Efficacy of Timolol Maleate (0.5%) in Preventing Rise of Intraocular Pressure (IOP) Post Neodymium: Yttrium Aluminum Garnet (Nd: YAG) Capsulotomy

Nazia Iqbal, Waqar Muzaffar, Muhammad Haroon Sarfaraz*, Saim Khan**, Ubaid Ullah Yasin***, Farooq Ul Abidin

Armed Forces Institute of Ophthalmology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *POF Hospital, Wah Pakistan,
**Prince Sultan Military Medical City, Riyadh Kingdom of Saudi Arabia, ***Pak Naval Ship Shifa Hospital, Karachi Pakistan

ABSTRACT

Objective: To determine the efficacy of 0.5% Timolol eye drops in preventing rise of intraocular pressure following Neodymium: Yttrium-Aluminum-Garnet laser posterior capsulotomy.

Study Design: Quasi-experimental study.

Place and Duration of Study: Outpatient Department of Ophthalmology, Combined Military Hospital Multan Pakistan, from May to Nov 2019.

Methodology: Patients presenting with posterior capsule opacification, undergoing elective Neodymium: Yttrium Aluminum Garnet (Nd: Yag) Capsulotomy were enrolled in the study. Patients were alternatively assigned to two groups; group-1 was administered 0.5% Timolol Maleate eye drops, while group-2 was administered placebo natural team eye drops. Intraocular pressure for all the patients was measured at three-time points a). First measurement was baseline intraocular pressure at presentation/before the treatment. Second measurement was 1-hour post laser capsulotomy and third measurement was 3 hours post laser capsulotomy.

Results: At 1-hour follow up, the mean intraocular pressure was significantly raised in the patients belonging to control group as compared to treatment group (21.45 ± 8.33 mm Hg vs 15.33 ± 3.37 mm Hg, p<0.001). At 3-hours follow-up the mean intraocular pressure decreased a bit for control group but still was significantly higher than the treatment group (17.40 ± 3.00 mm Hg vs 15.60 ± 2.30 mm Hg, p<0.001).

Conclusion: Prophylactic use of Timolol successfully reduces the post-procedural acute rise in intraocular pressure due to Neodymium: Yttrium Aluminum Garnet laser posterior capsulotomy.

Keywords: Intraocular pressure, Neodymium, Posterior capsule opacification, Secondary cataract, Timolol maleate, Yttrium-aluminum-garnet (nd: yag) laser posterior capsulotomy.


INTRODUCTION

One of the leading causes of loss of vision is glaucoma and/or cataract worldwide. Cataract surgery is the most common surgical procedure in Ophthalmology.1 Posterior capsule opacification (PCO), also termed as secondary cataract is considered to be a normal variant of cataract surgery. It constitutes a global incidence of 7-31% in the 2-years after surgery.2 The development of posterior capsule opacification had been demonstrated to be faster in eyes with hydrophilic compared to hydrophobic acrylic intraocular lenses, where the design of optic, haptics, the optic haptic junction and the posterior edge of the IOL optic play an important role.3

Posterior capsule opacification is formed due to growth and trans-differentiation of equatorial epithelial cells along the intact posterior capsule, forming monolayers. In 10% of the cases, the remaining outer cells of the previous lens also proliferate.4 In young patients, posterior capsule opacification develops earlier and rapidly due to the effect of age-related fibroblast growth factor on the lens fibers. The posterior capsule opacification decreases in Best Corrected Visual Acuity (BCVA), glare and mono-ocular diplopia.5 Nd: YAG laser capsulotomy is an established technique which uses its photo-disruption property to create a central opening in PCO with energy of few millijoules but a number of complications exist. Improvement in visual acuity after the procedure is well documented.6 Post-procedural rise in intraocular pressure is one of the most troublesome complication reported for Neodymium: Yttrium Aluminum Garnet (Nd: YAG) laser capsulotomy. In 67% of the patients, a rise in intraocular pressure of at least 10 mmHg or more was reported to be associated with this surgical procedure, which peaks in first 3 hours.7 The sudden rise in intraocular pressure is a result of debris clogging the trabecular...
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meshwork or trabeculum, inflammation of the iris root or ciliary body and pupillary block which depends on the size of capsulotomy and other humoral factors. This complication poses a serious threat to the vision, which may even drop to the perception of light only.8

Literature reports that a number of drugs can be used to treat and prevent rise in intraocular pressure post Nd:YAG laser capsulotomy.9 Timolol Maleate, a non-selective β1 and β2 adrenergic receptor antagonist, lowers the intraocular pressure by reducing the production of aqueous humor. It is reported to be helpful in avoiding post-procedural rise in intraocular pressure among posterior capsule opacification patients.10

In this study, we aimed to determine the utilization of Timolol Maleate in preventing the intraocular pressure related complication in our local settings where there is no established practice to administer prophylactic medications following elective Neodymium: Yttrium Aluminum Garnet (Nd:YAG) laser capsulotomy for treating posterior capsule opacification.

METHODOLOGY

This quasi-experimental study was conducted at the Outpatient Department of Ophthalmology, Combined Military Hospital, Multan, from May 2019 to Nov 2019. Ethical approval was taken from Hospital Ethical Committee and consent was taken from the participants prior to their enrolment in the study. Sample size of 208 was calculated by using WHO online calculator, with an effect size of 1.5,10 pooled standard deviation of 3.85,10 80% study power, 95% confidence level. The patients were recruited by using non-probability consecutive sampling technique.

Inclusion Criteria: Patients with age ≥20 years, presenting with posterior capsule opacification to the outpatient ophthalmology department, who underwent elective Neodymium: Yttrium Aluminum Garnet (Nd: Yag) capsulotomy were enrolled in the study.

Exclusion Criteria: Patients on any medication which can alter the intraocular pressure, patients of glaucoma or those having relative or absolute contraindications to YAG capsulotomy (e.g. macular edema, anterior uveitis, corneal edema, corneal ulcer, corneal edema, corneal scarring) were excluded from the study. Patients with history of any prior surgery for glaucoma, ocular trauma, uveitis, retinal detachment, vitreous hemorrhage and/or angle anomalies, and patients contraindicated for Timolol Maleate eye drop (e.g. patients with asthma or cardiac diseases) were also excluded from the study.

After explaining the study procedure and possible complications, written informed consent was taken. Patients were alternatively assigned to two groups; patients belonging to group 1 were administered 0.5% Timolol Maleate eye drops pre-capsulotomy, while patients of group 2 were administered placebo natural team eye drops. Patients and outcome accessor were blinded to the treatment allocation. The data was collected using a structured proforma. Information related to patients’ age, gender, involved eye, date of cataract surgery, comorbidities, visual acuity, pre and post intraocular pressure values and follow-up times were noted. Pre-capsulotomy assessment of patients was done including assessment of visual acuity, intraocular pressure by Applanation Tonometer, Slit lamp examination to look for any contraindications and presence of posterior capsule opacification. An hour prior to laser treatment, one drop of treatment/placebo eyedrops was administered and patients were instructed to press over the puncta for 5 minutes and keep the eyes closed, where group-1 was given 0.5% Timolol Maleate eye drops and group-2 was instilled placebo tears natural eye drops. Cornea was topically anaesthetized with 0.5% Proparacaine and dilated with Medicarpine. Capsulotomy YAG contact lens was used along with Qswitched Zeiss VISULAS YAG III (Nd: YAG) laser system to make a hole in the posterior capsule. Nd:YAG laser contact lens was placed over the anesthetized cornea with a viscoelastic substance used as a coupling agent. Laser shots with low energy (1 milli joules) were used and increased gradually, if required, with an aim to use minimum amount of total laser energy to create a 2-3mm opening in the posterior capsular opacification. Only one surgeon performed all the capsulotomies to avoid bias. Intraocular pressure for all the patients was measured by Goldman Applanation Tonometer as per following protocol: a) first measurement: baseline intraocular pressure at presentation/before the treatment; b) 2nd measurement: 1-hour post laser capsulotomy, c) 3rd measurement: 3-hours post laser capsulotomy.

The data was analyzed using Statistical Pack-age for Social Sciences (version 23). Descriptive statistics for qualitative variables were presented by using frequency and percentages, while for quantitative variables mean and standard deviation were used. Primary outcome variable, intraocular pressure was compared between treatment and control group by using independent sample t-test, while other categorical variables were compared via Chi-square test. The confidence level of the study was kept at 95%, hence p-value ≤0.05
indicated a statistically significant intergroup difference.

RESULTS

A total of 208 patients were considered for analysis in this study, divided into two groups of 104 patients each. There were 102 (49%) males and 106 (51%) females in the study group, with a mean age of 55.83 ± 13.1 years. Patients belonging to group-1 were administered Timolol Maleate prior to capsulotomy, whereas group-2 was administered artificial tear drops. There were 46 (44.2%) males and 58 (55.8%) females in group-1 with mean age of 54.08 ± 12.6 years, while in group-2 there were 56 (53.8%) and 48 (46.2%) males and females respectively, with mean age of 58.10 ± 13.2 years as shown in Table-I.

Table-I: Summary of baseline characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study Groups</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group-1 (n=104)</td>
<td>Group-2 (n=104)</td>
</tr>
<tr>
<td>Age in years (Mean ± SD)</td>
<td>54.08 ± 12.6</td>
<td>58.10 ± 13.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46 (44.2%)</td>
<td>56 (53.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>58 (55.8%)</td>
<td>48 (46.2%)</td>
</tr>
<tr>
<td>Time to Posterior Capsule Opacification, n(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>36 (34.6%)</td>
<td>44 (42.3%)</td>
</tr>
<tr>
<td>1-3 years</td>
<td>56 (53.8%)</td>
<td>56 (52.3%)</td>
</tr>
<tr>
<td>4-5 years</td>
<td>12 (11.5%)</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>Type of Posterior Capsule Opacification, n(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eschiling Pearl</td>
<td>31 (29.8%)</td>
<td>34 (32.7%)</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>58 (55.8%)</td>
<td>60 (57.7%)</td>
</tr>
<tr>
<td>Mixed Type</td>
<td>15 (14.4%)</td>
<td>10 (9.6%)</td>
</tr>
</tbody>
</table>

The baseline intraocular pressure, assessed preoperatively, was found to be statistically similar for both the groups i.e. 15.21 ± 3.10 mm Hg and 15.19 ± 3.08 mmHg for group-1 and group-2 respectively (p= 0.964). After performing Nd:YAG laser capsulotomy, the intraocular pressure was assessed for each patient in group-1 and 2, at one-hour and three-hours post operatively. Upon group comparisons, it was revealed that, at 1-hour follow up, the mean intraocular pressure was significantly raised in patients belonging to control group as compared to treatment group (21.45 ± 8.33 mm Hg vs 15.33 ± 3.37 mm Hg, p<0.001) as shown in Table-II. Similarly, at 3-hour follow up the mean intraocular pressure value decreased a bit for control group but still was significantly higher than the treatment group (17.40 ± 3 mm Hg vs 15.60 ± 2.30 mm Hg, p<0.001).

DISCUSSION

Neodymium: Yttrium Aluminum Garnet (Nd: Yag) laser posterior capsulotomy is a non-invasive, safe, cost-effective, less time consuming and less infection causing procedure but is associated with complications such as raised intraocular pressure, intraocular lens pitting, mild anterior uveitis and anterior hylloid membrane rupture. In the present study, the focus was kept on intraocular pressure changes following Nd: YAG laser capsulotomy with and without pre-capsulotomy use of 0.5% Timolol Maleate eye drops.

Table-II: Comparison of pre-operative and post-operative intraocular pressure between treatment and control group.

<table>
<thead>
<tr>
<th>Intraocular pressure (IOP)</th>
<th>Study Groups</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group-1 (n=104)</td>
<td>Group-2 (n=104)</td>
</tr>
<tr>
<td>Intraocular pressure at baseline, mm Hg (mean ± SD)</td>
<td>15.21 ± 3.10</td>
<td>15.19 ± 3.08</td>
</tr>
<tr>
<td>Intraocular pressure at 1-hour Post-op, mm Hg (mean ± SD)</td>
<td>15.33 ± 3.37</td>
<td>21.45 ± 8.33</td>
</tr>
<tr>
<td>Intraocular pressure at 3-hour Post-op, mm Hg (mean ± SD)</td>
<td>15.60 ± 2.30</td>
<td>17.40 ± 3.00</td>
</tr>
</tbody>
</table>

In this study, the baseline mean intraocular pressure in group-1 was 15.21 ± 3.10 mmHg as compared to 15.19 ± 3.08 mmHg in group-2, thus showing no significant difference in mean intraocular pressure values for two study groups pre-operatively. However, 1 hour after the procedure was performed, the mean intraocular pressure for the patients in group-1 was 15.33 ± 3.37 mmHg as compared to 21.45 ± 8.33 mmHg in group-2 thus showing mean intraocular pressure in group-2 to be significantly higher (p<0.001). Similarly, 3 hours after the procedure, the mean intraocular pressure in group-1 was 15.60 ± 2.30 mmHg and mean intraocular pressure in group-2 was 17.40 ± 3.00 mmHg thus showing mean intraocular pressure of group-1 to be significantly lower as compared to that in group-2 (p<0.001).

In a randomized controlled, single blinded, parallel group study conducted on 330 eyes by Garg et al,11 reported similar sort of results where post-operative mean intraocular pressure was significantly lower in patient group randomly assigned to Timolol treatment as compared to placebo i.e. 13.45 ± 3.92 vs. 15.41 ± 2.63 respectively (p<0.001) at one hour after procedure was performed. Similarly at three hours after the procedure was performed, the mean intraocular pressure remained significantly lower in Timolol treatment group as compared to placebo i.e. 14.25 ± 3.59 vs 15.61 ± 2.62 respectively (p<0.001).

In a quasi-experimental study conducted by Ahmed et al,12 70 patients equally divided into two...
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groups, were administered 0.5% Timolol Maleate eye drops or 0.2% Brimonidine Tartrate eye drops prophylactically before Nd:YAG capsulotomy. Results revealed that both drugs successfully prevented the post-operative rise in intraocular pressure assessed at one and three hours after the procedure. Timolol Maleate was found to be more effective in reducing the intraocular pressure as compared to the other drug 18.31 ± 2.15 vs 20.54 ± 2.43 mmHg respectively (p=0.002).

A randomized controlled trial conducted by Masoumi et al., on 200 patients with posterior capsule opacification, were assigned to either Timolol or Apraclonidine treatment group, reported that both the drugs were equally effective in maintaining the normal intraocular pressure after Nd:YAG capsulotomy procedure. No significant difference was reported between mean intraocular pressure for Timolol and Apraclonidine group i.e. 13.9 ± 4.6 vs 14.1 ± 3.3 mmHg respectively (p=0.12) at three hours post-procedure.

Similarly, in a study conducted by Celik et al., on 180 patients divided into two groups, were either administered combination of Timolol and Brinzolamide or Apraclonidine alone, reported that both treatment options were effective in reducing the incidence of intraocular pressure related complications of Nd: YAG capsulotomy, where Timolol combination treatment was more effective treatment option for patients with pre-existing glaucoma who were at higher risk of developing such complications. Another study conducted by Lakshmi et al., reported that no significant difference was observed in mean intraocular pressure of patients who were administered Timolol during the Nd:YAG procedure, and none of the patients required post-operative administration of drug except one, patient who had pre-existing glaucoma, required frequent administration of Timolol to stabilize the spiked intraocular pressure.

Other studies in which Timolol maleate was used post-operatively to blunt down the intraocular pressure spikes, rather than using it prophylactically also showed that Timolol maleate is very effective in normalizing the post-operative intraocular pressure spikes. In a study conducted by Reddy et al., reported post-operative use of Timolol Maleate to buffer the rise in intraocular patients and when assessed at 24-hours the values were almost back to normal in 43.26% patients with transient rise in intraocular pressure. Similarly, in another study conducted by Soni et al., it is reported that 37% of the patients had their intraocular pressures raised in first four hours after capsulotomy, which responded well to Timolol Maleate and the values came back to normal within 24 hours. In a study conducted by Nigam et al., it is reported that highest rise in intraocular pressure following Nd:YAG capsulotomy is noticed within three hours after the procedure, which in some cases can be very troublesome, so it is recommended to either administer intraocular pressure lowering drugs e.g. Timolol Maleate immediately after the procedure or pre-operatively to avoid such complications.

CONCLUSION

Prophylactic use of Timolol successfully reduces the post-procedural acute rise in intraocular pressure due to Neodymium: Yttrium Aluminum Garnet laser posterior capsulotomy.

Conflict of Interest: None.

Authors’ Contribution
NI: Conception, data collection and analysis, WM: Research supervision and approval, MHS: Statistical analysis and interpretation, SK: Data collection and manuscript drafting, UUY: Conception and research analysis, FU: Data collection and manuscript drafting.

REFERENCES


