

Phacoemulsification without preoperative topical mydriatics: Induction and sustainability of mydriasis with intracameral mydriatic solution

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Context: Intracameral mydriatic solution can eliminate the disadvantages of repeated eye drop instillation regimen and provide adequate mydriasis for phacoemulsification with added advantages. **Aims:** Evaluating the role of intracameral irrigating solution (0.5% lignocaine + 0.001% epinephrine) in initiating and maintaining the pupillary mydriasis during phacoemulsification. Secondary aims were to observe the effect of surgical time, nucleus density and ultrasound time on mydriasis during the procedure. **Settings and Design:** The study is a prospective interventional case series, conducted at tertiary care institution. **Materials and Methods:** Thirty patients underwent phacoemulsification under topical anesthesia for visually significant cataract. Pupillary dilatation was achieved by intracameral irrigation of mydriatic solution alone. Pupillary diameter was measured serially during surgery and ultrasound time and total surgical time were noted. **Statistical Analysis Used:** Paired samples student-*t* test was done to compare means. Spearman correlation coefficient was used to study the effect of various parameters on mydriasis. **Results:** Thirty eyes completed the study. The pupil size increased from 2.1 mm (Range 2-3.5 mm SD \pm 0.32) to 6.9 mm (Range 5-9 mm SD \pm 1.02) in 30 seconds time after intracameral mydriatic solution delivery, and was 7.0 mm (Range 3.5 - 9 mm SD \pm 0.20) at the end of surgery. Duration of surgery, grade of nucleus and ultrasound time had statistically insignificant effect on mydriasis. **Conclusions:** Intracameral solution containing 0.5% lignocaine and 0.001% epinephrine provides rapid mydriasis which is adequate for safe phacoemulsification and is unaffected by other parameters.

Key words: Cataract, intracameral mydriatic solution, no preoperative mydriatic, phacoemulsification

Modern cataract surgery either by phacoemulsification or manual small incision cataract surgery (MSICS), both require good pupillary dilatation, which at present, is achieved by repeated administration of mydriatic/cycloplegic and NSAID (non-steroidal anti-inflammatory drug) eye drops. This preparation for surgery has definite disadvantages like 1 to 1.5 hour holding of patient in preparation room, contamination of the ocular surface, epithelial toxicity due to preservatives in the topical formulas and discomfort due to frequent instillation of the drops. Systemic safety of these topical formulae containing beta agonists and parasympatholytics is doubtful as they are known to cause a rise in blood pressure,^[1] ataxia, dizziness and dry mouth.^[2] Often due to noncompliance of the patient or staff there may be no dilatation or poor dilatation leading to delay in start of surgery causing wastage of man hours and resources. Due to these problems there has been an attempt to search for alternatives to this repeated eye drop instillation regimen. Various options like single drop instillation,^[3] Ocular inserts,^[4] depot preparation of mydriatic,^[5] and intracameral irrigation of mydriatic-cycloplegic drugs have been used with comparable results.^[2,6,7] Out of these only intracameral irrigation can obviate the need of pre-operative preparation. For this purpose many drugs have been used, namely

- Lignocaine (0.75%-1%) with epinephrine 0.025%,^[2,8]

- Lignocaine solution 1%,^[9-11]
- Cyclopentolate 0.1%, phenylephrine 1.5%, and lignocaine 1%.^[7,8,12]

We have not considered using cyclopentolate solution as studies have confirmed that the use of cyclopentolate does not enhance the action provided by intracameral lignocaine.^[8]

Apart from lignocaine, the other component of this intracameral mydriatic solution is sympathomimetic, for which we have two options, namely phenylephrine and epinephrine. The dual effects of epinephrine to contract the dilator musculature by its α receptor actions and relax the sphincter by β effect could act synergistically to dilate the pupil more than phenylephrine.^[13] Potential of intracameral epinephrine to cause macular edema has been studied and it has been reported that intracameral epinephrine at 0.2 mg/ml concentration or less does not increase this risk.^[14] Systemic safety of intracameral epinephrine has been established in medically controlled hypertensive patients.^[15]

Going by the present evidence intracameral irrigation of lignocaine with epinephrine is an effective and safe option for initiating and maintaining pupillary dilatation during cataract surgery. In this study we aimed at evaluating the role of intracameral irrigating solution of 0.5% lignocaine + 0.001% epinephrine in initiating and maintaining the pupillary mydriasis during phacoemulsification under topical anesthesia, without any topical mydriatic or NSAID use. Secondary aims were to observe the effect of surgical time, ultrasound time and nucleus density on sustainability of mydriasis during the procedure.

Access this article online

Website:

www.ijo.in

DOI:

10.4103/0301-4738.109521

Quick Response Code:



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Manuscript received: 05.05.11; **Revision accepted:** 26.01.12

Materials and Methods

Sample Size

Using 1% α (avoiding false positive outcome, as good pupillary dilatation is important for safe surgery), the power calculation determined that at least 18 observations were needed to reach 95% power for a mean value of 7 mm (SD 1.2).^[16,17] We have kept the critical value of pupil size as 6 mm for safe phacoemulsification. To enhance the reliability of our observations and to compensate for dropouts, we have taken a sample size of 30.

Patient Selection and Study Design

The study was a prospective interventional case series. Patients who were planned for phacoemulsification under topical anesthesia for visually significant cataract were screened for exclusion criteria [Table 1] and included in the study after obtaining their informed consent. Patients were not screened for Pseudoexfoliation or intake of alpha blockers; however, pupillary dilatation of less than 6 mm (measured using slit lamp, with topical solution of Tropicamide 0.8% + Phenylephrine Hydrochloride 5%) was one of the exclusion criteria. Patients who had per-operative complications like iris trauma or vitreous loss during the study were to be excluded from the study. All the patients were examined with dilated pupils two days before the surgery to grade the nucleus grade using LOCS III^[18] and to verify adequate pupillary dilatation (>6 mm).

Pupillary Dilatation and Surgical Technique

The mydriatic solution was prepared by injecting 2 ml of epinephrine solution (0.1% or 1:1000) into 50 ml solution of preservative free lignocaine 2% (Injection Xylocard, Astra Zeneca India Ltd). This was prepared freshly before surgery and used within 2 h of preparation, owing to degradation of epinephrine in sunlight and normalization of pH. This solution was further diluted fourfold by mixing 0.5 ml of this cocktail with 1.5 ml of BSS (Balanced Salt Solution), thus achieving the final concentration of lignocaine 5 mg/ml (0.5%) and epinephrine ~0.01 mg/ml (0.001% or 1:100,000).

Topical anesthesia was provided by the use of lignocaine jelly 2% (Xylocain Jelly 2% Astra Zeneca India Ltd).^[19,20] After making the keratome entry, anterior chamber was irrigated with the intracameral mydriatic solution. There was no specific dose of irrigating fluid delivered; the aim was to replace the aqueous with the irrigating fluid. On an average approximately 0.3 to 0.5 ml of this fluid was irrigated into the anterior chamber. After measurement of pupillary dilatation this mydriatic solution was replaced by 2% methylcellulose and capsulorhexis was completed. This mydriatic solution

was the only mydriatic agent used during the surgery and epinephrine was not added to the irrigating BSS used during the phacoemulsification procedure. Phacoemulsification using direct chop technique with in the bag implantation of foldable hydrophilic acrylic Intra Ocular Lens (IOL) (RYCF model, Intra Ocular Care Pvt. Ltd, India) using cartridge and injector through 2.8 mm incision was done.

Pupil Size Measurement

Surgical caliper having a least count of 0.5 mm was used to measure the horizontal and vertical diameter of the pupil thrice during the surgery. This was done under microscope view with monocular view using only the right eye of the observer, to avoid any parallax error. Measurement of pupil size was done at following stages during the surgery.

1. Before making the incision (undilated pupil size under the microscope illumination).
2. Thirty seconds after instillation of the mydriatic solution in the anterior chamber.
3. At the termination of the surgery after wound hydration and just before removal of the lid speculum.

Statistical Analysis

Statistical software Medcalc ver. 11.4.2.0 for windows was used to perform analysis of the observations. Descriptive analysis was done on the age distribution of the subjects. Undilated pupil size, pupil size after mydriatic solution irrigation and at the termination of surgery was compared using paired samples student *t*-test. Influence of the grade of nuclear sclerosis, duration of surgery and ultrasound time on the pupil size was analyzed using spearman correlation coefficient.

Results

Thirty eyes of thirty patients completed the study; there were no dropouts due to surgical complications. There were 15 male patients. The age distribution of subjects was normal (D'Agostino-Pearson test $P = 0.37$) with average age being 64.3 years (Range 40-75 SD ± 8.8).

The average pupil size without any mydriasis under the microscope illumination was 2.1 mm (Range 2-3.5 mm SD ± 0.32) which increased to an average of 6.9 mm (Range 5-9 mm SD ± 1.02) at 30 seconds time after anterior chamber irrigation with the mydriatic solution. This change was statistically significant with $P < 0.0001$ (paired samples student *t*-test). When compared to a test value of 7 mm (pupillary dilatation required for comfortable and safe phacoemulsification) using one sample student-*t* test, there was no statistically significant difference ($P = 0.5$).

At the end of surgery the average pupillary diameter was 7.0 mm (Range 3.5-9 mm SD ± 0.20). Thus, pupillary mydriasis was not only maintained throughout the surgery but rather there was an increase (0.10 mm average difference) in the size of the pupil at the end of surgery. Though this difference was statistically insignificant (paired student-*t* test, $P = 0.24$).

The pupillary dilatation achieved by the use of intracameral mydriatic solution was adequate for the entire surgical procedure which took 13 min on an average (Range 9- 18 min SD ± 1.6). There was a weak positive correlation between the pupil size and the surgical duration, which was statistically insignificant (Spearman correlation coefficient 0.13, $P = 0.46$).

Nucleus density and pupillary dilatation at the end of the

Table 1: Exclusion criteria for case selection

Pregnancy /Breast feeding
Unable to understand and follow verbal commands
Previous same eye ocular surgery
Pupillary deformity
Allergy to components of the medicine
Using topical or systemic NSAID/prostaglandins/para sympathomimetics
Maximum pupillary dilatation <6 mm
Ocular diseases other than cataract

procedure had weak positive correlation which was statistically insignificant (Spearman correlation coefficient 0.09, $P = 0.60$) Fig. 1.

Ultrasound time had weak positive correlation to final pupillary dilatation at the end of surgery, which was statistically insignificant (Spearman correlation coefficient 0.02, $P = 0.91$) Fig. 2.

Thus the pupillary dilatation achieved by the use of intracameral mydriatic solution was unaffected by the duration of surgery, grade of nucleus and ultrasound time.

Discussion

Adequate pupillary dilatation and maintenance of mydriasis are important for an uncomplicated phacoemulsification.^[21] The efficacy of mydriatic solution composed of lignocaine (0.75%-1%) with epinephrine 0.025% in inducing and maintaining pupillary mydriasis during phacoemulsification has been demonstrated earlier.^[2,8]

One percent Intracameral lignocaine has been demonstrated to be safe for corneal endothelium, but as this toxicity is concentration related,^[22] Thus it can be safely presumed that using a lower concentration which can provide effective anesthesia and mydriasis would be enhancing its' safety. In our study we have demonstrated that using 0.5% lignocaine in intracameral solution can provide adequate mydriatic effect comparable to a similar study.^[8]

There are conflicting reports in literature regarding the corneal endothelial toxicity of epinephrine. Experimental and clinical reports claiming safety of epinephrine solutions with concentrations ranging from 1 mg/ml to 0.01 mg/ml are there,^[23,24] and on the other hand there are studies and case reports claiming endothelial toxicity of epinephrine at similar concentrations.^[25,26]

We further analyzed these antagonistic reports and found that going by the present evidence endothelial toxicity is related to the buffer capacity of the epinephrine solution, which is in turn is controlled by the concentration of the antioxidant (sodium bisulfite) as well as by the vehicle formulation and a low pH value.^[27] Thus epinephrine solution toxicity to

endothelium is the byproduct of formulations rather than the molecule itself. So, either an endothelial friendly formulation^[28] or maximum dilution of available formulation (which is corneal endothelium compatible with regard to concentration and pH) appear to be the possible answers for safe use of intracameral epinephrine.

Thus, use of lower concentration of lignocaine and epinephrine can enhance the safety by reducing the toxicity to intraocular structures apart from retaining all the advantages offered by intracameral mydriatic solution.^[1,2]

Combination of epinephrine with lignocaine as an intracameral irrigation solution has many advantages apart from providing anesthesia and pupillary dilatation, as it provides better duration of action and more efficacy,^[8] aids in hemostasis, and markedly reduces or eliminates risk for IFIS (Intraoperative Floppy Iris Syndrome) in eyes with risk factors such as exposure to alpha Blockers and Tamsulosin.^[29-31]

We found that the pupillary dilatational in our study was comparable to the findings in a study done by William *et al.*, using similar (but more concentrated) intracameral mydriatic solution. In that study the average pupillary dilatation achieved using their higher concentration intracameral mydriatic solution was 7.1 mm \pm 0.7 against our average pupillary dilatation of 6.9 mm \pm 1.02.^[8] Similarly at the end of surgery the average diameter was 7.3 mm \pm 0.7 and 7.0 mm \pm 0.20, in their and our study respectively. This indicates a slight increase in the diameter during the surgical procedure in both studies.

As the surgical time, nucleus density and ultrasound time increase for any given surgical machine they cause tissue damage and which in turn causes release of prostaglandins leading to pupillary miosis. Topical NSAIDs (Non- Steroidal Anti-inflammatory Drugs) are used as preoperative medication routinely to prevent this pupillary constriction.^[32-36] In this study we have not used any preoperative NSAID, and yet the pupillary dilatation was maintained. This is an important requirement for safe removal of lens matter and is well catered by our technique of mydriasis.

There are few limitations of this study, particularly, the lack of control arm (receiving conventional preoperative

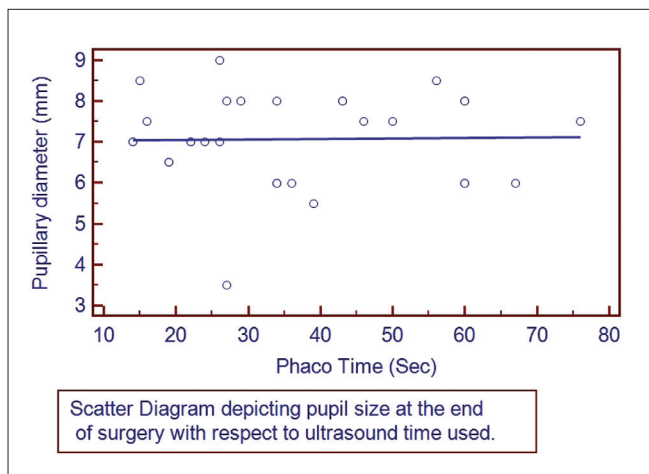


Figure 1: Scatter diagram depicting relation between pupillary diameters at the end of surgery to ultrasound time used

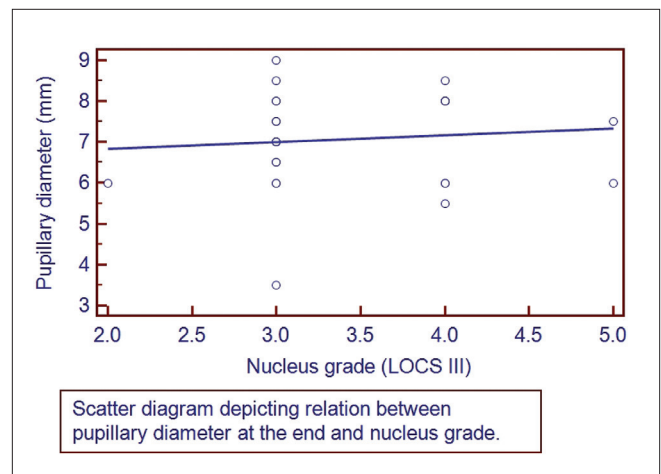


Figure 2: Scatter diagram depicting relation between pupillary diameter at the end and nucleus grade

topical mydriatic regimen). However the study intended to demonstrate feasibility of this method of mydriasis with lower concentration formulation rather than demonstrate comparison to various mydriatic regimens in practice.

The study demonstrates that the intracameral solution alone, containing lower concentration of lignocaine and epinephrine provides rapid mydriasis which is adequate for safe phacoemulsification with intraocular lens implantation and this mydriasis is maintained throughout the procedure.

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Cite this article as: Gupta SK, Kumar A, Agarwal S, Agarwal S. Phacoemulsification without preoperative topical mydriatics: Induction and sustainability of mydriasis with intracameral mydriatic solution. *Indian J Ophthalmol* 2014;62:333-6.

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