were randomized into two groups, Group A (Ropivacaine 0.1%) or Group B (Lignocaine 1.0%). The pain experienced by the patients during the surgery, mydriasis, post-op inflammation and endothelial cell change at six weeks after the procedure was evaluated. Surgeon's feedback was recorded to evaluate the cooperation of the patient during surgery. **Results:** A total of 210 subjects were screened and 184 were randomized to have 92 subjects in each group. There was no statistically significant difference seen on comparing Group A and B with respect to Age (P = 0.05), painful surgical steps (P = 0.85), visual analog scale scores (P = 0.65), surgeon's score (P = 0.11), postoperative inflammation (P = 0.90) and average ultrasound time during phacoemulsification (P = 0.10). Subjects in Group A fared better when compared to Group B with respect to endothelial cell loss (P = 0.0008), and augmentation in mydriasis (P < 0.001). **Conclusion:** Intracameral Ropivacaine and Lignocaine, both are equally effective in providing analgesia during phacoemulsification. However, intracameral Ropivacaine is superior to Lignocaine with regards to corneal endothelial cell safety, and augmenting mydriasis.

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Cataract surgery is the most common eye surgery with excellent and exceptionally cost-effective outcomes, second only to vaccination.[1] It is also one of the commonest surgical procedure worldwide.[2] Phacoemulsification and Manual Small Incision Cataract Surgery (MSICS) are the two most popular and comparable methods of removal of cataract (combined with implantation of Intra Ocular Lens) which provide complete rehabilitation of these patients.[3] Both can be done under topical anesthesia,[4] which is the anesthesia of choice due to least complications and being patient friendly when compared to contemporary techniques like Peribulbar, Retrobulbar, Sub-tenon, and subconjunctival anesthesia.[5] Cataract surgery under topical anesthesia is less painful with better patient comfort when augmented with intracameral anesthesia using Lignocaine 0.5–1% solution.[6]

However, Lignocaine is known to have dose related toxicity to corneal endothelium.[7] The studies have concluded that the Ropivacaine is safer than Lignocaine on tissue and a comparatively lower dose is effective and less toxic.[8] In comparison to Lignocaine a novel anesthetic agent, Ropivacaine is safer and equally effective local anesthetic agent when compared to Lignocaine for local anesthesia during intraocular surgery.[8-10] It has also been evaluated for toxicity to corneal endothelium, *in vitro* and animal studies.[7,8,11,12] It is also known that the intracameral injection of anesthetic agents can percolate into the vitreous cavity and cause toxicity to the retina,[13] thus the relative safety of Ropivacaine to retinal tissue[9,14] is also a relevant issue when being used as an intracameral anesthesia agent.

This study was designed to compare the safety and efficacy of intracameral Ropivacaine 0.1%to Lignocaine 1.0% in patients undergoing phacoemulsification under augmented topical anesthesia for uncomplicated senile cataract.

Methods

This was a double blinded randomized control trial to compare the patients' pain experience, surgeon's experience and the outcome of cataract surgery under augmented topical

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anesthesia using Ropivacaine or Lignocaine at a tertiary care Government hospital in North India. The study adhered to the Tenants of the Declaration of Helsinki and was conducted after approval from the Institutional Review Board.

Patients of age above or equal to 40 years with senile uncomplicated cataracts who were planned for cataract surgery were screened for exclusion criteria [Table 1] and included in the study after obtaining informed consent. Subjects included were randomized into Group A (Ropivacaine) or Group B (Lignocaine). The subject, surgeon and observer were masked to the randomization. The preoperative diagnostic workup protocol included demographic details of the patients, and ophthalmological examination, including Cataract LOCS III grading. Preoperative and postoperative (6 weeks post-surgery) endothelial cell count was done using a specular microscope (Specular microscope em-4000, Tomey Corporation, Japan).

Surgeries were done by a single surgeon using INFINITI vision system (Alcon Labs, Fortworth, USA) phacoemulsifier. After making a 2.8 mm two planer superior corneal tunnel, either 0.2 ml preservative-free 0.1% Ropivacaine (Neon Laboratories Ltd, India) or 1.0% Lignocaine (Sunways Pvt Ltd, India) was injected in the anterior chamber through the main tunnel as per the group assigned. After 20 seconds, phacoemulsification was done with implantation of Foldable 6 mm optics, hydrophilic acrylic IOL. Pupil size at the end of the surgery and total Phaco time was noted.

Patients were instructed to inform verbally about any discomfort or pain during the surgery. Any need of rescue analgesia due to operative discomfort, sufficient to warrant supplemental topical or peribulbar or retrobulbar anesthesia or sedation was noted. At the end of the surgery, Visual Analog Scale (VAS) was given to the patient to report their pain experience by marking at the appropriate point. For those patients who could not comprehend the scale, there was an integrated modified Wong Scale in the local language.[15] The surgeon graded their experience regarding the patient cooperation and ease of surgery as per the questionnaire described by Gupta *et al.* [Table 2].[15] Postoperative anterior chamber reaction was evaluated next day by quantification of aqueous flare and cells using SUN (Standardization of Uveitis Nomenclature) criteria. Intraocular pressure was measured postoperatively at day one by applanation tonometer. IOP >20 was considered high and anti-glaucoma was given.

Sample size calculation and statistical tests

Sample size of 93 in each group was reached upon assuming population of 3000 (total number of cataract surgeries performed at the department in a year) with confidence level 95% and confidence interval of 10%. Descriptive statistics were used to analyze the parameters and their distribution. Chi-square Test was used for categorical data and for numerical data, Student-t test or Rank sum tests were used.

Results

Patients

A total of 210 subjects presenting with senile cataract were screened against inclusion criteria and finally 184 subjects were included in the study and randomized into groups A and B with 92 subjects in each group. During the study period 5 patients were lost to follow-up or did not report, these subjects were excluded from the data analysis [CONSORT flow diagram, Fig. 1]. The distribution of patients in the groups and demographic data is depicted in Table 3. The cataract distribution as per LOCS classification among the groups is depicted in Fig. 2. This distribution was symmetrical and the proportion of different grades of nuclear sclerosis was statistically similar among the two groups (P = 0.18). The average intraocular pressure at the time of enrolment was 14.2 mm Hg (SD 1.98, Range 10–20) and the IOP among the subjects in the groups (Group A = 14.53 mm Hg (SD 1.93, Range 12–20), group B = 14.16 mm Hg (SD 2.01, Range 10–20)) was similar statistically (P = 0.17). The average endothelial cell density before the surgery was 2561.0 cells/mm^2 for all the subjects in the study. The endothelial cell density was not symmetrical among the groups as the mean cell density was 2657.7, and 2463.3, in group A and group B and this difference was statistically significant (P = <0.001) [Table 4].

Table 1: Exclusion criteria for screening patients for Phacoemulsification under augmented topical anesthesia

Exclusion criteria for patients enrolled in the comparative study for intracameral Ropivacaine vs. Lignocaine
Any previous intraocular surgery.
Patients with known hypersensitivity to Ropivacaine or Lignocaine.
Uncooperative attitude (intellectually challenged, involuntary movements).
Communication problems (hearing disability, language barrier).

Table 2: Surgeon's score questionnaire for phacoemulsification under augmented topical anesthesia

Per-op parameter	1	2	3
Patient cooperation	Excellent	Good	Poor
Difficulty due to ocular movements	None	Some	Great
Anterior chamber stability	Excellent	Good	Poor
Complications	None	Yes (Mention)	
Pupillary size (in mm)	Preoperative	After intracameral	

Anesthesia and pain evaluation

There were no complications due to the method of anesthetic administration. The maximum number of subjects felt pain during bisection of the nucleus in both the groups and this was the same among the groups (P = 0.85). No patient in either group experienced operative discomfort sufficient to warrant rescue anesthesia, and none reported discomfort beyond mild stinging with topical administration of anesthetic. The average VAS scores recorded at the end of the surgery was 2.29 (SD 0.70, Range 2–4) and the distribution was not normal (P < 0.001). The VAS scores in Group A (Ropivacaine) to Group B (Lignocaine) were statistically similar (P = 0.65).

Surgical safety evaluation

Pupillary dilatation at the start of the surgery averaged 6.36 mm (SD 0.46, Range 5–7.5 mm) in all the subjects and was 6.42 (SD 0.47) and 6.29(SD 0.44) mm among the group A and B, respectively (P = 0.06). At the end of the study, the average pupillary diameter increased from baseline to 7.52 mm (SD 0.49,

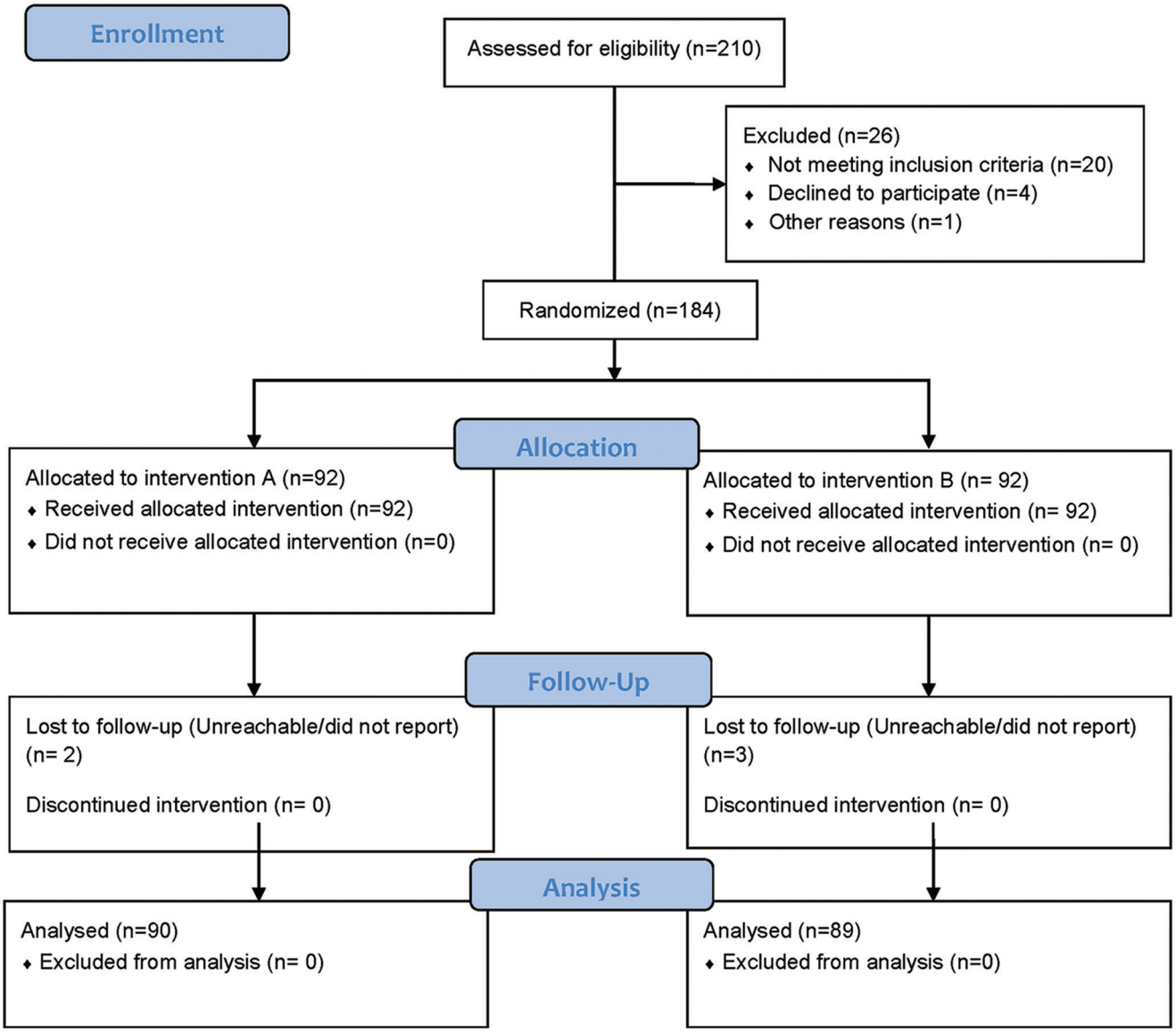

Figure 1: CONSORT 2010 Flow Diagram for the double-blind randomized control clinical trial to study and compare the effect of intracameral Ropivacaine 0.1% vs. Intracameral Lignocaine 1% in subjects undergoing cataract surgery by Phacoemulsification technique under augmented topical anesthesia

Table 3: Demographic details of the subjects in the study groups

n=162	Group A (Ropivacaine)	Group B (Lignocaine)	*P*
Number	90 (50.3%)	89 (49.7%)	
Male	62 (68.9%)	70 (78.7%)	0.18 (Chi-sq test)
Female	28 (31.1%)	19 (21.3%)	
Average age in years (SD, Range)	61.8 (5.9, 53-79)	63.43 (5.55, 49-73)	0. 05 (Student *t* test)
Average Pre-op IOP (mm Hg)	14.53	14.16	0.17 (Mann-Whitney test)

Range 6–8 mm). Thus, there was an increase in the pupillary dilatation (Average 1.16 mm SD, 0.42, Range 0.0–2 mm) at the end of the surgery in all the patients in the study. Intergroup comparison showed that this increase in the size of the pupil size was greater in group A (Average 1.28 mm) vs group B (1.05 mm) and this difference was statistically significant [Table 5, $P < 0.001$]. The endothelial cell count reduced in all the subjects as per the evaluation at 6 weeks after the cataract surgery by an average of 155.56 cells/mm^2 (SD 91.46, Range 3–629 cells/mm^2, $P < 0.0001$). the endothelial cell loss was significantly less in Group A when compared to Group B ($P < 0.001$). Table 4. The endothelial cell loss was related

to the EPT with a correlation coefficient of 0.3, ($P < 0.0001$). Post-surgery anterior chamber flare was similar in both the groups ($P = 0.90$) which indicates similar postoperative inflammation in both the groups. No reaction was seen in 86.7% and 85.4% in Group A and B, respectively. Grade I reaction was seen in 7.8%and 11.2% of patients in group A and B, respectively. Grade II reaction was more in group A (5.6%) than group B (3.4%). Average effective ultrasound time (Infinity Vision system, Alcon India) during the cataract surgery of all the subjects was 6.20 seconds. None of the subjects had IOP more than 20 mm Hg at day 1 post-op. The difference in the ultrasound time during phacoemulsification among the groups was statistically insignificant ($P = 0.1$) Table 5.

Patient cooperation evaluation

Surgeon's experience as measured by the surgeon's feedback on the patient's cooperation and other parameters during the surgery was statistically similar in both the groups ($P = 0.11$). The parameters evaluated were patient's cooperation during the surgery (Group A = 1.1, group B = 1.25, $P = <0.006$, Mann-Whitney test), anterior chamber stability (Group A = 1.12, group B = 1.2, $P = 0.07$), and overall surgical difficulty as judged by the surgeon (Group A = 1.13, group B = 1.19, $P = 0.11$).

Discussion

This study compares the efficacy and safety of intracameral Ropivacaine 0.1% with Lignocaine 1.0% in elective phacoemulsification cataract surgery under augmented topical anesthesia for the first time. Though there are studies which have investigated the safety and efficacy of Ropivacaine as topical and local anesthetic agent and have concluded that Ropivacaine has better efficacy and safety profile when compared to Lignocaine,[11,16] but at the time of reporting there were no human studies available regarding the safety of intra-cameral Ropivacaine and/or comparison to other intracameral medications in practice.

To assess the efficacy of randomization and to evaluate the presence of confounding factors, we compared the two groups with respect to demographic and clinical variables viz. age, sex, preoperative intraocular pressure, cataract grading (Lens Opacities Classification System III Grading). There was no statistically significant difference in these variables between the 2 groups. Thus, we can safely assume that these factors would not have affected our outcome.

The pre-op endothelial cell counts, however, were significantly different between the two groups ($P < 0.001$). This difference was induced in spite of randomization and the impact of this difference in comparing the safety profile of the two anesthetic agents was excluded by comparing the net reduction in the endothelial cell density in the two groups at 6 weeks after the procedure.

Augmentation of topical anesthesia by intra-cameral anesthesia has been conclusively proven to improve the pain experience of the patients undergoing phacoemulsification.[6] An important goal of our study was to compare per-operative analgesia between the two groups. No statistically significant difference was seen in the VAS on comparing Group A and B ($P = 0.41$), thus supporting equal analgesic efficacy of Ropivacaine and Lignocaine. Intra-operative anesthesia and analgesia to the patient and comfort to the surgeon can be indirectly reflected well by the need for rescue analgesia requirement which was not required in both, Group A and Group B.

The painful steps during phacoemulsification surgery are bisection of the nucleus, rotation of nucleus, and cortical aspiration in decreasing order of frequency as discussed in other reports.[17,18] Our patients also reported similar experience and this was comparable between the two groups ($P = 0.91$), supporting the equal efficacy of Lignocaine and Ropivocaine in providing analgesia.

Phacoemulsification through a small pupil is associated with increased operating time and a higher incidence of intraoperative complications like endothelial cell loss, nucleus drop, and posterior capsular tear.[19] It is known that the pupillary dilatation can be initiated and maintained by intracameral anesthesia, and it is sufficient to allow surgery without the use of pre-operative mydriatics.[19,20] In our study, we found that pupillary dilatation augmentation by intracameral anesthesia was statistically significant in both the groups. However, this increase in the pupillary diameter was statistically more pronounced in group A when compared to group B ($P < 0.001$).

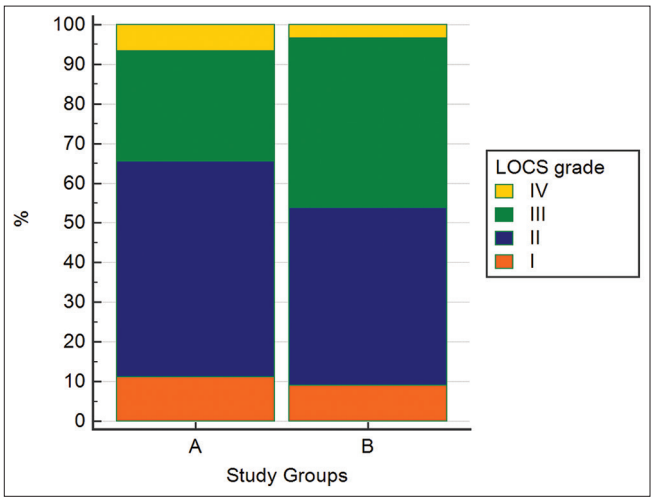

Figure 2: Cataract nucleus grading (LOCS) distribution among the study groups (Group A = Ropivacaine, Group B = Lignocaine) ($P = 0.18$)

Table 4: Endothelial cell density and changes after cataract surgery: Comparison between intracameral Ropivacaine and Lignocaine

Endothelial cells/sq mm	Group A (Ropivacaine)	Group B (Lignocaine)	*P* (Mann-Whitney test)
Pre surgery Average cell density	2657.7	2463.3	<0.001
Post-surgery	2520.2	2289.4	<0.001
Change in cell density after cataract surgery	-137.4 (5.1%) *P*<0.001	-173.8 (7.0%) *P*<0.001	<0.001

Table 5: Comparison of EPT and change in pupil size in intracameral Ropivacaine vs. Lignocaine

	Average EPT (sec)		Change in pupil size (mm)	
Group A (Ropivacaine)	6.17	*P*=0.05	1.28	*P*<0.001
Group B (Lignocaine)	6.37		1.05	

Endothelial cell density reduction is expected after routine uncomplicated cataract surgery with Posterior chamber Intra-Ocular Lens implantation and has been estimated by various studies to be in the range of 8–19% depending on various surgery and patient-related factors.[21-23] In our study, the average endothelial cell loss was 7.8 and 9.7% in group A and group B respectively which is comparable to other studies under local anesthesia and topical anesthesia alone. Group A subjects had significantly less loss of endothelial cells, when compared to group B subjects (P = 0.001). There was no significant difference in Effective Phaco Time between the two groups in our study.

Flare and cells response in the immediate postoperative period was acceptable in both the groups and was not statistically similar (P = 0.94). There was a short-term rise in the IOP in patients of Group B (P < 0.05) with spontaneous resolution at 6 weeks.

Surgeon's satisfaction was assessed by various questionnaires in similar studies[24-26] in which the surgeon's satisfaction was assessed on the basis of patient discomfort and surgeon stress. We assessed the surgeon's satisfaction on the basis of the questionnaire in our study. It included the patients' cooperation, difficulty due to ocular movements, anterior chamber stability, complications and an increase in pupillary size during surgery. In both the groups, the parameters judged by the surgeon with respect to the surgical safety and ease were favorable and the surgeon's score was statistically similar (P = 0.17).

The study shows that the pain experienced during phacoemulsification under augmented topical anesthesia using intracameral Ropivacaine or Lignocaine is comparable and acceptable to the patients. At the same time, the analgesia is sufficient to complete the procedure safely without causing the surgeon any significant difficulty. The use of intracameral Lignocaine or Ropivacaine is safe to corneal endothelium; it augments the pupillary dilatation and does not affect the IOP or increase inflammation. When compared, Ropivacaine is significantly safer to endothelium when compared to Lignocaine, thus Ropivacaine may be a preferred choice in view of similar efficacy and better safety for the endothelium.

Conclusion

Intracameral Ropivacaine is equally effective to Lignocaine in providing analgesia and superior in maintaining mydriasis and safety of endothelial cells. Which makes it a preferable choice for intracameral use as anesthetic agent.

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Conflicts of interest

There are no conflicts of interest.

References

1. Ellwein LB, Lepkowski JM, Thulasiraj RD, Brilliant GE. The cost-effectiveness of strategies to reduce barriers to cataract surgery. The Operations Research Group. Int Ophthalmol 1991;15:175-83.
2. Kessel L, Andresen J, Erngaard D, Flesner P, Tendal B, Hjortdal J. Indication for cataract surgery. Do we have evidence of who will benefit from surgery? A systematic review and meta-analysis. Acta Ophthalmologica 2016;94:10-20.
3. Jaggernath J, Gogate P, Moodley V, Naidoo KS. Comparison of cataract surgery techniques: Safety, efficacy, and cost-effectiveness. Eur J Ophthalmol 2014;24:520-6.
4. Gupta SK, Kumar A, Agarwal S. Cataract surgery under topical anesthesia using 2% lignocaine jelly and intracameral lignocaine: Is manual small incision cataract surgery comparable to clear corneal phacoemulsification? Indian J Ophthalmol 2010;58:537-40.
5. Zhao LQ, Zhu H, Zhao PQ, Wu QR, Hu YQ. Topical anesthesia versus regional anesthesia for cataract surgery: A meta-analysis of randomized controlled trials. Ophthalmology 2012;119:659-67.
6. Ezra DG, Allan BD. Topical anaesthesia alone versus topical anaesthesia with intracameral lidocaine for phacoemulsification. Cochrane Database Syst Rev 2007;:CD005276. Review. PubMed PMID: 17636793.
7. Borazan M, Karalezli A, Oto S, Akova YA, Karabay G, Kocbiyik A, *et al*. Induction of apoptosis of rabbit corneal endothelial cells by preservative-free lidocaine hydrochloride 2%, ropivacaine 1%, or levobupivacaine 0.75%. J Cataract Refract Surg 2009;35:753-8.
8. Pescosolido N, Scarsella G, Tafani M, Nebbioso M. Cataract surgery complications: An *in vitro* model of toxic effects of ropivacaine and lidocaine. Drugs R D 2012;11:303-7.
9. Zhou YL, Tong Y, Wang YX, Zhao PQ, Wang ZY. A prospective, randomized, double-masked comparison of local anesthetic agents for vitrectomy. Br J Ophthalmol 2017;101:1016-21.
10. Kashyap A, Varshney R, Titiyal GS, Sinha AK. Comparison between ropivacaine and bupivacaine in deep topical fornix nerve block anesthesia in patients undergoing cataract surgery by phacoemulsification. Indian J Ophthalmol 2018;66:1268-71.
11. Caça I, Kavak V, Unlü K, Ari S, Nergis Y, Take G. The histopathological effect of intracameral ropivacaine in different concentrations on corneal endothelium. Ann Ophthalmol (Skokie) 2006;38:43-8.
12. Soker S, Cakmak S, Olmez G, Buyukbayram H, Nergiz Y. Investigation of the toxic effects of ropivacaine corneal endothelium by the impression cytological method. Saudi Med J 2007;28:1018-20.
13. Gupta SK, Kumar A. Temporary complete vision loss after intracameral lignocaine in a post-vitrectomy eye: A single case report. Egypt Retina J 2014;2:83-5.
14. Olmez G, Soker Cakmak S, Ipek Soker S, Nergiz Y, Yildiz F. Effects of intravitreal ropivacaine on retinal thickness and integrity in the guinea pig. Curr Ther Res Clin Exp 2005;66:394-400.
15. Gupta SK, Kumar A, Kumar D, Agarwal S. Manual small incision cataract surgery under topical anesthesia with intracameral lignocaine: Study on pain evaluation and surgical outcome. Indian J Ophthalmol 2009;57:3-7.
16. Martini E, Cavallini GM, Campi L, Lugli N, Neri G, Molinari P. Lidocaine versus ropivacaine for topical anesthesia in cataract surgery. J Cataract Refract Surg 2002;28:1018-22.
17. Waheeb S. Topical anesthesia in phacoemulsification. Oman J Ophthalmol 2010;3:136-9.
18. O'Brien PD, Fulcher T, Wallace D, Power W. Patient pain during different stages of phacoemulsification using topical anesthesia. J Cataract Refract Surg 2001;27:880-3.
19. Nikeghbali A, Falavarjani KG, Kheirkhah A. Pupil dilation with intracameral lidocaine during phacoemulsification: Benefits for

the patient and surgeon. Indian J Ophthalmol 2008;56:63.

20. Gupta SK, Kumar A, Agarwal S, Agarwal S. Phacoemulsification without preoperative topical mydriatics: Induction and sustainability of mydriasis with the intracameral mydriatic solution. Indian J Ophthalmol 2014;62:333-6.
21. Werblin TP. Long-term endothelial cell loss following phacoemulsification: Model for evaluating endothelial damage after intraocular surgery. Refract Corneal Surg 1993;9:29-35.
22. Dhasmana R, Singh IP, Nagpal RC. Corneal changes in diabetic patients after manual small incision cataract surgery. J Clin Diagn Res 2014;8:3-6.
23. Maggon R, Bhattacharjee R, Shankar S, Kar RC, Sharma V, Roy S. Comparative analysis of endothelial cell loss following phacoemulsification in pupils of different sizes. Indian J Ophthalmol 2017;65:1431-5.
24. Crandall AS, Zabriskie NA, Patel BC, Burns TA, Mamalis N, Malmquist-Carter LA, *et al*. A comparison of patient comfort during cataract surgery with topical anesthesia versus topical anesthesia and intracameral lidocaine. Ophthalmology 1999;106:60-6.
25. Tseng S-H, Chen FK. A randomized clinical trial of combined topical-intracameral anesthesia in cataract surgery. Ophthalmology 1998;105:2007-11.
26. Pandey SK, Werner L, Apple DJ, Agarwal A, Agarwal A, Agarwal S. No-anesthesia clear corneal phacoemulsification versus topical and topical plus intracameral anesthesia. J Cataract Refract Surg 2001;27:1643-50.