

## The effect of 0.25% apraclonidine in the prevention of intraocular pressure elevation following Nd: YAG laser posterior capsulotomy

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**Objective** The efficacy and adverse effects of 0.25% apraclonidine on intraocular pressure (IOP) following Nd: YAG laser posterior capsulotomy were investigated and the results were compared with placebo, 0.50% timolol maleate and 1% apraclonidine.

**Methods** The study was carried out in the Anterior Segment Division of the Department of Ophthalmology of Uludağ University Medical Faculty between September 1994 - November 1995.

In this study, 80 eyes were randomly assigned into four groups each consisting of 20 eyes. In double masked study, the groups were treated with placebo (group-1), 0.50% timolol maleate (group-2), 1% apraclonidine (group-3), 0.25% apraclonidine (group-4) 1 hour before and 5 minutes after Nd: YAG laser posterior capsulotomy. Intraocular pressure of patients was measured 1 hour before and 1, 3, 24 hours following the capsulotomy.

**Results** IOPs increased 3.90 (5.35, 5.95 (5.32, 1.15 (3.20 mmHg in the first group (control group), and 0.40 (4.08, 0.75 (5.33, 0.80 (6.03 mmHg in the second group in respect to the average baseline IOP in 1, 3, 24

hours posttreatment respectively ( $p=0.025$ ,  $p=0.002$ ,  $p=0.822$ ). In the third group it decreased 3.70 (2.40, 3.30 (2.47, 2.65 (1.56 mmHg in the corresponding times ( $p=0.0001$ ,  $p=0.0001$ ,  $p=0.0001$ ). In the fourth group, IOP increased 0.35 (3.32mmHg in one hour, but decreased 1.25 (3.41, 0.90 (2.07mmHg in 3 and 24 hours ( $p=0.017$ ,  $p=0.010$ ,  $p=0.022$ ). There were statically difference between the 3rd and the 4th groups in 1, 3, 24 hours ( $p=0.0001$ ,  $p=0.03$ ,  $p=0.05$ ), but no difference were seen between the 2nd and the 4th groups in the corresponding times.

Some systemic and local side effects were seen in the second and third group, but no side effect was seen in the fourth group.

**Conclusion** As a result, 0.25% apraclonidine is also effective in preventing the early elevation of IOP after Nd: YAG laser posterior capsulotomy and may be preferred to 1% apraclonidine and 0.50% timolol maleate.

**Key words** Nd: YAG laser, posterior capsulotomy, apraclonidine, timolol maleate

### Introduction

Extracapsular cataract extraction (ECCE) with or without IOL implantation is the preferred surgery for the rehabilitation of cataract. Posterior capsule opacification is the most common complication of the surgery in the first five years seen in 50% and in 10% of the cases after ECCE and ECCE+IOL implantation, respectively (1, 2).

This complication was treated surgically until Aron-Rosa introduced the use of Nd: YAG laser to open the posterior capsule, which is a noninvasive and much safer intervention (3).

Elevation of IOP in the early phase after Nd: YAG laser capsulotomy may cause serious visual disturbances. IOP increase is more frequent, more dangerous and long lasting in glaucomatous patients than others (4-7). Many studies have been carried out to overcome this outmost important complication since the first application of this therapy method (2, 4, 8). Acetazolamide, (beta)blockers, clonidine, apraclonidine and (beta)blockers+ apraclonidine combinations were

used for this purpose. Some side-effects of these drugs urged the investigators to search for new alternatives. Apraclonidine, a relative selective alpha-2 adrenergic agonist, was found to decrease IOP in both normotensive and hypertensive eyes by decreasing aqueous inflow. This drug was also found to be very effective in decreasing the IOP elevation following Nd: YAG laser capsulotomy (6-13).

In this study, we compared the effectiveness and side effects of 0.25% apraclonidine with 1% apraclonidine and 0.50% timolol maleate in decreasing the IOP elevations after Nd: YAG laser capsulotomy.

### Material and Method

The study was carried out in the Anterior Segment Division of the Department of Ophthalmology of Uludağ University Medical Faculty between September 1994-November 1995. Eighty eyes of 76 patients who had ECCE + PC IOL implantations having capsular opacification were included in the study.

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Patients using anti-hypertensive drugs or who had had glaucoma surgery, and those having ocular surface problems and high corneal astigmatism that might decrease the reliability of applanation tonometry, and patients with pulmonary or liver or renal disorders were not included in the study. IOP exceeding 22 mmHg before capsulotomy was another exclusion criterion.

All patients had routine ophthalmic examinations. Before Nd: YAG laser capsulotomy, IOPs were measured twice with an applanation tonometry in order to determine the baseline IOPs. Systolic and diastolic blood pressures and pulse rates were also recorded. Pupil diameter and interpupillary distance were measured under normal room illumination with calliper, and recorded.

After this first examination these eyes were randomly assigned into four groups and every group included 20 eyes. Double masked, group-1 was treated with placebo coll., group-2 with 0.5% timolol maleate coll., group-3 with 1% apraclonidine hydrochloride coll., group-4 with 0.25% apraclonidine hydrochloride coll. Drugs were instilled one hour before and 5 minutes after laser treatment. The operation was carried out with MQL-10 Q-Switched Nd-YAG laser (pulse duration: 8nsec., spot size: 100  $\mu$ m) by only one person after mydriasis obtained by 10%

Table 1. The effects of placebo, 0.50% timolol, 1% and 0.25% apraclonidine to baseline average IOPs (mmHg).

Drug	Baseline IOP	1st hour	3rd hour	24th hour
placebo	12.40 $\pm$ 2.25	3.90 $\pm$ 5.35	5.95 $\pm$ 5.32	1.15 $\pm$ 3.20
0.50% timolol	13.15 $\pm$ 2.54	0.40 $\pm$ 4.08	0.75 $\pm$ 5.33	0.80 $\pm$ 6.03
1% apraclonidine	12.40 $\pm$ 3.26	-3.70 $\pm$ 2.40	-3.30 $\pm$ 2.47	-2.65 $\pm$ 1.56
0.25% apraclonidine	11.95 $\pm$ 3.23	+0.35 $\pm$ 3.32	-1.25 $\pm$ 3.41	-0.90 $\pm$ 2.07

The average baseline IOPs increased 3.90 (5.35, 5.95) (5.32, 1.15) (3.20 mmHg in the first group and 0.40 (4.08, 0.75) (5.33, 0.80) (6.03 mmHg in the second group in 1, 3, 24 hours posttreatment respectively ( $p=0.025$ ,  $p=0.002$ ,  $p=0.822$ ). In the third group, it increased 3.70 (2.40, 3.30) (2.47, 2.65) (1.56 mmHg at the corresponding times ( $p=0.0001$ ,  $p=0.0001$ ,  $p=0.0001$ ). In the fourth group it increased 0.35 (3.32 mmHg in 1st hour, but decreased 1.25 (3.41, 0.90) (2.07, mmHg in 3 and 24 hours ( $p=0.017$ ,  $p=0.011$ ,  $p=0.022$ ). (Table-1, Figure-1). There were statically difference between the 3rd and the 4th groups in 1, 3, 24 hours ( $p=0.0001$ ,

phenylephrine hydrochloride coll., and Peyman Nd: YAG capsulotomy contact lens (OPY-12.12) was used. We applied minimum energy and shooting numbers to obtain plus shaped 3-4 mm opening on the posterior capsule. The energy used was 119  $\pm$  70 mJ, 134  $\pm$  71 mJ, 125  $\pm$  58 mJ, 124  $\pm$  41 mJ totally in the groups respectively. When IOP was over 30 mm Hg 0.5 % timolol maleate and acetazolamide tablets 2x1 were given until IOP was decreased below 25 mm Hg. All the pretreatment measurements were done again at 1st, 3rd and 24th hours posttreatment. Pallor of the conjunctiva, xerostomia, dryness of nasal mucosa and exhaustion were asked, and recorded. All the patients were ordered with topical dexamethasone for 5 days.

The results were evaluated statistically with student t and oneway ANOVA tests.

## Results

Thirty-six of the cases were male (47.3%) and forty were female (52.7%). Both eyes of four patients were included in the study. The average age was 56 $\pm$ 11 years, ranging between 20-82 years. The average baseline IOPs were 12.40 $\pm$ 2.25 mmHg, 13.15 $\pm$ 2.54 mmHg, 12.40 $\pm$ 3.26 mmHg, 11.95 $\pm$ 3.23 mmHg in the groups respectively. There were not statistically differences among these values ( $p=0.621$ , Table 1).

$p=0.03$ ,  $p=0.05$ ), but no difference were seen between the 2nd and the 4th groups in corresponding times ( $p=0.97$ ,  $p=0.21$ ,  $p=0.25$ ).

IOP increases were seen in 14 eyes, 18 eyes, 10 eyes at 1st, 3rd and 24th hours posttreatment respectively in the first group, in 10, 6, 8 in the second group, and in 10, 8, 4 in the fourth group. There was only one eye the IOP of which increased in the first hour, whereas no increase was seen in 3 and 24 hours in the third group (Table 2, Figure 2).

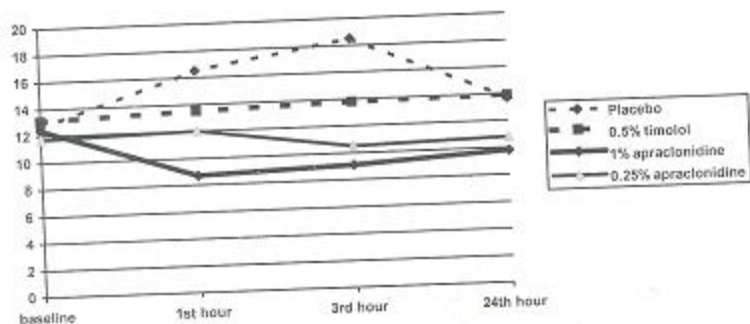


Figure 1. The alteration lines of IOPs.

Table 2. The alteration of IOPs and the number of patients at 1st, 3rd and 24th hours.

From baseline IOP	1 <sup>st</sup> hour				3 <sup>rd</sup> hour				24 <sup>th</sup> hour			
	G1	G2	G3	G4	G1	G2	G3	G4	G1	G2	G3	G4
0-5 mmHg decrease	1	6	12	7	1	10	14	10	4	9	19	12
5-10 mmHg decrease	-	1	6	-	-	1	6	2	-	1	-	-
Unchanged	5	3	1	3	1	3	-	-	8	6	-	4
0.5 mm Hg increase	9	8	1	8	10	2	-	6	2	2	-	-
5-10 mm Hg increase	3	2	-	2	4	2	-	2	-	-	-	-
10 mm Hg < increase	2	-	-	-	4	2	-	-	-	-	-	-

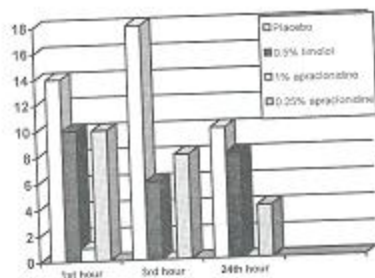


Figure 2. The number of eyes exceeding baseline IOPs.

The number of eyes which exceeded 5mmHg were 5, 8, 2 in the first group 2, 4, 2 in the second group, 2, 2, 0 in the fourth group in 1, 3, 24 hours respectively, whereas there was not any in the third group. The number of eyes exceeding 10 mmHg were 2 and 4 at 1st and 3rd hours respectively in the first group posttreatment, and 2 at 3rd hour in

the second group. These increases were lower than 10 mmHg at 24th hour. In no eyes, IOP increased over 10 mmHg in the third and fourth groups in any measurement (Table 2, Figure 3).

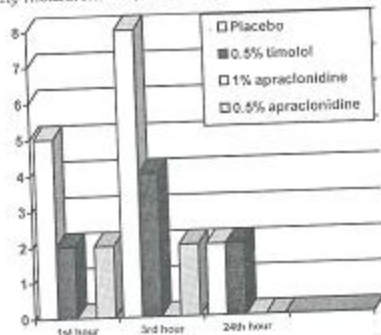


Figure 3. The number of eyes over 5 mmHg exceeding baseline IOPs.

In the second group, there were punctate keratitis in 2 cases (10%), bronchospasm and anxiety in 1 case (5%), anterior chamber (++) flare in 5 cases (25%). In the third group, there were lid retraction over 1 mm in 6 eyes (30%), mydriasis over 1mm in 8 eyes (40%), pallor of conjunctiva in 10 eyes (50%). However in the fourth group no prominent side effect was seen. Symptoms like bradycardia, rhythm disorders, sweating and exhaustion were not seen in all groups

## Discussion

Nd: YAG laser application causes molecular bond rupture and macromolecular break up (photodisruption) in the tissues. It has a wide range of application in ophthalmology including both the anterior and posterior segments, but widely used for posterior capsulotomy (6-11). Although an easy and noninvasive method, it may cause some serious side effects such as IOP increase in about 60% of the cases requiring urgent treatment (9, 10).

The resulting tissue damage is due to shock wave, thermal and electromagnetic effects as well as the sensitivity of the target tissue and its surroundings.

The IOP increase encountered after Nd: YAG laser application is a result of mechanical obstruction of the trabecular meshwork by the capsular remnants causing decrease in the outflow facility and blood-aqueous barrier breakdown by the release of prostaglandins from the iris tissue as a result of mechanical trauma (7, 11, 14). Apraclonidine, a relative selective alpha-2 adrenergic agonist is used to avoid this complication. It decreases the aqueous inflow also by decreasing c-AMP with the effect of adenylyl cyclase enzyme.

IOP increase is generally seen at the third hour posttreatment, which subsides by the 24th hour, but may be permanent in about 2-3% of the cases (15). Terry et al. reported that it continued six week in 4% of the cases (16). Richter et al. reported an average of 8mmHg of IOP increase, whereas we have found an increase of  $6.3 \pm 5.3$ mmHg at third hour in the control group (7). Both the number of eyes with increased IOP and with maximum increase was seen at the 3rd hour posttreatment in the control group of the study and decreased at the 24th hour (10 eyes, 50%). Two eyes exceeding 5 mmHg at the first 3 hours were still high at 24 hours (10%).

Channel et al. reported that they did not see IOP increase higher than 10mmHg in the cases not

exceeding 5 mmHg in the first four hours posttreatment, whereas in our study, there were 14 eyes (17.5%) exceeding 5 mm in the first three hours in all groups, none of which exceeded 10 mmHg afterward (6). For this reason, although it is reported that an increase of IOP might occur in the late period, we took at the 1st, 3rd and 24th hours values into consideration for the evaluation of the early IOP increase (17).

The energy used, was  $4 \text{ mJ/pulse}$  and  $119 \pm 70 \text{ mJ}$ ,  $134 \pm 71 \text{ mJ}$ ,  $125 \pm 58 \text{ mJ}$ ,  $124 \pm 41 \text{ mJ}$  totally in the groups respectively. It was suggested that there was a correlation between the submitted total energy and IOP increase (3, 6, 10). However, this correlation was not supported by the studies performed later (2, 14). For this reason, we did not make a particular evaluation regarding the submitted energy.

Apraclonidine 0.5% and 1% were used both in normotensive and hypertensive eyes, but no differences were found except for few side effects (18, 19). Jampel et al. used 0.25% apraclonidine in the treatment of glaucomatous eyes (20). No research has been done on its effect on IOP after posterior capsulotomy. Therefore we compared the effectiveness and side effects of 0.25% apraclonidine with 1% apraclonidine and 0.5% timolol maleate in decreasing the IOP elevations after Nd: YAG laser capsulotomy in the study.

The average baseline IOPs increased  $4.6 \pm 5.5$ ,  $6.3 \pm 5.3$ ,  $1.6 \pm 3.6$  mmHg in the first group and  $0.5 \pm 4.4$ ,  $0.6 \pm 5.8$ ,  $0.5 \pm 5.5$  mmHg in the second group in 1, 3, 24 hours posttreatment respectively. In this way, timolol was seen to be relatively effective in 1st hour than 3rd and 24th hour. Migliori also reported that its effectivity decreased following the 5th hour (21).

In the third group, the average baseline IOP decreased  $3.0 \pm 2.4$ ,  $3.0 \pm 2.5$ ,  $3.0 \pm 1.4$  mmHg at the corresponding times. This decrease was highly significant compared to timolol and 0.25% apraclonidine. Although Pollack et al. reported 10 mmHg or higher IOP increase in 3% of the cases with 1% apraclonidine, we did not see any IOP increase higher than 5 mmHg. Özdamar et al. did not see such a high IOP increase either (22, 23). The effectivity of 1% apraclonidine was observed to start in the 1st hour and to continue in the 24th hour.

In the fourth group average IOP increased  $0.35 \pm 3.32$  mmHg in one hour, but decreased  $1.25 \pm 4.41$ ,  $0.90 \pm 2.07$  mmHg in 3 and 24 hours. Although pressure exceeding 5mmHg was observed at the 3th hour in two eyes, it was below 5mmHg at the 24th hour. No eyes demonstrated

increase exceeding 10 mmHg. The effectivity of 0.25% apraclonidine was lower at the first hour, but at 3rd hour reached maximum level and continued slightly decreasing at 24th hour.

In the second group, we encountered punctate keratitis, bronchospasm, anxiety and anterior chamber (+ +) flare. Frishman et al. reported heart rhythm disorders, bronchospasm, dyslipidemia in hypertensive eyes treated with timolol, whereas Letho reported decrease of visual acuity (24, 25).

Although similar side effects were not seen in Abram's study with 1% apraclonidine lid retraction, mydriasis, pallor of conjunctiva were seen in our study with 1% apraclonidine. On the other hand we confronted no side effects with 0.25% apraclonidine. We did not also see any systemic side effects such as systemic hypertension, change in pulse rate, dryness of mouth and nasal mucosae or exhaustion.

Although 0.25% apraclonidine is slow acting and weakly effective than 1% apraclonidine, it seems that this concentration is sufficient alone in preventing early IOP increases after Nd: YAG laser posterior capsulotomy. It can be an alternative drug to 0.50% timolol in decreasing the postoperative flare, and to 0.5% and 1% apraclonidine for having no side effects.

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