Efficacy and safety of intraoperative intracameral mydriasis in manual small incision cataract surgery - A randomized controlled trial

K Ajay, Srinivasan Saranya¹, Divya Dabir Sundaresh¹, HR Hithashree², BC Hemalatha¹, Malavika Krishnaswamy¹, Sathyendranath B Shetty¹

Purpose: The purpose of this study is to assess the efficacy and safety of intracameral mydriatic solution, as compared to preoperative topical mydriatics, in patients undergoing manual small incision cataract surgery (MSICS) under peribulbar anesthesia. To assess the sustainability of intracameral mydriasis in MSICS by monitoring pupil size at specific junctures during the surgery. Methods: This trial recruited 127 patients, who underwent MSICS under peribulbar block. Mydriasis in topical group was achieved with preoperative topical dilating drops while patients in intracameral group were taken up for surgery without dilation, and mydriasis was achieved intraoperatively with intracameral solution. Pupil sizes were measured serially, at six different junctures during surgery. Time duration of surgery, any intraoperative complications and first postoperative day visual acuity, corneal edema score, and anterior chamber inflammation score were noted in all patients. Results: Mean pupil size just before peribulbar block was 7.3 mm in topical group and 3.3 mm in intracameral group (P < 0.001). Mean pupil size in intracameral group increased to 7.3 mm 30 s after injecting intracameral dilating solution. Mean pupil size in both groups progressively reduced, reaching 5.5 mm (topical group) and 6.2 mm (intracameral group) just before intraocular lens implantation (P = 0.001), and measured 5.1 mm and 5.5 mm, respectively, at the end of surgery (P = 0.048). On first postoperative day, there was no significant difference in distribution of corneal edema scores, AC inflammation scores, and in median logMAR visual acuity between the two groups. Conclusions: MSICS can be performed effectively and safely utilizing intracameral mydriatic solution, without the use of preoperative dilating drops.

Key words: Intracameral, manual small incision cataract surgery, mydriasis

Trial registration: CTRI/2016/06/007036

Adequate pupillary dilation is crucial for safe and effective cataract surgery. A study performed by Gupta et al.[¹] reported that intracameral solution containing 0.5% lignocaine and 0.001% epinephrine provided rapid mydriasis which was adequate for safe topical phacoemulsification cataract surgery, and the dilation achieved was unaffected by other parameters. The mydriasis required for phacoemulsification cataract surgery in this study was achieved by the surgeon himself, using intraoperative intracameral solution, without preoperative topical administration of mydriatics.

In India and the developing world, manual small incision cataract surgery (MSICS) is hugely popular²⁴ and is probably the most commonly performed method of cataract surgery in community-based high-volume surgical campaigns (camp surgeries).²⁵ Yet, studies evaluating the efficacy and safety of intracameral mydriatic solution for MSICS have not been reported.

We report the results of this randomized controlled trial, wherein intracameral mydriatic solution as prepared by Gupta et al.,¹¹ was compared with preoperative topical mydriasis, with respect to efficacy, sustainability, and safety for the performance of MSICS under peribulbar anesthesia.

Methods

This study was conducted at a medical college hospital in South India. Institute Ethics Committee approval was obtained before commencement of the study. The study was designed as a prospective, randomized comparative controlled trial, and registered with Clinical Trials Registry-India. Patients scheduled for elective MSICS were screened for exclusion criteria and were recruited for the study after obtaining informed consent. Exclusion criteria were pregnancy/breastfeeding, uveitis, intake of alpha blockers, use of topical or systemic nonsteroidal anti-inflammatory drugs/prostaglandins/miotics, presence of corneal opacities, pupillary deformities, history of surgery in same eye, and hypersensitivity to any component of medicines used. In addition, any eye not dilating to at least 6 mm直径 was excluded from the study.

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preoperatively and eyes where intraoperative complications such as iris trauma or vitreous loss were encountered were excluded from the study. Excluding eyes with significant iris trauma or vitreous loss would mean that the patient was being excluded from the analysis after having been randomized. However, the number of such cases were expected to be small and we felt that the occurrence of such complications could cause inaccuracy in the estimation of pupil size. In addition, in the event of such a complication (expected to be rare), it would be preferable to let the surgeon concentrate on successfully completing the case and preventing further mishap than to continue measuring pupil sizes. For this reason, we also recruited nine cases more than the minimum sample size.

All patients were also examined with dilated pupils before surgery, to assess the amount of pupillary dilation (using surgical caliper, to within half a millimeter) and to evaluate nucleus grade. Nucleus grading was done by observing the color of nucleus on slit-lamp examination and was graded as 1 for white to pale yellow, 2 for yellow, 3 for brownish yellow, and 4 for brown, including reddish and black brown.[10] Although not as comprehensive as the Lens Opacities Classification System, version III,[9] this system of classification was chosen as it was the grading method routinely performed in our medical college and was deemed to be feasible and adequate for the limited purpose of this study.

Once a patient was recruited, he/she was randomized into topical or intracameral group. Computerized randomization was performed by “blocked randomization method,” tabbed before study, and patients serially allocated into each group as and when recruitment happened.

Patients allocated to topical mydriatic group (topical group) underwent pupillary dilation on day of surgery with preoperative topical drops, using the standard regimen of alternate tropicamide 0.8% plus phenylephrine 5% drops (Tropicacyl Plus, Sunways, India) and flurbiprofen 0.03% drops (Ocuflu, FDC, India) at 15 min intervals for 1 h before surgery. Patients allocated to intracameral mydriatic group (intracameral group) were not administered any topical dilating drops. Mydriasis in this group was achieved intraoperatively by the surgeon, by injection of solution containing 0.5% lignocaine, and 0.001% epinephrine immediately after first entry into the anterior chamber (AC). This solution was prepared and injected as detailed by Gupta et al.[10] 2 ml of epinephrine solution (0.1% or 1:1000 adrenaline as Adrenaline Bitartrate, Harson laboratories, India) was injected into 50 ml solution of preservative free lignocaine 2% (Loxicard 2%, Neon Laboratories, India). 0.5 ml of this cocktail was then mixed with 1.5 ml Balanced Salt Solution (BSS, Alcon, India), to achieve a final concentration of lignocaine 5 mg/ml (0.5%), and epinephrine ~ 0.01 mg/ml (0.001% or 1:100,000). Epinephrine is a known risk factor for pseudophakic cystoid macula edema, but intracameral epinephrine at a concentration of 0.2 mg/mL or lesser (1:5000) has been shown as not to be associated with increased risk of central macular edema.[14] The solution was used within 2 h of preparation to prevent degradation in sunlight, and the amount of solution injected was on an average 0.5–0.6 ml.

All patients in both groups were administered peribulbar block anesthesia employing a solution of 1:1 compounded 2% lidocaine plus adrenaline 1:200,000 (Lox 2%, Neon Laboratories, India) and 0.5% bupivacaine (Anawin 0.25%, Neon Laboratories, India), with hyaluronidase (Hynidase, Shreya Life Sciences Pvt. Ltd., India) added at 7.5 turbidity units/ml to the solution.

All surgeries were done by experienced surgeons (had independently performed at least 300 MSICS) using similar surgical technique. The nucleus prolapse into AC was done by partial hydropulsion and rotation technique and nuclear extraction from the AC to exterior was done by sandwich method (vectis and dialer).

On the day of surgery, the investigator administering peribulbar block anesthesia measured pupillary dilation (P1) in all cases before blocking the case, using surgical calliper, to within half a millimeter. The same investigator measured the pupil size in both groups of patients just before the patient lay down on the operation table (P2). The operating surgeon measured the pupil size in both groups at four further junctures: First recording (P3) 1 min after entering AC through scleral tunnel in topical group and 30 s after intracameral instillation of mydriatic solution in intracameral group, second recording (P4) just after extracting nucleus from AC to exterior, third recording (P5) just before intraocular lens (IOL) implantation and fourth recording (P6) at the end of surgery before the removal of lid speculum.

If at any point of time during surgery in intracameral group patients, the operating surgeon felt that the pupil dilation is inadequate or has constricted to an unsafe level, s/he was free to decide whether intracameral mydriatic solution has to be reinjected, or to apply mechanical methods such as iris hooks or sphincterotomy.

In topical group patients, if the operating surgeon encountered constriction of pupil to a level perceived unsafe, s/he would inject the standard mydriatic solution employed for such situations in our center, which was 0.1 ml epinephrine 0.01% in 0.9 ml of balanced salt solution giving a concentration of 1:100,000.[11]

The time duration of surgery and any intraoperative complications in both groups were noted.

On the first postoperative day, uncorrected and pinhole visual acuity were determined in both groups, and all patients were graded for corneal edema from 0 to 3 as none, mild (Descemet folds only), moderate (stromal edema with Descemet folds), and severe (stromal and epithelial edema). AC inflammation was evaluated by estimating the number of cells in a 1 mm by 1 mm slit-beam field and was graded from 0 to 4 as 0 (no cells seen), 0.5 (1–5 cells), 1 (6–15 cells), 2 (16–25 cells), 3 (26–50 cells), and 4 (>50 cells). Investigators assessing visual acuity, corneal edema, and AC inflammation on the first postoperative day were blinded to which group the patient belonged.

Sample size

The sample size was calculated as 118 (59 in each arm). Torron et al.[12] had observed that the dilation at presurgery time using standard preoperative mydriatic agents was 9.44 ± 1.17 mm. In the present study, expecting similar result while comparing with intraocular instillation of mydriatic solution, with 90% power and 95% confidence level, and with effect size of 0.59, the study required a minimum of 59 subjects per arm.
Statistical analysis

The data were analyzed using commercial software (SPSS version 18.0, SPSS Inc., Chicago, Illinois, USA). Independent t-test was used to compare mean pupil sizes between the two groups. Chi-square test was used to compare the distribution of first postoperative day corneal edema and AC inflammation scores and Mann–Whitney U-test was used to compare median values of visual acuity between the two groups. The statistical calculations of visual acuity were performed after converting Snellen visual acuity to logMAR visual acuity, based on the methods explained by Jack Holladay in his guest editorial on Visual acuity measurements. Median visual acuity has been used to estimate central tendency of visual acuity, as the data were not normally distributed. \( P < 0.05 \) was considered for statistical significance.

Results

A total of 127 patients (66 males, 61 females) were recruited for the study (63 in topical group, 64 in intracameral group). Posterior capsule rent with vitreous loss occurred in two patients in topical group and one patient in intracameral group. These three patients (all females) were excluded from data analysis. In one patient in topical group, the surgeon encountered inferior zonular dialysis of three clock hours but continued the case uneventfully after inserting a capsular tension ring. This patient was not excluded from the data analysis.

Table 1 presents the demography and cataract surgical profile of the patients analyzed in the study.

Table 2 gives the details of pupil size measured at the designated time-points, along with surgical duration.

Table 3 presents the details of the median first postoperative day logMAR visual acuity, in both groups.

The first postoperative day corneal edema scores for patients in topical group were 48 (79%) Grade 0, 7 (11%) Grade 1, 6 (10%) Grade 2, and 0 Grade 3. The corresponding scores for patients in intracameral group were 50 (80%) Grade 0, 7 (11%) Grade 1, 4 (6%) Grade 2, and 2 (3%) Grade 3. The distribution and difference in corneal edema scores between the two groups were not statistically significant \( (P = 0.492) \).
Table 3: Median first postoperative day logarithm of the minimum angle of resolution visual acuity (equivalent Snellen visual acuity in italics below)

|                         | Median (IQR) | P     |
|-------------------------|--------------|-------|
|                         | Topical group (n=61) | Intracameral group (n=63) |       |
| Uncorrected visual acuity | 0.40 (0.30-0.48) | 0.40 (0.30-0.50) | 0.530 |
| Pinhole visual acuity    | 6/15 (6/12-6/18) | 6/15 (6/12-6/19) |       |
|                         | 0.18 (0.0-0.25) | 0.05 (0.0-0.30) | 0.950 |
|                         | 6/9 (6/6-6/10)  | 6/6 p (6/6-6/12) |       |

IQR: Interquartile range

The first postoperative day AC inflammation scores for patients in topical group were 1 (2%) grade 0.5, 42 (75%) grade 1, 12 (21%) grade 2, 1 (2%) grade 3, and 0 grade 4. These scores in intracameral group were 4 (6.5%) grade 0.5, 34 (56%) grade 1, 22 (36%) grade 2, 0 grade 3 and 1 (1.5%) grade 4. The difference in AC inflammation scores between the two groups was not statistically significant (P = 0.117).

Discussion

Currently, the most prevalent method for achieving mydriasis for cataract surgery is repeated administration of mydriatic and NSAID eye drops topically.[14] This method of preoperative topical dilation usually depends on additional manpower and resources, entails increased preparation time of patients and can potentially contaminate ocular surface, not to mention the occasional noncompliance of staff or patients leading to inadequate dilation.[1,14]

To obviate these disadvantages, intraoperative intracameral mydriatic solutions were introduced. Many authors have reported such solutions to be effective and safe.[15-18] However, there is a caveat-every single report has shown intracameral mydriasis is effective for phacoemulsification cataract surgery. MSICS, unlike phacoemulsification, involves the prolapse of cataractous nucleus into the AC during surgery.[20] It is possible that the prolapse of the nucleus into AC in MSICS may influence the sustainability of intracameral mydriasis. To the best of our knowledge, this is the first study evaluating the practical feasibility and safety of intraoperative mydriasis for MSICS.

From an analysis of Table 2, it can be seen in intracameral group patients that the mean pupil diameter increased from 3.3 mm (P1) to 4.8 mm (P2) after peribulbar block with lignocaine and adrenaline solution and was 7.3 mm (P3) 30 s after intracameral injection of mydriatic solution. Mydriasis to this extent permitted the operating surgeon to go ahead with MSICS. The corresponding mean readings in topical group patients were 7.3, 7.4, and 7.4, which meant that there was no much change in pupil sizes after block.

As the surgery progressed, the mean pupil size in both groups gradually decreased. In intracameral group patients, this was evidenced by mean pupil values just after extracting nucleus from AC (P4) being 6.8 mm, just before IOL implantation (P5) as 6.2 mm and finally, just before the removal of lid speculum (P6) being 5.5 mm. Although the mean pupil size decreased to 6.2 mm just before IOL implantation, this extent of reduction in mydriasis did not prevent the surgeon from implanting the IOL. In one case, P5 was 3 mm, and in this case, the operating surgeon decided to reinject mydriatic solution. The pupil size in this case just before removing lid speculum (P6) was 8 mm. This was the only case where the operating surgeon elected to go in for repeat dilation of pupil during surgery.

The progressive constriction of pupil size during surgery was seen in topical group also. The mean pupil diameter just before IOL implantation (P5) in this group was 5.5 mm, and two cases had P5 readings <4 mm (3 and 3.5 mm). In these two cases, the operating surgeon injected the standard mydriatic solution employed for such situations in our center (as detailed in methods section) and successfully completed the case after implanting the IOL.

The mean pupil diameter at the end of surgery in intracameral group patients was 5.5 mm, a decrease of nearly 25% from the mean dilation size achieved intracameraly (7.3 mm). This was in contrast to the study by Gupta et al.,[1] who reported an average intracameral dilation size of 6.9 mm increasing to 7.0 mm at the end of surgery, in their series of patients undergoing phacoemulsification cataract surgery. We believe that the increased intraoperative iris manipulations of MSICS contribute to this decrease unlike in phacoemulsification. We also noted that surgeons in our center had the habit of stroking the iris after implanting IOL to ensure all viscoelastic substance is removed, and this would also influence the significant decrease in pupil size by the end of MSICS.

The mean amount of constriction in topical group (7.4 mm to 5.1 mm) was more than that seen in intracameral group (7.3 mm to 5.5 mm), and this was statistically significant too (P = 0.048); but just as in topical group, the decrease in pupil size did not prevent implantation of IOL in all except the two cases mentioned earlier, wherein the surgeon elected to inject mydriatic solution and successfully completed the case. While we had no specific answer as to why topical group patients displayed more constriction, we noted that Lundberg and Behndig also had reported similarly increased constriction in topical group, in their trial of intracameral versus topical mydriatics for phacoemulsification surgery.[15]

There was no statistically significant difference between distribution of corneal edema scores and AC inflammation scores among the two groups on first postoperative day. There was also no statistically significant difference in postoperative median logMAR visual acuity between the two groups, as can be observed from Table 3.

Anecdotally, intracameral dilation for MSICS also had the benefit of reducing the workload of the ward nurses, who were tasked with preparing patients for cataract surgery, in our hospital. They were quite pleased to learn that the need to instill drops frequently before surgery and to check pupils regularly for effect was not required in the study patients. A workflow analysis was conducted on two selected days during the study, and it was found that an extra hour of preparation time was required for topical group patients, during which time the ward nurses instilled dilating drops and checked for mydriasis. Sengupta et al.[21] had reported on the use of a mydriatic cocktail with a wick for preoperative mydriasis in cataract surgery. A standard-sized wick soaked for a minute in mydriatic cocktail regimen (equal parts of phenylephrine, cyclopentolate, moxifloxacin, and flurbiprofen) was placed in
the inferior fornix for 45 min, and this was found to be superior to topical dilation with regard to size of dilation, cost, patient comfort, and compliance and the main benefit being reduction in nursing time to administer drops. Intracameral dilation would be a step further in achieving the same goals and would result in enhanced patient comfort and compliance since even the placement of a pledget in the fornix would be avoided.

We believe that performing MSICS employing intracameral mydriatic solution would be extremely beneficial in high volume surgical lists (such as “camp surgeries,” common in India) as the need to dilate patients preoperatively is obviated. This will not just render free, manpower for other duties; it will also reduce the time taken to complete surgical lists.

Conclusions
Intracameral mydriatic solution is effective in inducing adequate mydriasis for MSICS. The mydriasis induced does not sustain through the entire duration of MSICS, but the amount of pupillary constriction that occurs does not prevent the surgery from being performed successfully.

MSICS performed using intracameral mydriatic solution without preoperative topical mydriasis is effective and safe with respect to vision and AC inflammation on the first postoperative day.

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Conflicts of interest
There are no conflicts of interest.

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