Thai J Ophthalmol 2025;39(1):10-20.

Original Article/นิพนธ์ต้นฉบับ

Intracameral Anaesthetic Mydriatics as Adjuvant Aids in Small Pupil Cataract Surgery to Reduce the Use of Pupillary Expansion Devices: A Randomized Prospective Cohort Study from Central Kerala, India

Merine Paul, MS, DNB, FAICO

Abstract

Aims: To determine if intracameral anesthetic mydriatics (ICAM) can improve pupillary dilatation and reduce the use of pupillary expansion devices (PED) in small pupil cataract surgery.

Material and Methods: A randomized prospective cohort study of 94 patients who met the inclusion criteria was conducted in a private hospital setting in Central Kerala. Patients were randomized into two groups A and B, with Group A given intracameral "Phenocaine Plus" prior to capsulorhexis and none given in Group B. Pupillary measurements were taken at preoperative, start of surgery, post "Phenocaine Plus" injection, post-hydrodissection, post-phacoemulsification and post-IOL implantation stages of surgery. The demographic and clinical data collated were subject to statistical analysis.

Results: Thirty-six (75%) patients in Group A dilated to 6 mm or beyond, prior to capsulorhexis with the use of ICAM. This advantage in pupillary dilation was present in all stages of the surgery at statistically significant levels. The use of PED did not vary significantly between the groups. Group B had more intraoperative complications compared to group A, but the difference was not statistically significant.

Conclusions: ICAM as an adjuvant in small pupil cataract surgery helps to dilate and maintain dilation of the pupil at all stages of surgery. ICAM did not significantly impact the use of PED in this study, however, multicenter studies with a larger pool of cataract surgeons are required to further explore the lack of difference.

Key words: intracameral anesthetic mydriatics, small pupil cataract surgery, Phenocaine Plus, pupillary expansion devices.

Ophthalmology Department, Trinity Eye Hospital, Thrissur, India

Introduction

Small pupil cataract surgery is one of the last frontiers of safety in phacoemulsification. Pharmacological aids in the form of topical eye drops, intracameral injections and mechanical aids like pupil expansion devices (PED) and stretch pupilloplasty are available to overcome the difficulties of small pupil cataract surgery. There will be inter-surgeon variations in the skill required to safely navigate small pupil cataract surgery, but guidelines on the management of small pupils are not clear. Anecdotal evidence suggests that intracameral anesthetic mydriatic (ICAM) agents may act as pharmacological adjuvants to regular topical dilating drops used preoperatively and can help to further dilate the poorly dilating pupil during surgery. They are also used to manage unexpected intraoperative miosis during the procedure.

Mydrane (Laboratories Thea, Clremont-Ferrand, France) is an intracameral anesthetic and dilating agent that was introduced in Italy in 2016, as an alternative to mydriatic drop instillation in cataract surgery. It consists of a standardized combination of tropicamide 0.02%, phenylephrine 0.31% and lidocaine 1.0%[1]. Its safety and efficacy have been demonstrated by multiple studies and a phase 3 multicenter clinical trial.[2-4]. A similar combination of agents has been introduced in India under the brand name "Phenocaine Plus" (1 ml, Entod Pharma, Gujarat, India). Most studies on Mydrane and Phenocaine demonstrate the ability of this drug cocktail to dilate normal pupils when used intracamerally. Their equivalence with topical dilating drops in ensuring adequate dilatation perioperatively has been established[5]. Various studies have shown the safety of ICAM in complicated cases and pediatric cataract surgery[5-7]. However, there is a lack of literature on whether this drug cocktail can be used effectively in small pupils and whether it aids in the surgery of cataractous eyes with poor dilatation. Most of the studies on Mydrane were designed to show equivalence with topical dilating agents and hence small pupils (any pupil less than six mm) on preoperative evaluation were considered as exclusion criteria, and therefore not included in any of the studies[3,4]. Similarly, eyes with the possibility of inconsistent mydriasis like Intraoperative Floppy Iris Syndrome (IFIS) were also part of the exclusion criteria of many studies[8]. Hence no study has thus far supported the claim of ICAMs being helpful for small pupil cataract surgery.

In this manuscript, we report the results of a study that aimed to explore whether ICAM can be used as adjuvant dilating agents in small pupil cataract surgery to reduce the use of pupil-expanding devices in these surgeries. The secondary aim was to estimate the percentage of small pupils dilating to 6 mm or beyond with ICAM.

Material and Methods

Consecutive patients who were referred for cataract surgery by the operating surgeon (OP) at two Ophthalmic hospitals in Central Kerala, between 1st January 2022 to 30th March 2022, were selected. All patients underwent detailed preoperative workup including a dilated fundus examination, at least two days prior to the day of surgery to prevent pupillary fatigue. The study included subjects who had < 6 mm of pupil dilation (measured on the slit lamp) at 30 minutes after instillation of a single drop of Tropicamide 1% repeated three times every 10 minutes along with one time instillation of Phenylephrine 10% eye drop. Uncomplicated cataracts of all grades with poor pupillary dilation were included in the study. Patients with a history of trauma with evident damage to pupillary margins or subluxation/dislocation of the lens, corneal diseases, chronic uveitis with any signs of posterior synechiae and retinal pathologies were excluded from the study. Subjects that met the

eligibility criteria were randomized to either the control group or the intervention group using a computer-generated randomization schedule after obtaining informed consent. The sample size for the study was estimated as 47 subjects in each group for 90% power and a two-sided alpha of 0.05 based on the proportion of subjects that needed expanders in both groups in a pilot study. The study protocol that adhered to the tenets of the Declaration of Helsinki was approved by the institutional ethics committee.

All patients underwent identical preoperative management including topical antibiotics and NSAID drops in the eye to be operated, three times a day for two days prior to surgery. All the patients were dilated an hour prior to surgery with topical dilating drops (Tropicamide 1%, Cyclopentolate 1% and Phenylephrine HCl 10%) on the day of surgery. Patients in group A were administered intracameral Phenocaine 0.2 ml at the pupillary plane just before starting capsulorhexis. The size of the pupil before and after injection was measured with Castroviejo calipers. Routine phacoemulsification was done if the pupil dilated to > 6 mm. Zyonate Injection (14 mg Sodium Hyaluronate Ophthalmic Solution, Zydus Cadila. India), a high molecular weight viscoelastic, was used to maintain the pupil size if the pupil remained between 4.5 to 6.0 mm. Pupillary dilating devices like Iris Hooks (Appasamy Associates, India) or B-Hex Pupil Expander (Med Invent Devices, India) were used to dilate the pupil if the pupil size became 4.5 mm or less. Stretch pupilloplasty was done to dilate the pupil mechanically in select cases. Pupillary measurements were also taken after hydrodissection when the pupil size normally tends to decrease. Final pupillary measurements were done at the end of phacoemulsification of the nucleus and after IOL implantation.

In group B, Phenocaine Plus was not used despite pupil size reducing to less than 6 mm. High molecular weight viscoelastic, Zyonate Injection, was used to maintain pupil size. However, pupillary expansion devices were employed to keep the pupil at an adequate size if the pupil size reduced to 4.5 mm. Pupillary dilation was measured at the same points during the stages of surgery as in Group A. In both groups, the rigidity of the pupils was noted by inducing slight mechanical pressure using viscoelastic in the anterior chamber and expansion, if any, was measured. Other parameters measured included the size of the capsulorhexis (as smaller pupils tend to reduce the size of the capsulorhexis inadvertently) and the amount of epinuclear material remaining at the end of phacoemulsification of nucleus, which is also an indirect indication of the grade of difficulty in operating on small pupils. Other variables noted were total phaco time, grade of the hardness of the nucleus, intraoperative complications and immediate postoperative complications. Systemic and ocular comorbidities were noted in both groups. Broad groups of medications used by the patients were recorded. Ease of surgery from the surgeon's perspective was recorded at end of surgery. and graded on a scale of 0 to 4 with 0 indicating a routine case with no stress and 4 indicating a case that could not be completed to satisfaction. Patients were asked to grade their comfort during surgery, in the immediate postoperative phase (within 10 minutes of returning to their rooms) to get accurate data and prevent dissociative amnesia from clouding their judgement. They were specifically asked about pain in the eye or orbital area and responses were graded on a 4-point ordinal scale, with 0 indicating no pain or discomfort and 4 indicating severe pain.

Primary and secondary outcomes of interest included a reduction in the use of PED, if any, with the use of ICAM and estimation of the proportion of subjects with eyes dilated to 6 mm or beyond with the use of ICAM. Data were entered into an MS Excel

spreadsheet and exported to the statistical software STATA version 12.0 (college station, Tx, USA) for statistical analysis. Continuous data were expressed as mean (SD) and compared using a student's *t*-test. Categorical variables were expressed as proportions and compared using the chi-square test or Fisher's Exact test as appropriate. A p-value < 0.05 was considered statistically significant.

Results

The study enrolled 94 subjects including 48 subjects in the Phenocaine group and 46 subjects in the control group. The mean age of patients in Group A was 70 ± 9.3 years and 69 ± 7.3 years in Group B. Table 1 presents the baseline clinical and demographic details of both groups. The pupil sizes measured at various stages during the surgery are shown in Table 2 and Figure 1, 2 and 3.

Table 1 Baseline characteristics of the "Phenocaine Plus" group (Group A) and the control group (Group B)

Characteristics	Subgroups	Group A (n = 48)	Group B (n = 46)
Age ± SD	-	69.97 ± 9.36	69.02 ± 7.29
Gender (%)	M	23 (47.92)	24 (52.17)
	F	25 (52.08)	22 (47.93)
Laterality (%)	RE	28 (58.33)	29 (63.04)
	LE	20 (41.67)	17 (36.96)
VA (%)	6/9 – 6/12	3 (6.25)	8 (17.39)
	6/18 – 6/24	15 (31.25)	9 (19.57)
	6/36 – 6/60	11 (22.92)	10 (21.74)
	< 6/60	19 (39.58)	19 (41.30)
Nucleus Grade (%)			
	1	10 (20.83)	15 (32.61)
	2	19 (39.58)	20 (43.48)
	3	11 (22.92)	6 (13.04)
	4	8 (16.67)	5 (10.87)
Elastic/rigid pupils (%)			
	Elastic	23 (47.92)	32 (69.57)
	Rigid	25 (52.08)	14 (30.43)
Comorbidities (%)			
	Hypertension	27 (56.3)	22 (47.8)
	Diabetes	26 (54.1)	19 (41.3)
	Dyslipidaemia	8 (16.6)	9 (19.6)
	IHD	8 (16.6)	6 (13.0)
	Thyroid disorders	2 (4.2)	4 (8.7)
	COPD	4 (8.3)	5 (10.8)
	BPH	4 (8.3)	6 (13.0)

(SD- Standard Deviation, RE -Right Eye, LE- Left Eye, VA- Visual Acuity Snellen's), IHD- ischemic Heart disease, COPD- Chronic Obstructive Pulmonary Disease, BPH- Benign Prostatic Hypertrophy)

Table 2 Distribution of pupil sizes from preoperative assessment to the end of surgery in the "Phenocaine Plus" group (Group A) and the control group (Group B)

Pupil Size (mm)	Group A (N=48)			Group B (N=46)			*p* Value
	Mean	SD	95%CI	Mean	SD	95%CI	
Preoperative	5.03	0.69	4.8-5.2	5.32	0.59	5.1-5.5	0.03*
Start of surgery	5.57	0.68	5.4-5.8	5.84	0.64	5.6-6.0	0.06*
Post-hydrodissection/ capsulorhexis	5.62	0.62	5.4-5.8	5.41	0.48	5.2-5.5	0.63 (A) ** <0.001(B) **
Post-phacoemulsification	5.80	0.75	5.5-6.0	5.58	0.62	5.3-5.7	0.04(A) ** 0.03(B) **
Post-IOL insertion	5.52	0.78	5.3-5.8	5.16	0.77	4.9-5.3	0.65(A) ** < 0.001(B) **

[1]SD- Standard Deviation, CI-Confidence Interval, IOL- Intraocular lens,

p – Value by : Two-sample t test in preoperative and start of surgery assessments (*)

: Paired t test for comparing start of surgery pupils with post-hydrodissection, Post-phacoemulsification and Post-IOL insertion pupils. (**)

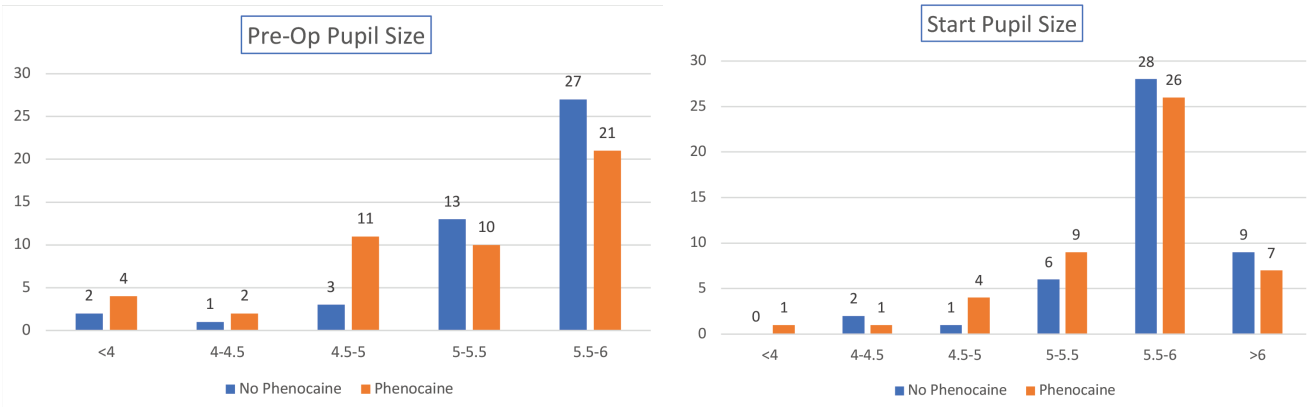

Figure 1 Comparison of pupil sizes in mm at preoperative evaluation to that at start of surgery after intensive topical dilatation in Group A (n = 48) and B (n = 46).

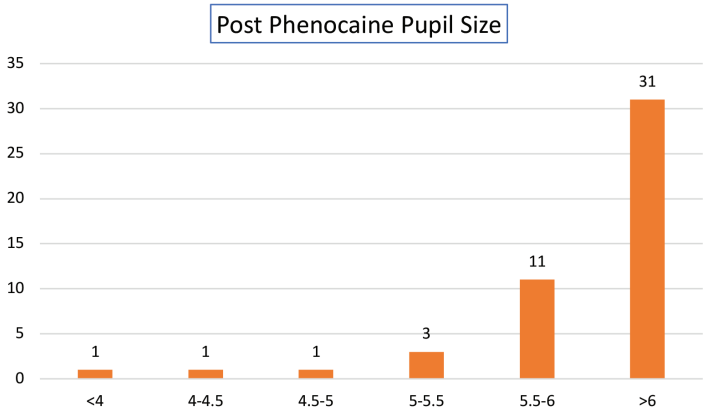

Figure 2 Representation of pupil size in mm in Group A (n = 48) after injection of Phenocaine at pupillary plane.

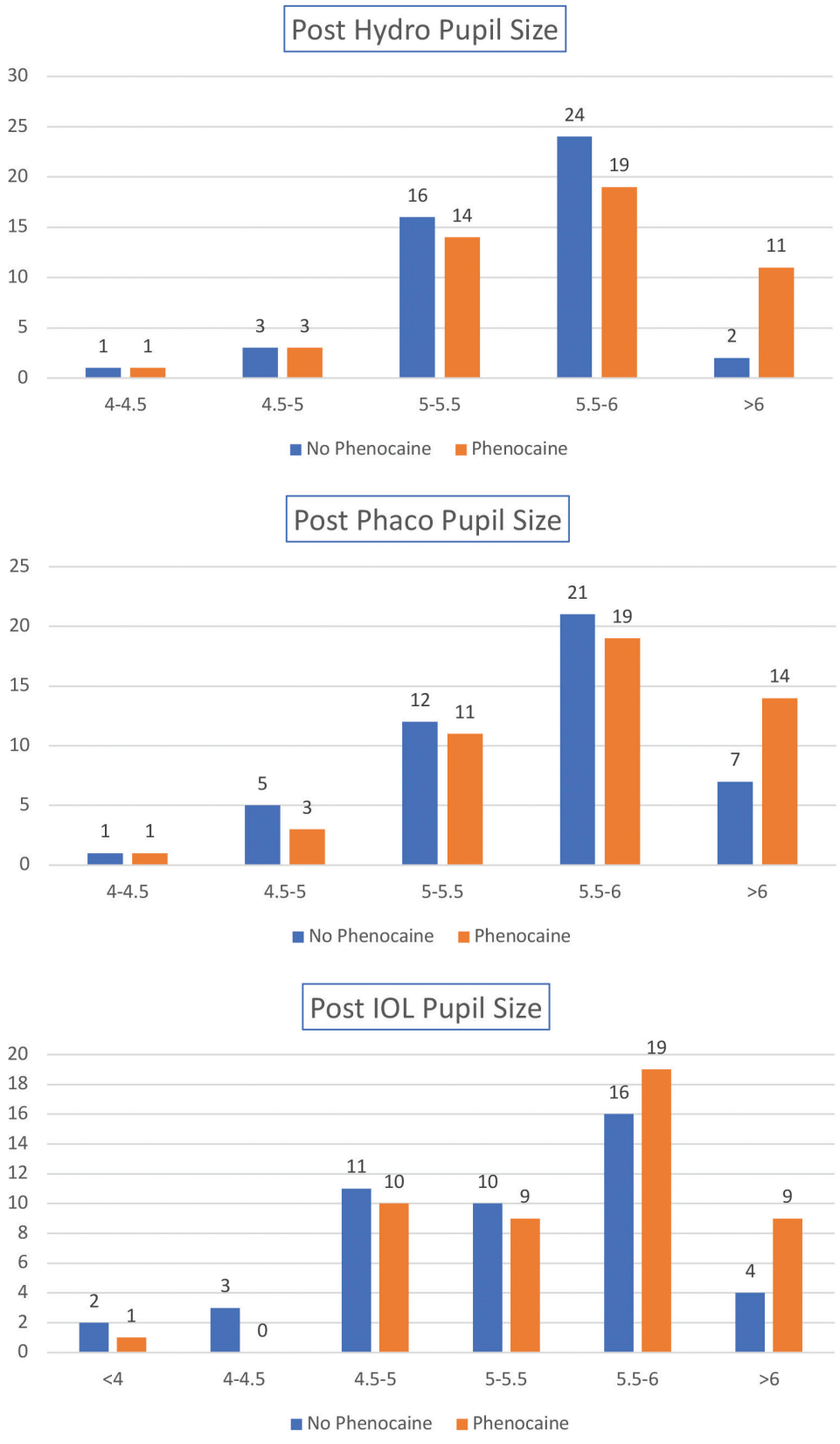

Figure 3 Comparison of pupil sizes in mm in Groups A (n = 48) and B (n = 46) at various stages of surgery.

Group A had more rigid pupils (n = 25, 52.08%) as compared to Group B (n = 14, 30.43%) (p = 0.03). This finding was reflected in the mean expansion in the two groups, where Group A pupils had a mean pupillary size of 5.72 ± 0.72 mm versus 6.05 ± 0.66 mm in Group B, after injection of viscoelastic prior to capsulorhexis (p = 0.03). Significantly, 36 (75%) of the patients in Group A dilated to 6.0 mm or more after injection of Phenocaine prior to capsulorhexis (Figure 2). The mean capsulorhexis size was 5.13 ± 0.37 mm in Group A and 5.11 ± 0.31 mm in Group B and the difference was not statistically significant.

The use of PED did not differ significantly between the two groups (Table 3). The proportion of subjects without epinuclear remnants after phacoemulsification did not differ significantly between the two groups (n = 42, 87.5% in Group A and n = 38, 82.61% in Group B). The average total phaco time in Group A was 88.1 ±0.64 seconds and 74.6 ± 0.59 seconds in Group B. Patient and surgeon comfort level during surgery also did not vary significantly between the groups (Table 3).

Table 3 Outcome Measures of the "Phenocaine Plus" group (Group A) and the control group (Group B)

Outcomes	Subgroups	Group A n = 48 (%)	Group B n = 46 (%)	Fisher's exact test
Use of PED	B Hex	1 (2.08)	1 (2.17)	
	Iris Hooks	5 (10.42)	5 (10.86)	1.0
	Stretch Pupilloplasty	1 (2.08)	0	
Surgeon comfort (grade)	0	40 (83.33)	41 (89.13)	
	1	6 (12.50)	2 (4.35)	
	2	1 (2.08)	2 (4.35)	0.613
	3	1 (2.08)	1 (2.17)	
Patient comfort (grade)	0	38 (79.17)	35 (76.09)	
	1	5 (10.42)	9 (19.57)	0.296
	2	5 (10.42)	2 (4.35)	

[i]PED: Pupillary expansion device, Surgeon comfort grades: 0- routine case/no stress, 1- mildly challenging case, 2- moderately challenging case, 3- highly challenging case, 4- case could not be completed to satisfaction.
Patient comfort grades: 0- no pain/discomfort, 1- no pain but mild discomfort, 2- mild pain, 3- moderate pain, 4- severe pain.

There were no major intraoperative complications in both groups, with 4 (8.33%) in Group A and 11 (23.91%) in Group B having iris touch, which was the most common reported complication. Other complications included iris prolapse and pupillary sphincter damage in 2 (4.2%) in Group A and 3 (6.5%) in Group B and 3 (6.25%) in Group A and 2 (4.34%) in Group B respectively. IFIS was reported in 1 (2.1%) and 5 (10.8%) patients in Group A and B respectively.

Discussion

Prevalence of small pupils in the general population is not well documented, but a study from Greece, has reported a prevalence of 6.8% small pupils in patients coming for cataract surgery[9]. Another study from rural India shows that 22.1% of cataract surgery patients have pseudoexfoliation and small pupils during surgery is the commonest complication[10] Using a pharmacological agent is usually easier and

safer than mechanical devices to dilate the pupil in most cases of cataract surgery. The use of mechanical devices adds to the time taken for surgery and requires an additional skill set on the part of the surgeon, for learning to insert the device and safely remove it at the end of surgery. From the patient's point of view, there may be a marginal reduction in the safety due to multiple openings into the anterior chamber in case of iris hooks, pupillary sphincter damage, potential damage to the cornea, and risk of an anterior capsular tear with all types of pupillary expanders[11]. From the nurse's perspective, it gives additional work in preparing a patient for surgery and can disrupt the workflow of the operation schedule due to inadequate dilatation delaying the surgical queue. The use of pharmacological agents can also positively impact the budget model for hospitals looking to optimize the costs of surgery[12]. A downside to pharmacological agents is potential contamination but this is a negligible risk given the safety of the current generation of intracameral agents[11]. A few retrospective studies in patients receiving intracameral phenylephrine and ketorolac combinations during surgery seems to suggest a reduction in the use of PED[13,14]. This study however does not show a significant difference in the use of PED with ICAM even in small pupil cataract surgery. This could have been due to the confounding factor introduced by the higher percentage of rigid pupils in Group A, (Table 1).

In busy operation theatres with high volume of cataract surgeries, it may be difficult to distinguish between inadequate pupil dilatation due to preexisting pathology or inadequate dosing of dilating drops. Even with standard preoperative assessment, evaluation of pupils may err on the side of poor dilation as seen in this study (Table 2). The unpredictability of time to mydriasis can lead to the use of rescue mydriatics in 15 to 18% of surgeries[12]. Intensive dilatation on the day of surgery can improve dilation results as seen by the data on pupil size at the start of surgery compared to preoperative pupil size measurements, (Figure 1). However, it is significant that Group A (Phenocaine group) patients who had smaller pupils preoperatively and a higher percentage of rigid pupils with poorer expansion did show expansion to 6 mm or more in 75% of the cases (Figure 2), indicating higher efficiency with ICAM.

The measurements of pupils at various times during the procedure as in, post-hydrodissection, post nucleus removal and post-IOL implantation all showed significant improvement and consistent pupil dilatation in the Phenocaine Group. The pupil size showed a significant reduction at the end of hydrodissection when compared to the start of surgery in Group B ($p < 0.001$). Mean pupil size was 0.04 mm larger in Group A, as compared to a 0.42 mm reduction in pupil size in Group B, when measured between start of surgery to end of hydrodissection. Similarly, comparing pupil measurements at the start of surgery to the post-phaco pupil size also revealed significant differences between both groups. In Group A the mean pupil size was 0.22 mm ($p = 0.004$) larger at the end of phacoemulsification as compared to the size at the start of surgery. In Group B, the mean pupil size was 0.26 mm ($p = 0.03$) smaller when measured at the same point during surgery (Figure 3, Table 2). The measurements at the end of IOL implantation also revealed significant differences between both groups. Compared to the start of surgery, Group A had a mean reduction of 0.05 (SD-0.78) mm ($p = 0.65$) in pupil size as opposed to 0.67 (SD-0.86) mm ($p < 0.001$) in Group B after IOL implantation (Table 2).

This is an indication that ICAMs can improve safety in small pupil cataract surgery. Intraoperative complications, though mild, were more in Group B with iris touch and IFIS reported in larger numbers in

this group. The slightly longer phaco time in Group A is explained by the higher number of harder Nucleus in group A. However, these findings were not statistically significant.

Patient comfort and surgeon comfort during the procedure were similar in both groups. This may be due to the operating surgeon experience which played a role in dealing with challenging situations and the threshold for using PED may vary between surgeons. Both patient comfort and surgeon comfort were subjective variables which were largely dependent on the surgeon's skill. The operating surgeon was not masked to the use of ICAMs and there was only a single surgeon's perspective in this study, which are limitations. A larger study in a multi-center setting and with a larger cohort of surgeons can help generate more evidence on the role of ICAMs in small pupil cataract surgery.

Conclusions

This study has shown that the use of ICAM as adjuvants in small pupil cataract surgery is warranted as pupil diameters in 75% of patients dilated to 6 mm or beyond at all stages of the procedure, ensuring safe surgery. Use of PED did not vary significantly in this study but a larger study is needed to further explore the impact of ICAM on PED use.

References

1. Srinivasan S. Intracameral mydriatics during cataract surgery. J Cataract Refract Surg. 2018 Mar;44(3):257-258.
2. Agnieszka Kubicka-Trzaska, Anna Markiewicz. Mydrane intracameral injection can be an alternative to mydriatic drops instillation in cataract surgery. J Physiol Pharmacol [Internet]. 2020 [cited 2022 Mar 28]; Available from: https://doi.org/10.26402/jpp.2020.2.08
3. Chiambaretta F, Pleyer U, Behndig A et al. Pupil dilation dynamics with an intracameral fixed combination of mydriatics and anesthetic during cataract surgery. J Cataract Refract Surg. 2018;44(3):341-347.
4. Labetoulle M, Findl O, Malecaze F et al. Evaluation of the efficacy and safety of a standardised intracameral combination of mydriatics and anaesthetics for cataract surgery. Br J Ophthalmol. 2016;100(7):976-985.
5. Nuzzi R, Baratozzi V, Sole Polito M, Tridico F. Efficacy and Safety of an Intracameral Combination of Two Mydriatics and an Anesthetic for Phacoemulsification in Complicated Patients. Open Ophthalmol J. 2018;12(1).
6. Labetoulle M, Behndig A, Tassignon MJ et al. Safety and efficacy of a standardized intracameral combination of mydriatics and anesthetic for cataract surgery in type-2 diabetic patients. BMC Ophthalmol. 2020 Dec;20(1):81.
7. Kaur S, Korla S, Ram J, Gupta PC, Sukhija J. Intracameral anesthetic mydriatic (ICAM) assisted pediatric cataract surgery. Eur J Ophthalmol. 2022 Mar;32(2):1157-1162.
8. Hovanesian JA, Sheppard JD, Trattler WB, et al. Intracameral phenylephrine and ketorolac during cataract surgery to maintain intraoperative mydriasis and reduce postoperative ocular pain: integrated results from 2 pivotal phase 3 studies. J Cataract Refract Surg. 2015;41(10):2060-2068.
9. Halkiadakis I, Chatziralli I, Drakos E et al. Causes and management of small pupil in patients with cataract. Oman J Ophthalmol. 2017;10(3):220.
10. Joshi, RS, Singanwad, SV. (2019). Frequency and surgical difficulties associated with pseudoexfoliation syndrome among Indian rural population scheduled for cataract surgery: Hospital-based data. Indian journal of ophthalmology, 2019;67(2),221-226.
11. Al-Hashimi S, Donaldson K, Davidson R et al. Medical and surgical management of the small pupil during cataract surgery. J Cataract Refract Surg. 2018 Aug;44(8):1032-1041.
12. Davey K, Chang B, Purslow C, Clay E, Vataire AL. Budget impact model of Mydrane®, a new intracameral injectable used for intra-operative mydriasis, from a UK hospital perspective. BMC Ophthalmol. 2018 Apr 19;18(1):104.

13. Visco D. Effect of phenylephrine/ketorolac on iris fixation ring use and surgical times in patients at risk of intraoperative miosis. Clin Ophthalmol. 2018 Feb;Volume 12:301-5.

14. Bucci F, Jr., Michalek B, Fluet AT. Comparison of the frequency of use of a pupil expansion device with and without an intracameral phenylephrine and ketorolac injection 1%/0.3% at the time of routine cataract surgery. Clin Ophthalmol. 2017 Jun;Volume 11:1039-1043.

Intracameral Anaesthetic Mydriatics as Adjuvant Aids in Small Pupil Cataract Surgery to Reduce the Use of Pupillary Expansion Devices: A Randomized Prospective Cohort Study from Central Kerala, India

Merine Paul, MS, DNB, FAICO

Footnotes and Financial Disclosures
Originally receive: 30/5/2024
Final revision: 20/3/2025
Accepted: 23/5/2025

Corresponding author: -
Financial Disclosure(s)
-