Efficacy and Tolerability of Latanoprost 0.005% in Treatment of Primary Open Angle Glaucoma (POAG)

Muhammad Imran Janjua, Saira Bano, Ali Raza

Purpose: Glaucoma is considered as a type of optic neuropathy for which intraocular pressure (IOP) is accepted as an important causative factor. Previous research has emphasized the value of IOP reduction in treatment of glaucoma. There are many treatment modalities available including medical and surgical options. This study was undertaken to show the effectiveness and safety profile of latanoprost 0.005% in reducing the intraocular pressure to acceptable levels.

Materials and Methods: This study was carried out at Department of Ophthalmology, Holy Family Hospital, Rawalpindi, from July to December 2015. Fifty patients diagnosed with primary open-angle glaucoma (POAG) were included in the study. Following baseline measurements of IOP, topical latanoprost 0.005% was administered once daily in the evening for 12 weeks. Patients were followed up with visits at two, six and twelve weeks. Mean IOP reduction was taken as the primary parameter. The ocular side effects of the drug were also assessed by patient’s history and slit lamp examination.

Results: Fifty patients, 22 (44%) males and 28 (56%) females, were enrolled for the study. The age ranged from 28 to 70 years with a mean of 59.56 (± 9.24) years. The mean IOP at baseline was 22.48 mmHg (± 6.4). The IOP at 2 weeks was 17.72 mmHg (± 4.70), at 6 weeks 14.88 mmHg (± 4.19) and at 12 weeks 13.20 mmHg (± 3.03) showing a mean reduction of 9.28 mmHg (± 5.36) from baseline. There was marked difference (± 41.28%) between the baseline and final IOP readings (p < 0.001). 12 (24%) patients had ocular side effects of medication. The side effects reported were ocular irritation in 8 (16%), conjunctival hyperemia in 2 (4%) and watering of eyes in 2 (4%) patients. None of them required discontinuation of medication. 38 (76%) patients did not develop any side effects.

Conclusion: Latanoprost can be regarded as an effective ocular hypotensive drug, having good compliance profile and no serious side effects.

Key words: Latanoprost, Primary Open Angle Glaucoma (POAG).

Primary open-angle glaucoma (POAG) is a type of optic neuropathy which damages the optic nerve head, causing cupping of the optic disc and thinning of the neuroretinal rim. These changes result in characteristic peripheral visual field defects. High intraocular pressure (IOP) is regarded as an important risk factor for development and progression of POAG. Progression of ocular damage can be prevented by lowering the IOP. Different treatment modalities are available including both surgical and medical options. The most commonly used drugs for the treatment of POAG are beta-blockers, carbonic
Aqueous humor production and IOP levels follow a circadian rhythm, being high in morning and decreasing by night. Similarly the systemic blood pressure also decreases during sleep hence affecting the ocular perfusion pressure. This gives more importance to the nocturnal control of IOP in management of glaucoma. Previous research has demonstrated variability in the effectiveness of topical medications used for IOP control during different times of the day. This includes decreased effect of beta-blockers during sleep. Also, acetazolamide and apraclonidine decrease the rate of aqueous flow at night.

Prostaglandin analogs have been in clinical use in the management of glaucoma since 1995. Latanoprost reduces the IOP by increasing the aqueous drainage through the uveoscleral route. Topical prostaglandin analogs generally have no significant systemic side effects. The adverse effects associated with the use of topical latanoprost are blurred vision, burning, itching or redness of the eye, changes in eyelash color and length and pigmentary changes in the iris and periocular skin.

This study was undertaken to show the effectiveness and safety profile of latanoprost 0.005% in reducing the intraocular pressure to acceptable levels.

MATERIALS AND METHODS
This prospective non-randomized open-label study was carried out at the Department of Ophthalmology, Holy Family Hospital, Rawalpindi from July to December 2015. Fifty patients with primary open-angle glaucoma (POAG) were enrolled. Following baseline measurements of IOP, topical latanoprost 0.005% was administered once daily in the evening preferably at 8 pm. The total duration of treatment was three months (twelve weeks) with follow up visits at two, six and twelve weeks. A deviation of ±2 days for first follow up visit (i.e. at 2 weeks) and ±5 days for second and third visits at six and twelve weeks was allowed. Patients with adverse events at the end of study period were followed up for further 2 to 4 weeks. At each follow-up visit a complete ophthalmic examination including slit lamp examination, IOP measurement and dilated fundus examination was performed. The adverse effects were diagnosed on the basis of patient’s history and clinical examination. Severity was graded by the examiner as mild, moderate or severe. For patients treated for both eyes, only one randomly selected eye was included for analysis.

Patients were instructed to instill the medication in the evening, preferably at 8 pm (±1 hr). If the patients were already using some other topical medication for POAG they were instructed to continue it along with latanoprost. The total duration of treatment was three months (twelve weeks) with follow up visits at two, six and twelve weeks. A deviation of ±2 days for first follow up visit (i.e. at 2 weeks) and ±5 days for second and third visits at six and twelve weeks was allowed. Patients with adverse events at the end of study period were followed up for further 2 to 4 weeks. At each follow-up visit a complete ophthalmic examination including slit lamp examination, IOP measurement and dilated fundus examination was performed. The adverse effects were diagnosed on the basis of patient’s history and clinical examination. Severity was graded by the examiner as mild, moderate or severe. For patients treated for both eyes, only one randomly selected eye was included for analysis.

The baseline visit comprised of complete medical history including treatment history, complete slit lamp examination, Goldman applanation tonometry, gonioscopy and dilated fundus examination with special emphasis on the optic disc and peri-papillary area for typical glaucomatous changes. IOP was measured at 10 am (±1 hr) and the mean of three readings was noted. Status of the eyelashes, periocular skin and iris color was also noted. No anterior segment photographs were taken.

Patients having closed or barely open anterior chamber angle or those with a history of acute angle closure in the past were excluded from the study. Also, patients having ocular inflammation or infection, those who had previously used topical prostaglandin analogues, had surgical or laser treatment for glaucoma, those using contact lenses or having any condition preventing applanation tonometry, known hypersensitivity to any component of the study medication were excluded.

The data was analyzed by Statistical Package for Social Sciences (SPSS) version 20.0 and values were expressed in terms of frequencies, percentages and means. The mean IOP reduction was analyzed by comparing mean IOP at follow up visits to the mean IOP at baseline using Student’s t-test. A P-value of <0.05 was taken as significant. The occurrence of side effects was assessed by patient’s history and slit lamp examination.
effects was also analyzed and was expressed in terms of frequencies and percentages.

RESULTS
Fifty patients were enrolled for the study, 22 (44%) were male and 28 (56%) were female. The age ranged from 28 to 70 years with a mean of 59.56 (± 9.24) years. Left eye was selected for analysis in 31 (62%) and right eye in 19 (38%) patients. 40 (80%) patients were newly diagnosed and 10 (20%) were already using topical IOP reducing medications other than latanoprost (Table 1, Fig. 1). Table 2 shows the topical medications used by patients.

The mean baseline IOP was 22.48 mmHg (± 6.4). The IOP at first follow up visit i.e. 2 weeks was 17.72

### Table 1: Demographic Distribution of Patients (n=50).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22 (44)</td>
</tr>
<tr>
<td>Female</td>
<td>28 (56)</td>
</tr>
<tr>
<td>Eyes</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>31 (62)</td>
</tr>
<tr>
<td>Right</td>
<td>19 (38)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>New cases</td>
<td>40 (80)</td>
</tr>
<tr>
<td>Old cases</td>
<td>10 (20)</td>
</tr>
</tbody>
</table>

A total of 12 (24%) patients had ocular side effects of medication. 8 (16%) patients reported ocular irritation. Of these, 4 (8%) had mild symptoms and 4 (8%) had symptoms of moderate degree. None of them required discontinuation of medication. 2 (4%)
Table 3: IOP Values (n = 50).

<table>
<thead>
<tr>
<th></th>
<th>Mean IOP mmHg (± SD)</th>
<th>Mean IOP Reduction mmHg (± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>22.48 (± 6.4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>17.72 (± 4.70)</td>
<td>4.76 (± 3.26)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>6 weeks</td>
<td>14.88 (± 4.19)</td>
<td>7.60 (± 4.80)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>12 weeks</td>
<td>13.20 (± 3.03)</td>
<td>9.28 (± 5.36)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table 4: Adverse Effects and Their Severity (n = 50).

<table>
<thead>
<tr>
<th>Side Effects</th>
<th>Intensity of Side Effects</th>
<th>Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nil N (%)</td>
<td>Mild N (%)</td>
</tr>
<tr>
<td>Nil</td>
<td>38 (76)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Irritation</td>
<td>0 (0)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Conj. Hyperemia</td>
<td>0 (0)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Watering</td>
<td>0 (0)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Total</td>
<td>38 (76)</td>
<td>8 (16)</td>
</tr>
</tbody>
</table>

Fig. 3: Percent IOP Reduction.

patients developed conjunctival hyperemia and another 2 (4%) had watering of eyes after using the drops. Both conjunctival hyperemia and watering were of mild degree. None of the patients developed any serious adverse effects. 38 (76%) patients tolerated the medication well and did not develop any side effects (Table 4, Fig. 4 and 5).

DISCUSSION

As new treatment modalities are being introduced for glaucoma management, research on the IOP lowering efficacy and safety is important in clinical decision-making. Numerous topical medications can be used in glaucoma patients. The six classes of drugs (miotics, beta-blockers, alpha-agonists, adrenalin derivatives, carbonic anhydrase inhibitors and prostaglandin analogs) are commonly being used either as a single drug therapy or in different combinations offering multiple medication options.

Fig. 4: Adverse Effects According to Gender (n = 50).

This short term study was designed to evaluate the effect and safety profile of latanoprost 0.005% in
controlling the IOP. Latanoprost was given to patients with inadequate IOP control, and the drugs already being used by previously diagnosed patients of POAG were not washed out before adding latanoprost. The results showed a significant decrease in IOP at two, six and twelve weeks of therapy. The mean IOP reduction at 12 weeks was 9.28 mmHg. Previous literature also showed a similar IOP reduction pattern. This was achieved in patients who were newly diagnosed with POAG, and were given only latanoprost for treatment, as well as in patients previously diagnosed and already using other topical IOP lowering agents.\textsuperscript{16,17}

This study did not compare the IOP lowering effect of latanoprost with other topical drugs or IOP reducing modalities. Several previous studies showed that latanoprost had a similar, and in some cases better IOP lowering profile as compared to beta blockers and topical carbonic anhydrase inhibitors.\textsuperscript{2,6,18,19} Nagar et al. showed that latanoprost had a better effect in controlling IOP as compared to selective laser trabeculoplasty (SLT).\textsuperscript{20}

A major concern in glaucoma management is poor compliance with topical therapy. Most of the drugs usually require twice or thrice daily administrations. Hence, another advantage of using latanoprost is better compliance of treatment since it has to be administered once daily in the evening.

The safety profile of topical latanoprost is excellent. The reported side effects were only of mild to moderate degree and none of the patients needed to discontinue the treatment. Previous literature also demonstrated a similar side effect profile with no serious local or systemic adverse effects with the use of topical latanoprost.\textsuperscript{1,13,17} In patients with systemic diseases e.g. heart disease and asthma, bradycardia and bronchospasm have been reported by the use of topical beta blockers. Therefore, caution is necessary in treating such patients. Latanoprost has no effect on the circulatory and respiratory systems and can safely be used in cardiac or asthmatic patients.\textsuperscript{18} Eyelash thickening and lengthening, iris and periocular hyperpigmentation are other reported side effects of long term use of topical prostaglandin analogs.\textsuperscript{11,17} Since this was a short term study, so no such adverse effects were seen in any of the patients.

**CONCLUSION**

It can be concluded that topical latanoprost 0.005% is very effective in reducing the IOP in glaucomatous patients. It also demonstrates good pharmacological effects when used along with other drugs that have not been able to keep the IOP at desired level. It has excellent safety profile with no significant side effects and offers more convenience to the patients as a result of once daily administration.

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REFERENCES


