Introduction

Normal-tension glaucoma (NTG) is a clinical entity defined as a chronic progressive optic neuropathy resulting in characteristic optic nerve head changes, retinal nerve fiber layer defects, and visual field defects. In NTG, the intraocular pressure (IOP) values are lower than 22 mmHg, which differentiates it from primary open-angle glaucoma (POAG).1,2 Despite many controversies about the origin and pathogenesis of NTG, major treatment modalities for NTG are directed toward IOP reduction. Currently, latanoprost is being prescribed frequently for the management of NTG. Latanoprost is a prostaglandin(PG) analogue and reduces IOP by stimulating uveoscleral outflow.1 Although the exact cellular mechanism for this effect is not clarified, it is well known that these drugs are associated with a reduction of collagen fibers within the uveoscleral outflow pathway.

Considering the fact that the cornea is mainly composed of collagen fibers, many previous studies of prostaglandin analogs have been shown to decrease the central cornea thickness (CCT) values in patients with various type of glaucoma. As influence of CCT on IOP measured by Goldmann applanation tonometer4, it is important to determine CCT values serially during the follow up of glaucoma, especially NTG patients who medicated prostaglandin analogs.

Purpose

This study was performed to evaluate the effect of latanoprost on the CCT in patients with unilateral NTG during 24 months follow-up periods.

Methods

We retrospectively reviewed the records of all patients who were newly diagnosed unilateral NTG and medicated with latanoprost 0.005% monotherapy over 24 months. Unilateral NTG was defined as open angle detected by gonioscopy, an IOP lower than 21 mmHg, characteristic glaucomatous optic nerve head damage, such as notched and neurotinal rim thinning in only one eye, glaucomatous visual field (VF) loss in only one eye, no neurologic disorder that could affect the optic nerve. Patients with ocular disease other than glaucoma, contact lens users and patients that had undergone refractive surgery, intraocular surgery or laser photocoagulation treatment were excluded. Also patients with myopia or hypermetropia greater than 3D or astigmatism more than 1D that could potentially affect our measurements were excluded. An unaffected eye in unilateral NTG patients was evaluated for the control group.

The CCT was measured with an ultrasound pachymeter (AL-2000; Bio & Pachymeter) in upright position by the same physician. We obtained an average value from 5 consecutive measurements. CCT measurements before treatment and 3, 6, 9, 12 and 24 months after treatment were analyzed. To evaluate the variation in CCT values at different time intervals within the groups, a paired-sample t-test was used. An independent sample t-test was used to compare the baseline IOP, and baseline CCT values serially during the follow up of glaucoma, especially NTG patients who medicated prostaglandin analogs.

Results

Patients demographics are shown in Table 1. Thirty-eight patients with unilateral NTG were included. The mean age of the patients was 55.51 ± 11.13 years. There were no statistically significant differences between the latentoprost group (affected eye) and the control group (unaffected eyes) for baseline IOP and CCT.

Mean CCT in both groups from baseline to 24 months after treatment were shown in Table 2. During follow up, mean CCT of latanoprost group was decreased except at 9 month treatment, but only statistically significant after 24 months of treatment. (544.6 ± 38.4 vs. 540.3 ± 37.8 μm, p=0.013)

There was no statistically significant change in CCT in the control group. (547.5 ± 33.7 vs. 545.3 ± 32.1 μm, p=0.789)

Table 1. Study Population Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total patients</th>
<th>Sex (M/F)</th>
<th>Age (Mean±SD)</th>
<th>Affected eye (Right/Left)</th>
<th>Control group (Unaffected eye)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>38</td>
<td>18/20</td>
<td>55.51 ± 11.13</td>
<td>13/25</td>
<td>25/13</td>
</tr>
<tr>
<td>Baseline IOP (mmHg)</td>
<td>Mean±SD</td>
<td>19.54 ± 2.68</td>
<td>15.63 ± 2.18</td>
<td>p=0.563</td>
<td></td>
</tr>
<tr>
<td>Latanoprost group</td>
<td>Mean±SD</td>
<td>544.65 ± 38.41</td>
<td>545.73 ± 33.71</td>
<td>p=0.897</td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>Mean±SD</td>
<td>545.2 ± 32.4</td>
<td>548.9 ± 36.8</td>
<td>546.6 ± 33.8</td>
<td></td>
</tr>
<tr>
<td>CCT (μm)</td>
<td>Baseline</td>
<td>545.2 ± 32.4</td>
<td>548.9 ± 36.8</td>
<td>546.6 ± 33.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 months</td>
<td>548.3 ± 37.5</td>
<td>548.3 ± 37.5</td>
<td>548.3 ± 37.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>548.9 ± 36.8</td>
<td>548.9 ± 36.8</td>
<td>546.3 ± 33.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 months</td>
<td>545.3 ± 32.1</td>
<td>545.3 ± 32.1</td>
<td>545.3 ± 32.1</td>
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<tr>
<td></td>
<td>12 months</td>
<td>545.3 ± 32.1</td>
<td>545.3 ± 32.1</td>
<td>545.3 ± 32.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 months</td>
<td>545.3 ± 32.1</td>
<td>545.3 ± 32.1</td>
<td>545.3 ± 32.1</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Mean Central corneal thickness at baseline and follow up period

We found that after 6 month of treatment, seventeen patients who had dry eye symptoms were prescribed the artificial tears consistently after 6 months. This study could reconfirm that CCT in dry eyes increases rapidly and significantly compared to normal eyes after application of artificial tears.

The predominant IOP effect of PG analogues is caused by MMP-1 (matrix metalloproteinases-1) activation in the smooth muscle of the ciliary body.6 Berfonzi et al7 suggested that prolonged treatment with PG can induce collagen degradation in the stromal extracellular matrix owing to activation of MMPs and inhibition of tissue inhibitors of metalloproteinases (TIMPs). A long-lasting consequence could be the reduction of CCT.

As influence of CCT on IOP measured by Goldmann applanation tonometer and thinner cornea in NTG than other glaucoma, it is important to determine CCT values serially during the follow up, especially NTG patients who medicated prostaglandin analogs. Therefore, clinicians have to pay attention for proper IOP targeting.

Discussion

In this study, statistical significant reduction in CCT was observed in latanoprost group at 24 month after treatment. In latanoprost group, the mean CCT was decreased during follow up period except at 9 month after treatment in spite of no statistically significant. Through retrospective chart review, we found that after 6 month of treatment, seventeen patients who had dry eye symptoms were prescribed the artificial tears. That might be the reason why the mean CCT was not decreased at 9 month after treatment. Katadayi et al5 showed that CCT in dry eyes increases rapidly and significantly compared to normal eyes after application of artificial tears.

Conclusions

As influence of CCT on IOP measured by Goldmann applanation tonometer and thinner cornea in NTG than other glaucoma, it is important to determine CCT values serially during the follow up, especially NTG patients who medicated prostaglandin analogs. Therefore, clinicians have to pay attention for proper IOP targeting.

References


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