COMPARISON BETWEEN 0.5% TIMOLOL MALEATE AND 0.2% BRIMONIDINE TARTRATE IN CONTROLLING INCREASE IN INTRAOCULAR PRESSURE AFTER NEODYMIUM: YTTRIUM-ALUMINIUM-GARNET LASER CAPSULOTOMY

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ABSTRACT

Objective: To compare the effectiveness of prophylactically given 0.5% Timolol maleate and 0.2% Brimonidine tartrate in controlling increase in intraocular pressure after neodymium (Nd) : yttrium aluminum garnet (YAG) laser capsulotomy.

Study Design: Randomized controlled trial.

Place and Duration of Study: This study was conducted at Ophthalmology Department, Jinnah Hospital, Lahore from 15-05-2009 to 14-05-2010 for a duration of 12 months.

Material and Methods: In this study, 90 consecutive patients were referred from outpatient department for Nd: YAG laser capsulotomy. Hospital ethical committee's approval for this research proposal and the informed consent was taken. These patients were equally divided into two groups A and B, comprising of 45 patients in each group. Group A was control group which received 0.5% Timolol maleate. Group B was experimental group which received 0.2% Brimonidine tartrate. Intraocular pressure was measured using Goldmann tonometer before instilling these topical medications. These medications were administered topically 1 hour before the laser procedure. Intraocular pressure (IOP) was recorded 1 and 3 hours after laser capsulotomy.

Results: In patients belonging to group A, 42 (93.3%) patients had effective control of IOP (raise of less than or equal to 5 mmHg from the baseline) after 3 hours of Nd:YAG laser capsulotomy whereas 28 (62.2%) patients had effective control of IOP after the same period of time in group-B with significant difference (p<0.001).

Conclusion: Use of prophylactic topical antiglaucoma medications before doing Nd: YAG laser capsulotomy is a effective way to reduce post laser spike of intraocular pressure. Present study showed that the use of 0.5% timolol maleate was safe and more effective than 0.2% brimonidine tartrate when given 1 hour before laser capsulotomy.

Keywords*:* Goldmann Tonometer, Intraocular Pressure, Nd: YAG Laser capsulotomy.

INTRODUCTION

Cataract is the leading cause of blindness and visual impairment in the world causing reversible blindness in more than 17 million people every year[1]. Phacoemulsification has become the preferred method of cataract extraction over extracapsular cataract extraction[2]. The enduring success of any lens surgery depends on the permanent clarity of the posterior capsule no matter which surgical technique is used otherwise the vision becomes blurred again and sensitivity of the macula to incoming light is reduced[3]. Its overall rate is 28% after 5 years[1]. Capsular opacification occurs secondary to proliferation of remaining viable lens epithelial cells after removal of natural lens.

In developed countries, the next most common surgical procedure after cataract extraction and IOL implantation (Nd: YAG laser capsulotomy) is to clear any opacity that may occur in the posterior capsule. This improves both best corrected visual acuity (BCVA) and sensitivity of the macula[3].

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Neodymium: Yttrium-Aluminum-Garnet (Nd: YAG) laser is the preferred modality for treating posterior capsular opacification nowadays[4]. It is performed on outdoor basis and is a painless procedure with pulse energy delivered between 0.8-2.0 mJ with either Q-switched or mode locked systems. The Nd: YAG laser emits radiation at a wavelength of 1064 nm (1). It acts by photo disruption using acoustic shock waves generated by ionization and plasma formation to cut the opacity without the need for pigment absorption and producing carbon dioxide and water. The physics of these reactions is discussed in detail by Puliafito and Steinert[5].

Nd:YAG laser is a very effective and successful technique but the procedure itself may lead to variety of untoward complications like damage and pitting the IOL or its dislocation, raise in intraocular pressure, precipitation of cystoid macular oedema or retinal detachment, or exacerbation of localized endophthalmitis. Fortunately, in experienced hands, these are very rare[6].

One of the common undesired outcomes of Nd: YAG laser capsulotomy is transient elevation of intraocular pressure (IOP) that peaks after 2-3 hours of the procedure[4]. This complication is a result of obstruction of trabecular meshwork by debris scattered after laser treatment[1]. Many topical ocular hypotensive agents are available to counter this side effect of which the routinely used medications include topical beta blockers (0.25-0.50% timolol maleate, 0.25-0.50% levobunalol, 0.25% betoxalol), topical alpha 2–agonists (1% apraclonidine HCL, 0.2% brimonidine tartrate), topical carbonic anhydrase inhibitors (2% dorzolamide, 1% brinzolamide) and topical prostaglandin analogs (0.005% latanoprost, 0.004% travoprost, 0.03% bimatoprost)[7].

In the absence of any prophylactic therapy, this intraocular pressure elevation is clinically significant, because it may lead to visual field loss, particularly in eyes with preexisting glaucomatous damage[8]. In one study, prophylactic use of timolol maleate was found to control IOP after Nd:YAG laser capsulotomy in 93.4% of cases, where as brimonidine was found to control IOP in 68.3% of cases after the laser procedure. It is appropriate to treat this pressure elevation on prophylactic basis by topical anti glaucoma medications[9].

The purpose of this study was to compare the effectiveness of 0.5% Timolol maleate and 0.2% Brimonidine tartrate in controlling the raise in intraocular pressure after Nd: YAG laser capsulotomy if these drugs are instilled prophylactically one hour before the laser procedure.

MATERIAL AND METHODS

These study was a randomized controlled trial conducted at Department of Ophthalmology, Jinnah Hospital Lahore, Pakistan for a duration of 12 months from 15th May 2009 to 14th May 2010.

Ninety consecutive patients meeting the below mentioned inclusion and exclusion criteria were referred from outpatient department (OPD) for Nd: YAG laser capsulotomy. Inclusion criteria included: age 45 years or more, both genders, pseudophakia as a result of age related cataract extraction at Jinnah Hospital, Lahore and posterior capsular opacity with visual acuity less than 6/18. Exclusion criteria included: complicated cataract extraction, history of trauma to eye resulting in traumatic cataract, history of, or ongoing uveitis and glaucoma, pseudoexfoliation and pigment dispersion syndrome, retinal detachment and history of, or current prolonged topical or systemic corticosteroid use.

An informed consent was taken where the procedure of Nd: YAG laser capsulotomy and the intervention using two different topical antiglaucoma medications and their side effects were explained. Hospital ethical committee's approval for this research proposal was taken. Posterior capsular opacification was identified using slitlamp biomicroscope. Patients were included using detailed medical and ocular

history, slitlamp biomicroscopy using 90 D lens and gonioscopy.

These patients were equally divided into two groups A and B, using random numbers table. Group A was control group which received 0.5% Timolol maleate. Group B was experimental group which received 0.2% Brimonidine tartrate. IOP of patients in both, control and experimental group was measured before instilling these topical medications. These medications were administered topically 1 hour before the laser procedure. Intraocular pressure was recorded 1 and 3 hours after Nd: YAG laser capsulotomy.

Data analysis: Data were analyzed by computer software SPSS version 13.0. Descriptive statistics were used to describe the data. The two groups were compared for effectiveness using Chi-Square test. *p* value (one tailed) equal or less than 0.05 was considered significant.

RESULTS

A total of 90 patients were included in this study. While analyzing the data regarding age of patients, the mean age in group A was 60.93 ± 11.65 years and that in group B was 60.5 ± 8.11 years

Twenty six (57.8%) patients in group A and 30 (66.7%) patients in group B were males. Both the groups were comparable with respect to age and gender ($p<0.666$).

The results showed that laser was applied to the right eye in 20 (44.4%) patients in group A and 25 (55.6%) patients in group B. In patients belonging to group A, 42 patients (93.3%) had effective control of IOP (raise of less than or equal to 5 mmHg from the baseline) after 3 hours of Nd:YAG laser capsulotomy whereas 28 patients (62.2%) had effective control of IOP after the same period of time in group-B (Table). There was statistically significant difference ($p<0.001$) in the control of IOP raise after laser capsulotomy between patients in group A and group B.

DISCUSSION

This study was designed to compare the effectiveness of the two routinely used anti glaucoma medications; 0.5% Timolol maleate and 0.2% Brimonidine tartrate in effectively controlling the raise in IOP after Nd:YAG laser capsulotomy when given on prophylactic basis.

In this study, 90 patients were divided into two equal groups. 45 patients were in group A (receiving prophylactic 0.5% Timolol maleate) and 45 patients were in group B (receiving prophylactic 0.2% brimonidine tartrate).

Table: Distribution of cases among groups A and B by controlling raise in intra ocular pressure (IOP).

Controlling raise of IOP	Group-A (Timolol maleate) (n=45)	Group-B (Brimonidine tartrate) (n=45)
	n (%)	n (%)
Yes	42 (93.3)	28 (62.2)
No	03 (06.7)	17 (37.8)

$p< 0.001$

Patients' characteristics included age, gender, visual acuity and cataract extraction with IOL implantation with either phacoemulsification or extracapsular technique following only age related cataracts. Patients with complicated or traumatic cataracts, uveitis, glaucoma, history of steroid use and other ocular conditions like pseudoexfoliation and retinal detachment were not included in this study.

The distribution of patients according to different age groups and gender is discussed. There was no statistically significant difference between the two groups.

IOP was successfully controlled in 42 (93.3%) patients in group A who prophylactically received 0.5% timolol maleate 1 hour before laser capsulotomy. 3 patients (6.7%) showed increase

of IOP more than 5 mmHg despite receiving prophylactic topical medicine.

Whereas in group B who received 0.2% brimonidine tartrate on prophylactic basis, 28 (62.2%) patients showed adequate control of IOP after Nd:YAG laser capsulotomy and 17 (37.7%) patients showed to have raised IOP after 3 hours of laser capsulotomy. Difference was statistically significant between two groups (p<0.001).

The results of this study are comparable to a study conducted by Cai et al (2008) who concluded that prophylactic use of 0.5% timolol maleate effectively controlled raise in IOP after Nd:YAG laser capsulotomy in 86 out of 91 patients (94.5% compared to 93.3% of our study) versus placebo group in which 85 out of 99 patients (85.8%) showed controlled IOP after laser capsulotomy. The parameters (cut off limits of IOP, drug schedule, dosage and strength, method of measurement of IOP and timing of IOP measurement) of both studies are comparable[10].

In a similar study conducted by Rakofsky et al (1997) showed the effectiveness to 0.5% timolol maleate in 51 out of 54 patients (94.4%) against the placebo group in which 18 out of 28 patients (64.3%) showed an IOP rise of less than 5 mmHg after laser capsulotomy. The settings of both studies were comparable[11].

Efficacy of timolol maleate in the discussed setting was further emphasized by Minello et al (2008) where he conducted comparison between timolol maleate, apraclonidine, brimonidine, latanoprost and dorzolamide. Prophylactic timolol maleate effectively controlled IOP spike after Nd:YAG laser capsulotomy[12].

The use of prophylactic brimonidine in similar settings was studied by Chen (2005). He concluded that brimonidine was effective in controlling IOP spike post laser capsulotomy in 28 out of 41 patients (68.3% compared to 62.2% in our study). He compared his results against the use of apraclonidine for the same purpose. Apraclonidine controlled IOP effectively in 71.8% of patients[9].

Use of 0.2% brimonidine tartrate was advocated by Seong et al (2000) when he found that brimonidine controlled the IOP spike laser capsulotomy in 38 out of 41 patients (92.7%). The debate between Seong's study and our study was related to the fact that his team instilled 0.2% brimonidine tartrate one hour before as well as immediately after the laser procedure where as in our study, this drug was administered only one hour before laser capsulotomy. The timing and method of IOP measurement was similar between the two studies[13].

In our study, we compared 0.5% timolol maleate with 0.2% brimonidine tartrate in controlling the spike of IOP after Nd:YAG laser capsulotomy when given on prophylactic basis. It was found that at one hour after the laser procedure, both the medications effectively controlled the IOP with no statistically significant difference between the two groups. When IOP was measured 3 hour post laser capsulotomy, it was found that group A (receiving 0.5% timolol maleate) had better control of IOP than group B (receiving 0.2% brimonidine tartrate). There was statistically significant difference (p value < 0.05) between the two groups and 0.5% timolol maleate was found to be more effective in controlling raise in IOP after Nd:YAG laser capsulotomy when given prophylactically.

There were a few other side effects noticed after the laser procedure apart from raise in IOP. Two patients (4.4%) in group A and one patient (2.2%) in group B had IOL pitting after laser capsulotomy which was responsible for causing visually significant glare and light scattering.

One patient in group A had prolonged inflammation after uneventful Nd:YAG laser capsulotomy which was successfully controlled after intensive topical steroid therapy for 3 months.

One patient in group B had uncontrolled rise of IOP after laser capsulotomy which had to be controlled with topical (latanoprost) and systemic (acetazolamide) anti glaucoma medications. This particular patient used topical latanoprost for 2

months which was later augmented with topical timolol to effectively control his IOP.

There was no reported case of intraoperative hyphema, post operative cystoid macular edema or retinal detachment.

CONCLUSION

Intraocular pressure (IOP) raise is a significant complication after Nd:YAG laser posterior capsulotomy, routinely done for visually significant posterior capsular opacity (PCO). Prophylactic use of anti glaucoma medications in a single dose provides efficient control of IOP spike after this laser procedure. In this regard, this study showed that the use of 0.5% timolol maleate was very safe and more effective than 0.2% brimonidine tartrate when given 1 hour before laser capsulotomy.

Further studies need to be conducted in our local settings to compare 0.5% timolol maleate with other anti glaucoma medications in controlling IOP spike after Nd:YAG laser capsulotomy and other common anterior segment laser procedures like Nd:YAG laser iridotomy and Argon laser trabeculoplasty.

In the mean while, timolol proves to be a safe option in this regard when it comes to the merits of effectiveness, cost affectivity and ready availability.

Ophthalmic surgeons should consider the regular use of 0.5% timolol maleate on prophylactic basis when performing Nd:YAG laser capsulotomy especially in those high risk cases where sudden spike of IOP can cause significant damage to vision.

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