Comparison between Intracameral Adrenaline Injection in Addition to Topical Mydriatics and Topical Mydriatics only in Phacoemulsification Surgery

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Received 17 February 2016
Accepted March 2016

The Egyptian Journal of Cataract and Refractive Surgery 2016, 22:15–20

Purpose
The aim of the present study was to compare the pupil diameter in cases injected with intracameral adrenaline intraoperatively, in addition to topical mydriatics, and cases that received topical mydriatics only. In addition, this study aimed at assessing the systemic and local side effects of the two techniques.
Patients and methods
The study was conducted on a total of 80 consecutive eyes that underwent phacoemulsification surgery. Patients with different types of cataract requiring phacoemulsification were included in this study. The patients were randomized and divided into two groups. The first group (50 cases) received intraoperative bolus adrenaline injection intracameraly, in addition to preoperative topical mydriatics. The pupil diameter was measured twice, once after topical mydriatics and the second time after intracameral adrenaline injection. The second group (30 cases) received benoxinate hydrochloride 4 mg (Benox) preoperatively as a topical anesthetic, and tropicamid 1% (Mydriacil) as mydriatic. The pupil diameter was measured by using a squint caliper after mydriacyl.
Results
The mean preoperative pupil diameter in the first group was 6.76 ± 0.90 mm. Patients in the first group had smaller pupils. The mean preoperative pupil diameter in the second group was 8.07 ± 0.68 mm. The difference between the two groups was statistically significant. On the other hand, the mean pupil diameter after intracameral adrenaline injection was 7.91 ± 1.01 mm, which was statistically different as adrenaline dilated the pupil.
Conclusion
The present study revealed better pupil dilatation in cases with narrower pupil when injected with intracameral adrenaline than in cases with topical mydriatic only, with no local or systemic side effects.

Keywords:
intracameral adrenaline, intracameral mydriatics, phacoemulsification

Egypt J Cataract Refract Surg 22:15–20

1687-6997

Introduction

Definition of cataract

A cataract is any opacity of the lens, whether it is a small local opacity or a diffuse general loss of transparency. To be clinically significant, however, the cataract must cause significant reduction in visual acuity (VA) or functional impairment [1]. Symptoms of cataract include reduced VA, photophobia, glare, myopia, and monocular diplopia.

In the continuous development of cataract surgery procedures, the field of preoperative pupil dilatation has recently taken some new steps. Intracameral mydriatics (ICM) has been evaluated as an alternative to traditional topical mydriatics (TMs) in phacoemulsification surgery, with the first study of ICM [2] concluding that it is a rapid, effective, and safe method. A clinical evaluation [3] confirmed the benefits from the method when used in high-volume surgery.

Surgically induced miosis commonly occurs during cataract extraction surgery [4] due to mechanical manipulation of the iris affecting the sensitive dilator muscle [5]. The induced miosis is significantly more pronounced in diabetes patients undergoing cataract surgery [6]. To perform a safe operation the pupil needs not only to be dilated preoperatively but preferably needs to remain dilated throughout the procedure.

Different techniques have been suggested for the maintenance of mydriasis [7], including preoperative diclofenac [8] naproxen [9], viscous phenylephrine hydrochloride [10], or intraoperative intracameral epinephrine, either in the irrigation solution [11] or as a single bolus dose [12].

Tropicamide is an antimuscarinic drug that produces short acting mydriasis (dilation of the pupil) and cycloplegia when applied as eye drops. Due to its relatively short duration of effect (4–8 h), it is typically used during eye examinations.

Epinephrine

Epinephrine (also known as adrenaline, adrenalin, or 4,5-β-trihydroxy-*N*-methylphenethylamine) is a hormone and a neurotransmitter [13].

Effect of pupillary constriction intraoperatively

Pupillary constriction during cataract surgery may increase the risk for complications, including iris damage, incomplete cortex removal, posterior capsule rupture, vitreous loss, and dislocation of the lens material [14].

Patients and methods

(1) The study was conducted on 80 eyes scheduled for phacoemulsfication surgery. The patients were divided into two groups: the first group received preoperative TMs in addition to intracameral adrenaline injection (50 cases), and the second group received only preoperative TMs (30 cases). Diabetic patients were included to know the effect of intracameral adrenaline injection on mydriasis in diabetics. Ethics commute at alexandria university, faculty of medicine approved this study.

Moreover, hypertensive patients were not excluded [to observe any increase in blood pressure during operation and early postoperative period (first day)].

Inclusion criteria

(1) Nondilatable pupil (when one or both pupils stay small and miotic 4–5 mm, after taking preoperative regimen of tropicamide 1% four times).
(2) Poorly dilatable pupil (when pupil does not fully dilate after TM regimen), 5–7 mm.

Exclusion criteria

(1) History of ocular trauma or intraocular surgery.
(2) Intraocular inflammation.

Study participants were subjected to a standard protocol consisting of the following:

(1) History taking, which included ophthalmological and general history.
(2) Examination, which included the following:
    (a) VA testing, including best spectacle corrected VA.
    (b) Manifest refraction.
    (c) Slit lamp examination of the anterior segment structures.
    (d) Intraocular pressure measurement (by using a Goldmann Haag-Streit AT 900 applanation tonometer (Haag Streit co., USA), Switzerland).
    (e) Fundus examination by slit lamp indirect ophthalmoscopy using 90 diopter lens.
    (f) Preoperative blood pressure and also fasting blood sugar level.
(3) Surgical techniques

    All patients received benoxinate hydrochloride, 4 mg (Benox: benoxate hydrochloride, EPICO, Egypt) preoperatively as a topical anesthetic, and tropicamid 1% (Mydriacil: tropicamide, Alcon, Egypt) as a mydriatic. Pupil diameter was measured by using a squint caliper after mydriacyl and after intracameral adrenaline injection concentration 1: 25 000.

    All surgeries involved a superior clear corneal incision, and 1.4% with sodium hyaluronate (HealonGv: sodium hyaluronate, Abott Medicaloptics, USA) as ophthalmic viscosurgical device.

    The nucleus was emulsified by using the stop and chop technique. An AcrySof foldable intraocular lens was implanted in all cases. Balanced salt solution with garamaycin was used as the irrigating solution.

    Intraoperative blood pressure was measured before and after the adrenaline injection.
(4) Follow-up visits:

    VA was measured on the first postoperative day (uncorrected visual acuity) and the best corrected visual acuity (BCVA) was measured 4 weeks after the surgery.

    Assessment of any postoperative complications locally (cells, flare in the anterior chamber, and/or increase in intraocular pressure) or systemically (shooting of the blood pressure).

(5) Statistical analysis of the data [15]:

Data were fed into the computer and analyzed using the IBM SPSS for Windows software package, version 20.0 (USA) [16] Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, SD, and median. Comparison between different groups regarding categorical variables was carried out using the χ^2-test. When more than 20% of the cells had an expected count less than 5, correction for χ^2 was conducted using Fisher's exact test or the Monte Carlo correction. The distributions of quantitative variables were tested for normality using the Kolmogorov–Smirnov test, Shapiro–Wilk test, and D'Agstino test. In addition, histogram and QQ plot were used for the vision test. If it revealed a normal data distribution, parametric tests was applied. If the data were abnormally distributed, nonparametric tests were used. For normally distributed data, comparison between the two independent populations were done using the independent *t*-test. Paired *t*-test was used to analyze two-paired data. For abnormally distributed data, comparison between two independent populations were done using the Mann–Whitney test. Significance of the obtained results was judged at the 5% level.

Results

The study was conducted on a total of 80 consecutive eyes underwent phacoemulsification surgery.

(1) The first group (the patient group), in which 50 patients received ICM in addition to TM.
(2) The second group (the control group), in which 30 cases received TM only.

In the first group, there were 15 male patients. The age distribution of the participants was normal, with average age being 63.24 ± 9.25 years. In the control group, there were 33.3% males. The age distribution of participants was normal, with average age being 63.20 ± 12.90 years (Table 1).

In the first group, 36 patients were complaining of right-sided cataract, whereas 14 patients were complaining of left-sided cataract. On the other hand, in the control group 20 patients were complaining of right-sided cataract.

Twenty-one patients were complaining of diabetes in the first group and 29 were not. In the control group, 11 patients were diabetic and 19 were not diabetic, which is not significantly different.

Preopertive fasting blood sugar level mean was 134.29 ± 33.99 mg/dl in the patient group and 135.82 ± 41.05 mg/dl in the control group, which is not statistically different.

Mean duration of diabetes was 11.06 ± 7.16 years in the first group and 10.73 ± 7.23 years in the control group, which is not statistically different.

Thirty-two patients were complaining of hypertension and 18 were not in the first group, whereas in the control group 12 patients were complaining of hypertension and 18 were not.

There were no statistically significance differences between the mean systolic blood pressure and the mean diastolic blood pressure in two groups, which supports the matching of the two groups (Table 2).

The mean pupil size preoperative under microscope illumination was 6.76 ± 0.90 mm in the first group, whereas in the control group it was 8.07 ± 0.68 mm, which was statistically different in the two groups (patients pupils were smaller in size) (Table 3).

When comparing preoperative pupil diameter (the mean was 6.76 ± 0.90 mm), which increased to 7.91 ± 1.01 mm after injection of intracameral adrenaline This change was statistically significant ($P < 0.001$) (paired *t*-test) (Fig. 1).

On comparing pupillary diameter in diabetic patients in the first and the control groups, there was a significant difference between the two groups as adrenaline dilated pupil more in the patient group (Table 4).

The mean systolic blood pressure in the first group was137.08 ± 24.94 mmHg preoperative and became 116.14 ± 20.46 mmHg after intracameral injection of adrenaline, whereas in the control group, preoperative systolic blood pressure mean was 137.1 ± 25.25 mmHg and became 117.60 ± 21.73 mmHg after anesthesia and beginning of operation, which was not statistically different in the two groups.

In addition, mean diastolic blood pressure was 80.76 ± 13.2 mmHg preoperatively and became 68.24 ± 11.0

Table 1 Comparison between the studied groups according to demographic data

	Patient ($n=50$) [n (%)]	Control ($n=30$) [n (%)]	Test of significance	P
Sex				
Male	15 (30.0)	10 (33.3)	$\chi^2=0.097$	0.755
Female	35 (70.0)	20 (66.7)		
Age				
Minimum–maximum	43.0–85.0	27.0–84.0	$t=0.016$	0.987
Mean±SD	63.24±9.25	63.20±12.90		
Median	62.50	64.0		

Table 2 Comparison between the studied groups according to hypertension and preoperative arterial blood pressure

	Patient ($n=50$) [n (%)]	Control ($n=30$) [n (%)]	Test of significance	P
Hypertension				
No	18 (36.0)	18 (60.0)	$\chi^2=4.364^*$	0.037*
Yes	32 (64.0)	12 (40.0)		
Hypertension systolic				
Minimum–maximum	90.0–210.0	90.0–190.0	$t=0.004$	0.997
Mean±SD	137.08±24.94	137.10±25.25		
Median	130.0	140.0		
Hypertension diastolic				
Minimum–maximum	42.0–120.0	55.0–110.0	$t=0.101$	0.920
Mean±SD	80.76±13.12	80.45±13.38		
Median	80.0	80.0		

t, Student's t-test. *Statistically significant at $P\leq0.05$.

Table 3 Comparison between the studied groups according to preoperative pupil and postadrenaline pupil

	Patient ($n=50$)	Control ($n=30$)	t_1	P
Preoperative pupil				
Minimum–maximum	4.50–8.50	7.0–9.25	6.919*	<0.001*
Mean±SD	6.76±0.90	8.07±0.68		
Median	6.75	8.0		
Postadrenaline pupil				
Minimum–maximum	5.0–10.0	7.0–9.25	0.751	0.455
Mean±SD	7.91±1.01	8.07±0.68		
Median	8.0	8.0		
t_2	11.082*			
P	<0.001*			

t_1, Student's t-test; t_2, paired t-test. *Statistically significant at $P\leq0.05$.

Table 4 Comparison between the studied groups according to preoperative pupil and postadrenaline pupil in diabetic patients

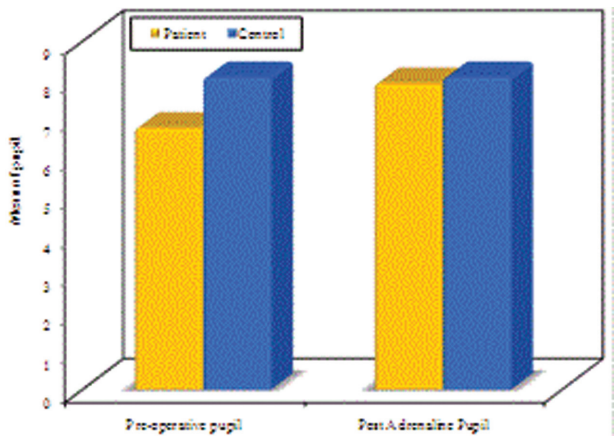
	Patient ($n=21$)	Control ($n=11$)	t_1	P
Preoperative pupil				
Minimum–maximum	5.0–8.50	7.0–8.50	4.486*	<0.001*
Mean±SD	6.63±0.90	7.93±0.45		
Median	6.50	8.0		
Postadrenaline pupil				
Minimum–maximum	5.0–9.50	7.0–8.50	0.885	0.383
Mean±SD	7.64±1.03	7.93±0.45		
Median	8.0	8.0		
t_2	6.707*			
P	<0.001*			

t_1, Student's t-test; t_2, paired t-test. *Statistically significant at $P\leq0.05$.

mmHg in the first group, whereas in the control group, preoperative mean diastolic blood pressure was 80.45 ± 13.38 mmHg and became 71.33 ± 10.90 mmHg, which was not statistically significant.

There was no statistically significant difference between the two groups as regards the preoperative specular microscopy, as the mean endothelial cell count in the patient group was 2558.90 ± 386.72

Figure 1



Comparison between the studied groups according to preoperative pupil and postadrenaline pupil.

cells and in the control group it was 2418.97 ± 345.05 cells.

Mean first day postoperative vision was 0.37 ± 0.15 in the first group and 0.29 ± 0.13 in the control group, which was statistically significantly different.

Forty-one patients did not get any complications in first postoperative day in the first group and nine patients got corneal edema (18%). On the other hand, in the control group 26 cases did not complicate and four cases got corneal edema (13%). All corneal edemas resolved at 1 month postoperative visit.

There was no statistically significant difference between the two groups that developed complications as regards preoperative specular microscope as the mean endothelial cell count in the patient group was 2535.25 cells, whereas in the control group it was 2366.70 cells.

When we compared BCVA 1 month postoperatively, the mean was 0.90 ± 0.10 in the patient group and 0.88 ± 0.10 in the control group, which was not statistically different.

Discussion

Cataract extraction is, in the majority of cases, a safe and effective procedure, but maintenance of mydriasis can contribute to the ease with which surgery can be performed [17]. A small pupil during surgery may increase the risk for damage to the iris, incomplete clearance of soft lens matter, or, more importantly, rupture of the posterior capsule [14].

To maintain mydriasis during surgery, some surgeons use adrenaline either in the intraocular irrigation fluid, or as a bolus injection into the anterior chamber [7].

In this study, we studied the effect of intracameral adrenaline injection in the study group (the first group). The mean preoperative pupil diameter was 6.76 ± 0.90 mm in the patient group, and in the control group it was 8.07 ± 0.68 mm, which is statistically different in the two groups (patients pupils were smaller in size).

In the first group, the mean preoperative pupil diameter was 6.76 ± 0.90 mm after TM and increased to 7.91 ± 1.01 mm after injection of intracameral adrenaline. This change was statistically significant ($P < 0.001$).

The mean pupillary diameter among diabetic patients was 6.63 ± 0.90 mm after TM and increased to 7.64 ± 1.03 mm after intracameral adrenaline injection. In the control group, it was 7.93 ± 0.45 mm. Thus, there was no significant difference between the two groups as adrenaline dilated the pupil more in the patient group. We found that the pupillary dilatational in our study was comparable with the findings in a study by Lundberg. He mentioned that the mean pupil size was smaller in the ICM group (6.7 ± 1.0 mm) than in the TM group (7.7 ± 1.0 mm) ($P < 0.001$), but the pupils in the ICM group often continued to enlarge throughout the cataract procedure (+4.5 ± 8.1%). When using ICM, the pupil was significantly larger at the end of the operation than at the beginning in the nonepinephrine group. In addition, the duration of mydriasis is longer with ICM compared with TM, which resulted in a larger pupil at the first postoperative day.

In their study, William *et al.* used a similar (but more concentrated) ICM solution. In that study, the average pupillary dilatation achieved using their higher concentration ICM solution was 7.1 ± 0.7 mm against our average pupillary dilatation of 6.9 ± 1.02 mm [18]. Similarly at the end of surgery, the average diameter was 7.3 ± 0.7 and 7.0 ± 0.20 mm in their and our study, respectively.

It was found that intracameral adrenaline injection did not affect arterial blood pressure neither systolic nor diastolic in hypertensive patients.

We found the blood pressure monitoring was comparable with that of Salima *et al.*, who mentioned that the mean of preoperative blood pressure was 117 ± 3/75 ± 2 mmHg. The pressure increased significantly after injection of local anesthesia. At the beginning of the surgery, blood pressure values dropped down to preoperative values.

Intraoperative and postoperative blood pressure after intracameral injection of epinephrine remained constant: 117 ± 2.5/65 ± 1.5 mmHg.

Björn Lundberg in Umeå university mentioned that the lower dose and the intracameral distribution of adrenaline may reduce the risk for cardiovascular side effects in certain groups of patients [19–21].

Forty-one patients did not develop any complications on the first postoperative day in the first group and nine developed corneal edema (18%), whereas, in the control group, 26 cases did not develop any complications and four got corneal edema (13%).

All eyes with corneal edema resolved at 1 month postoperative. The mean BCVA was 0.90 ± 0.10 in the first group 1 month postoperatively, and in the control group it was 0.88 ± 0.10, a difference that was not statistically significant.

When comparing complications and postoperative BCVA results with those obtained by Melanie *et al.*, who mentioned that early experience with intraocular adrenaline resulted in a few cases of severe corneal decompensation following use of the 1: 1000 concentration [22], but not 1: 5000, corneal endothelial damage was shown to result from toxicity due to the sodium bisulphite preservative in the adrenaline preparation, rather than the adrenaline itself.

Conclusion

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

It does not affect blood pressure even in hypertensive patients.

It dilates pupil more than does TM even in diabetic patients and older patients.

Financial support and sponsorship
Nil.

Conflicts of interest
All authors have no financial interest in any of drugs or devices used in this study.

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