ORIGINAL ARTICLE

Role of Prophylactic Use of Timolol Maleate (0.5%) in Preventing Rise of Intraocular Pressure (Iop) Post Neodymium: Yttrium Aluminum Garnet (Nd: Yag) Capsulotomy

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ABSTRACT

Purpose: To evaluate the role of prophylactic use of Timolol maleate (0.5%) eye drop in preventing rise of intraocular pressure (IOP) post Nd: YAG capsulotomy. **Materials and Methods:** A randomized, single-blinded, parallel group study conducted in 220 eyes, over a period of 18 months. Precapsulotomy baseline IOP, Slitlamp examination and grading of PCO was done. After instilling the test medication Nd: YAG laser capsulotomy performed. Post capsulotomy patients were assessed immediately, after 1 hour and 3 hours for IOP. **Result:** Precapsulotomy, mean IOP in Group I (use of placebo) was 15.30 ± 2.83 mm Hg as compared to 16.15 ± 2.48 mmHg in Group II (use of Timolol eyedrop), Group II mean IOP was significantly higher (P = 0.019). However, immediately after the procedure mean IOP in Group I was 14.55 ± 2.87 mmHg as compared to 13.16 ± 3.72 mmHg in Group II thus showing mean IOP in Group II to be significantly lower (P = 0.002). One hour and 3 hours after the procedure too, mean IOP in Group II was significantly lower as compared to that in Group I (P < 0.001). With increasing grade of PCO reduction in post-procedure IOP was lower and reduction in IOP was maximum in patients requiring <30 milliJoules of total energy. **Conclusion:** A judicious control over energy use and post laser IOP monitoring can influence the trend of IOP rise in a positive manner. Whenever anticipated that >60 mJ of laser energy is required as in higher grades and younger age, prophylactically Timolol maleate 0.5% eye drop should be instilled before Nd: YAG capsulotomy while all other patients in which Timolol is not used, should be kept under observation after laser capsulotomy.

Keywords: Capsulotomy, grade of posterior capsular opacification, intra ocular pressure, Nd: YAG laser, Timolol maleate

INTRODUCTION

Cataract surgery is currently the most common ophthalmic surgical procedure in the world. This procedure involves the extracapsular extraction of the opaque lens fibers and implantation of an intraocular lens (IOL) which restores good vision.[1] However, posterior capsular opacification (PCO), which is also termed as secondary cataract, is a common long-term complication of modern cataract surgery.[2]

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The PCO may lead to either partial or complete obstruction of the visual axis thus causing the problems of decreased vision, increased glare and interference in the day to day activities of the patient. So to restore back proper vision lost due to PCO, removal of PCO is the only remedy.

Of the various interventions available for treatment of PCO, Nd: YAG laser capsulotomy is an established and safe procedure[3] for which photodisruption property of Nd: YAG laser (1064 nm) using Q-switched mode is utilized

Nd: YAG laser clears the visual axis by creating a central opening in the opacified posterior capsule, but this procedure is not devoid of complications.

Transient rise of intraocular pressure (IOP) is the most common complication following laser capsulotomy,

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which peaks in the first 3 hrs of laser application.[4] The increase in IOP noted in previous literature is 5-10 mmHg which may lead to serious eye damage, especially in patients with advanced glaucoma who have higher frequency of this complication.[5]

For preventing the transient rise of IOP there are varied opinions about the use of Timolol maleate eye drops, which is a non-selective ß$_1$ and ß$_2$ adrenergic receptor antagonist and has an IOP lowering action by reducing aqueous humor production.[6]

Because of the lack of common consensus about the efficacy and need of pre-capsulotomy use of Timolol maleate in controlling different ranges of raised IOP spikes, this study was undertaken with the aim to evaluate the role and efficacy of prophylactic use of Timolol maleate (0.5%) eyedrop in preventing rise of IOP post Nd: YAG capsulotomy.

MATERIALS AND METHODS

This was a randomized parallel group study conducted over a period of 18 months from November 2010 to July 2012 at Era's Lucknow medical college and hospital, Lucknow. The study was conducted in 220 eyes which were divided into two Groups (Gp.) with 110 eyes in each group after randomization. Gp. I included eyes in which placebo (artificial tear substitute) was instilled before the laser treatment whereas Gp. II included eyes in which Timolol maleate (0.5%) was instilled before the laser treatment. Patients excluded were those already using antiglaucoma medications, having absolute or relative contraindications to YAG capsulotomy (e.g. corneal edema, corneal ulcer, corneal scarring, presence of glass IOL, anterior uveitis, macular edema) and in those where use of Timolol maleate eye drop was contraindicated (e.g. Asthmatic and cardiac patients). Precapsulotomy assessment of patients was done for vision, baseline IOP (by Applanation tonometery), slit-lamp examination for any contraindication for the procedure as well as to grade the PCO (using Madurai Intraocular lens study IV[7,20]) 110 eyes in group I were given placebo before capsulotomy while in the rest of 110 eyes comprising group II, 0.5% Timolol maleate eyedrop was instilled pre-casulotomy. Following instillation of eyedrops (Placebo/Timolol) patients were instructed to press over the puncta for 5 minutes and keep the eyes closed. Topical anesthetic 4% Paracaine was instilled and then a wide field spectral Nd.YAG laser contact lens (Abraham's contact lens) was placed over the cornea with viscoelastic substance as coupling agent. The slit-lamp beam was narrowed and obliquely angled (to help reduce miosis). Laser shots with low energy (1 milliJoule) were given initially and gradually increased as per requirement. Aim was to create a 2-3 mm diameter opening in the center of the opacified capsule with a minimum number of laser shots. Post capsulotomy, patients were assessed immediately, after 1 hour and 3 hours (hrs) respectively for IOP.

Statistical analysis

The data was analyzed using Statistical Package for Social Sciences. Independent samples "t"-test and analysis of variance has been used to compare the data. Chi-square test has been used to compare the proportions. The confidence level of the study was kept at 95%, hence a "*P*" value less than 0.05 is indicated as a statistically significant intergroup difference.

RESULTS

Age of patients ranged from 13 to 100 years with a mean age 57.86 ± 14.88 years in Group I and 60.70 ± 11.24 years in Group II. Majority of subjects in both the groups were females and had PCO grades I and II. Mean post-surgery time lag for PCO formation was 3.16 ± 2.14 years in Group I and 3.51 ± 3.31 years in Group II. The two groups were matched statistically for age, gender, PCO grade and mean post-surgery time lag for PCO formation [Table 1].

Before the procedure, mean IOP in Group I was 15.30 ± 2.83 mmHg as compared to 16.15 ± 2.48 mmHg in Group II, thus showing mean IOP in Group II to be significantly higher ($P = 0.019$). However, immediately after the procedure the mean IOP in Group I was 14.55 ± 2.87 mmHg as compared to 13.16 ± 3.72 mmHg in Group II thus showing mean IOP in Group II to be significantly lower ($P = 0.002$). One hour and 3 hrs after the procedure too, mean IOP in Group II was significantly lower as compared to that in Group I ($P < 0.001$) [Table 2].

On evaluating the impact of different demographic, clinical and procedural variables on IOP change, impact of intervention (0.5% Timolol maleate), time

Table 1: Baseline characteristics of patients receiving laser capsulotomy

	n = 110		*P* value
	Placebo group I	Timolol group II	
Mean Age±SD (range) in years	57.86±14.88 (18-100)	60.70±11.24 (13-86)	0.112
Male:Female	39:71	50:60	0.131
PCO grade			
I and II	81 (73.6%)	69 (62.7%)	0.082
III and IV	29 (26.4%)	41 (37.3%)	
Mean post surgery time lag for PCO formation±SD	3.16±2.14	3.51±3.31	0.354

PCO: Posterior capsular opacification, SD: Standard deviation, $P<0.05$ (significant)

lag since cataract surgery, grade of PCO and amount of total energy required were found to be significantly associated with the change in IOP.

Immediately after the procedure, mean reduction in IOP was 0.75 ± 1.92 mmHg in Group I as compared to 2.98 ± 2.91 in Group II ($P < 0.001$). At 1 hr after procedure, mean reduction in IOP was 0.11 ± 2.15 mmHg in Group I as compared to 2.69 ± 3.11 mmHg in Group II ($P < 0.001$). At 3 hrs after procedure interval, mean reduction in IOP was 1.90 ± 2.73 mmHg in Group II as compared to a mean increase in IOP to the tune of 0.31 ± 1.97 mmHg in Group I ($P < 0.001$) [Table 3].

With increasing grade of PCO reduction in post-procedure IOP was lower and reduction in IOP was maximum in patients requiring <30 mJ of total energy [Table 4].

DISCUSSION

Nd: YAG laser posterior capsulotomy is the treatment of choice for the PCO. This procedure has gained popularity as it is non-invasive, relatively safer, less time consuming and free from infections as compared to needle capsulotomy but has been associated with complications like corneal burns, intra ocular lens pitting and raised IOP varying from 1.6%[8] to 42.85%.[9] In the present study, the focus was kept on IOP changes following Nd: YAG laser capsulotomy with and without pre-capsulotomy use of Timolol maleate 0.5% eye drops. It has been shown in literature that Timolol maleate 0.5% is a useful intervention to inhibit IOP rise following Nd: YAG laser posterior capsulotomy.[8,10,11] In our study no rise in mean IOP was observed in either Gp. I or Gp. II, instead a nominal reduction in mean IOP was observed in both groups I and II (0.75 ± 1.92 and 2.98 ± 2.91 mmHg, respectively). This difference was statistically significant. At 3 hrs post-procedure interval, there was a rise in mean IOP in the placebo group (0.31 ± 1.97 mm Hg) whereas mean IOP in the Timolol maleate group was still lower by 1.90 ± 2.73 mm Hg as compared to precapsulotomy IOP which again was significant statistically. Contrary to our study, Cai *et al.* (2008)[12] observed a mean rise of 0.9 mmHg in the treatment group as compared to 2.1 mmHg in the placebo group and in another previous study by Rakofsky *et al.* (1997),[10] 7% of the Timolol group and 36% of the placebo group an IOP

Table 2: Comparison of change in IOP immediately after laser capsulotomy, at 1 hr, and at 3 hrs among two study groups (mmHg)

	n=110		*P* value
	Placebo group I	Timolol group II	
Before procedure	15.30±2.83	16.15±2.48	0.019
Immediately after procedure	14.55±2.87	13.16±3.72	0.002
1 hr after procedure	15.41±2.63	13.45±3.92	<0.001
3 hrs after procedure	15.61±2.62	14.25±3.59	<0.001

IOP: Intraocular pressure, hr: Hour, $P<0.05$ (significant)

Table 3: Postcapsulotomy change in mean IOP as compared to baseline IOP in the two study groups, at different time intervals (values are mean±SD mmHg)

Time interval	*n*=110		*P* value
	Placebo group I	Timolol group II	
Immediately after procedure	−0.75±1.92	−2.98±2.91	<0.001
1 hr after procedure	−0.11±2.15	−2.69±3.11	<0.001
3 hrs after procedure	0.31±1.97	−1.90±2.73	<0.001

IOP: Intraocular pressure, Hr: Hour, SD: standard deviation, $P<0.05$ (significant)

Table 4: Impact of different demographic and clinical variables on immediate change in intraocular pressure after Nd: YAG laser capsulotomy

Variable	No. of cases	Change in IOP		*P* value
		Mean	SD	
Group				
Control	110	−0.75	1.92	<0.001
Test	110	−2.98	2.91	
Age of patient				
<50	34	−0.91	2.08	0.079
50-70	163	−2.06	2.85	
>70	23	−1.91	2.15	
Sex				
Male	89	−1.51	2.82	0.105
Female	131	−2.11	2.59	
Duration (years)				
<1	3	0.00	0.00	0.017
1-5	180	−1.94	2.69	
6-10	31	−1.06	2.19	
>10	6	−4.50	3.99	
Grade				
I	73	−2.21	2.97	<0.001
II	77	−2.45	2.69	
III	34	−1.50	1.86	
IV	36	−0.25	2.16	
Total energy required (mJ)				
<30	86	−2.91	2.96	<0.001
30-60	59	−1.56	2.04	
60-90	50	−0.76	2.43	
>90	25	−1.20	2.50	
Preoperative BCVA (LogMAR)				
0	6	−1.17	2.79	0.284
0.1-0.3	60	−2.25	3.04	
0.4-0.6	54	−2.22	2.74	
0.7-0.9	40	−1.70	2.00	
1	60	−1.33	2.67	

IOP: Intraocular pressure, SD: Standard deviation, BCVA: Best corrected visual acuity, mJ: Millijoules, Nd: YAG laser: Neodymium doped yttrium aluminum garnet laser, LogMAR: logarithm of minimum angle of resolution, $P<0.05$ (significant)

rise of >5 mm Hg was observed. However, in our study, no such increase in IOP was observed in Group II (Timolol) while in Group I (placebo) also minimal rise of IOP was observed and that too only at 3 hour interval post laser capsulotomy. The reason for such nominal increase in IOP could be explained by the delivery of shorter energy packets per shot and lower total energy used in our study. In the present study, 86 (39.1%) eyes received total energy <30 mJ whereas only 75 (34.1%) eyes received total energy >60 mJ. The impact of amount of energy used on IOP rise has been shown by Waseem and Khan *et al.* (2010)[13] and in our study also there was a significant association between the total amount of energy used and change in IOP [Table 4]. In Gp. II, irrespective of total amount of energy delivered, at no post Nd: YAG capsulotomy stage there occurred any rise of IOP. While in Gp. I, there occurred an elevation of IOP only in those cases in which total laser energy was >60 mJ and it was also statistically not significant. But when laser energy was <30 mJ, instead of rise, a fall in IOP was observed immediately after YAG capsulotomy ($P < 0.001$). This was in concurrence with the study by Khanzada *et al.* (2008)[14] where low energy levels used for laser capsulotomy lead to, IOP rise in only 3.1% cases in their study. It was explained by use of less total energy delivered leading to minimal production of prostaglandins, thereby not leading to post laser rise in IOP. Apart from the laser intervention, we found that duration between cataract surgery and PCO formation as well as grade of PCO has a significant association with the amount of IOP rise. Similar associations have also been shown by Shaikh *et al.* (2010).[15]

Thus, the findings of the present study help us to conclude that judicious control over laser energy delivery can influence the trend of IOP rise. Whenever anticipated that >60 mJ of energy is required as in higher grades of PCO and younger age, prophylactically Timolol maleate 0.5% eye drop should be instilled before Nd: YAG capsulotomy while all the other patients should just be kept under observation.

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SUMMARY STATEMENT

A randomized, single-blinded, parallel group study conducted on 220 eyes, to evaluate the role of prophylactic use of Timolol maleate (0.5%) eyedrop in preventing rise of IOP post Nd: YAG capsulotomy. Precapsulotomy baseline IOP, Slit lamp examination and grading of PCO was done. After instilling the test medication Nd: YAG laser capsulotomy was performed. We found that with precapsulotomy use of Timolol, irrespective of total amount of energy delivered, at no post Nd: YAG capsulotomy stage there occurred any rise of IOP. While in other cases with precapsulotomy use of placebo, with energy amount >60 mJ there occurred an elevation of IOP (statistically not significant). Thus, prophylactically precapsulotomy Timolol maleate 0.5% eye drop should be instilled in higher grades, younger age and if >60 mJ total energy is required.

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