Original Article

Effect of Topical Latanoprost 0.005% Drops on Central Corneal Thickness in Patients with Primary Open Angle Glaucoma

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Purpose: To determine the effect of topical 0.005% Latanoprost on central corneal thickness in patients with Primary Open Angle Glaucoma.

Material and Methods: This study was conducted at Eye "A" unit, Khyber Teaching Hospital, Peshawar. Total sample size was 139 eyes. Baseline IOP measurement was taken with Goldman applanation tonometer. Central corneal thickness was measured by a single trained doctor using the Quantel® Pachymeter. All patients were prescribed Latanoprost 0.005% eye drops once daily in the evening. Follow up was at 2 weeks and 8 weeks.

Results: Mean age was 52 years with SD ±2.71. Sixty nine (55%) patients were male and 56 (45%) were female. Mean difference between baseline CCT and CCT after eight weeks was 4% as mean baseline CCT level was 538 µm with SD ± 1.87 and mean CCT level after 8 weeks was 534 µmwith SD ±2.12. Efficacy of effect of Latanoprost on central corneal thickness of patients with primary open angle glaucoma was analyzed as Latanoprost was effective in reducing CCT in 104 eyes (75%) of 94 patients and was not effective in 35 eyes (25%) of 31 patients.

Conclusion: Our study concludes that topical 0.005% Latanoprost eye drops reduces the central corneal thickness, so latanoprost therapy requires careful monitoring while treating patients with primary open angle glaucoma. However this reduction in CCT was not ≥ 25 µm from base line reading which is not significant enough and hence did not have an effect on IOP reading using Goldman applanation tonometer.

Key words: Latanoprost, central corneal thickness, Primary Open Angle Glaucoma.

Glaucoma has become an important cause of blindness worldwide especially in the aging age group. New statistics gathered by the WHO show that glaucoma is now the second leading cause of blindness globally.[1] It is the fourth commonest cause of Blindness in Pakistan.[2] Glaucoma affects about 60 million people globally and is the causative factor of 12% of global blindness.[3, 4] More than 3 million people are bilaterally blind from POAG worldwide, and more than 2 million people will develop POAG each year.[5]

Intra ocular Pressure (IOP) measurement is one of the key steps in diagnosis and monitoring and the gold standard is Goldman Applanation Tonometry (GAT). A linear correlation between Central Corneal Thickness (CCT) and IOP measured by Goldman Applanation tonometer has been described by several groups suggesting that Goldman Applanation Tonometry results in under estimation in thin corneas and overestimation in thick corneas.[6]

To prevent glaucoma progression and to preserve vision, mean intraocular pressure should be decreased

to a patient dependent target pressure.[7] The current treatment modalities for glaucoma include medical, laser (usually trabeculoplasty) and surgical (usually trabeculectomy).[8]

Regarding medical therapy Prostaglandin analogues are more cost-effective than beta-blockers for any stage of POAG.[9] Latanoprost is a prostaglandin F2α analogue. Latanoprost 0.005% decreases IOP by increasing outflow of aqueous humor through uveoscleral pathways.[8] Common side effects include conjunctival irritation and hyperemia, eyelash changes (increased length, thickness, pigmentation, and number of lashes), eyelid skin darkening, intraocular inflammation (iritis / uveitis), iris pigmentation changes, and macular edema, including cystoid macular edema.[8]

Evaluation of corneal thickness have been done in several populations. Comparison among different populations is difficult due to different measurement techniques and missing data. Aghaian et al. evaluated differences in central corneal thickness, and showed that the CCT of Japanese was significantly lower than that of Caucasians, Filipinos, Chinese, and Hispanics, and greater than that of African Americans., African Americans have thinner corneas compared to white subjects. [10]

In a study conducted on Pakistani population the mean (SD) CCT measurements were 531.08 +/- 33.37) and 531.29 +/- 33.33 micrometers in the right and left eyes respectively and were not significantly different from each other.[11]

Since no study has been done to look into the effects of topical latanoprost therapy on CCT in our population, this study will help to prove or disprove effect of topical latanoprost therapy on central corneal thickness. If found to cause reduction, it would be interesting to see whether this decrease in CCT significantly affects the IOP readings done by Goldman Applanation Tonometer. It would also prove beneficial in determining whether serial CCT measurement should be a part of monitoring effects of Latanoprost therapy.

Material and Methods

It was a descriptive Cross Sectional Study conducted at department of Ophthalmology, Eye "A" Unit Khyber Teaching Hospital Peshawar from April 2013 to October 2013. The total sample size was 139 eyes. Sample size was calculated by WHO software for sample size calculation using 77.10% proportion of decrease in CCT and 95% confidence interval and a 7% margin of error. Before starting study, approval was taken from hospital's ethical committee.

Patients were selected from outpatient department, department of Ophthalmology, Khyber Teaching Hospital, Peshawar. All newly diagnosed primary open angle glaucoma patients from either gender within 20-60 years age group were selected. Patients in whom Prostaglandin analogues are contraindicated e.g. patients with known allergy to prostaglandin analogues, patients with uveitis and other ocular inflammatory conditions, patients who require multiple drug therapy and patients with previous ocular surgery or corneal refractive surgery were excluded from the study.

Written informed consent was taken from the patient. Detailed history was taken followed by complete examination including assessment of best corrected visual acuity (BCVA), anterior segment examination with slit – lamp, baseline IOP measurement with Goldman applanation tonometer and fundus examination with 90 D lens. Humphrey Standard Perimetry was performed.

Central corneal thickness was measured in all patients by a single trained doctor using the Quantel® Pachymeter. The mean of 3 measurements was taken for analysis. All patients were prescribed Latanoprost 0.005% eye drops once daily in the evening. Patients were advised to come for follow up at 2 weeks and 8 weeks. Repeated Central corneal thickness readings were taken after 8 weeks by the same method as discussed above. CCT measurement was performed in the morning to avoid any possible alteration due to day – time fluctuations. Those patients who develop drug side effects and those who don't come for follow up were omitted from the study.

Latanoprost will be said to be efficacious in causing change in CCT if a difference in CCT was observed after 8 weeks of initiation of therapy compared to baseline value of CCT. This change in CCT would be considered significant if it was ≥25µ as correction factor need to be applied then.

SPSS version 20.0 was used for analysis of data. Quantitative variables include age and CCT (Base line and after 8 weeks); and qualitative variables include gender and involvement of eye. Mean ± standard deviation was calculated for quantitative variables; percentage and proportion was calculated for qualitative variables. Efficacy was stratified among age, gender and baseline CCT to see effect modifiers.

Table 1: Base Line CCT (n = 139 eyes).

Base line CCT	Frequency			Total
	Right eye	Left eye	Both eyes	
< 500 µm	5 (4%)	5 (4%)	3 (2%)	13 (10%)
500 - 525 µm	15 (11%)	15 (11%)	9 (6%)	39 (28%)
525 - 555 µm	22 (16%)	23 (17%)	13 (9%)	58 (42%)
555 - 570 µm	14 (10%)	12 (8%)	3 (2%)	29 (20%)
Total	56 (40%)	55 (40%)	28 (20%)	139 (100%)

Mean baseline CCT level was 538 µm with SD ± 1.87

Table 2: CCT at Eight Weeks (n = 139 eyes).

CCT at Eight Weeks	Frequency			Total
	Right eye	Left eye	Both eyes	
< 500 µm	6 (4%)	7 (5%)	4 (3%)	17 (12%)
500 -525 µm	19 (11%)	17 (11%)	6 (6%)	42 (30%)
525 -555 µm	20 (14%)	19 (14%)	16 (12%)	55 (40%)
555 -570 µm	10 (7%)	9 (7%)	6 (4%)	25 (18%)
Total	56 (40%)	55 (40%)	28 (20%)	139 (100%)

Mean CCT level after 8 weeks was 534 µm with SD ± 2.12

Table 3: Comparison of Base Line CCT and CCT at Eight Weeks.

	Baseline CCT	CCT at 8 Weeks
Mean	538	534
Standard deviation	1.87	2.12

T- test was applied in which P value was 0.0001

RESULTS

A total of 139 eyes of 125 patients were observed to determine the effect of topical 0.005% Latanoprost on central corneal thickness in patients with Primary Open Angle Glaucoma and the results were analyzes as: Age distribution among 125 patients (139 eyes), was analyzed as 2(2%) patients were in age range 20 – 30 years, 5(4%) patients were in age range 31 – 40 years, 30 (24%) patients were in age range 41 – 50 years and 88 (70%) patients were in age range 51 – 60 years. Mean age was 52 years with SD ± 2.71.

Gender distribution among 125 patients was analyzed as 69 (55%) patients were male while 56(45%) patients were female.

Involvement of eye among 125 patients was analyzed as 56 (45%) patients had right eye affected, 55 (44%) patients had left eye affected and 14 (11%) patients had both eyes (14 × 2 = 28 eyes) affected.

Base line CCT among 139 eyes was analyzed as 13 (10%) eyes had CCT level < 500 µm, 39 (28%) eyes had

Table 4: Efficacy and Stratification with Involvement of Eye (n = 139 eyes).

Efficacy	Involvement of eye			Total
	Right eye	Left eye	Both eyes	
Yes	42 (30%)	42 (30%)	20 (15%)	104 (75%)
No	14 (10%)	13 (9%)	8 (6%)	35 (25%)
Total	56 (40%)	55 (40%)	28 (20%)	139 (100%)

Chi square test was applied in which p value was 0.032

CCT level ranged from 500 – 525 µm, 58 (42%) eyes had CCT level ranged from 525 – 555 µm and 29 (20%) eyes had CCT level ranged from 555 – 570 µm. Mean CCT level was 538 µm with SD ± 1.87 (as shown in Table 1).

CCT at eight weeks among 139 eyes was analyzed as 17 (12%) eyes had CCT level < 500 µm, 42 (30%) eyes had CCT level ranged from 500 – 525 µm, 55 (40%) eyes had CCT level ranged from 525 – 555 µm and 25 (18%) eyes had CCT level ranged from 555 – 570 µm. Mean CCT level was 534 µm with SD ± 2.12 (as shown in Table 2).

Mean difference between baseline CCT and CCT after eight weeks was 4% as mean baseline CCT level was 538 µm with SD ±1.87 and mean CCT level after 8 weeks was 534 µm with SD ±2.12. P value has been calculated for pre-treatment and post-treatment CCT using T-test and is found to be less than 0.0001. By conventional criteria this difference is considered to be extremely statistically significant (Table 3).

Efficacy of Latanoprost in causing a reduction of central corneal thickness of patients with primary open angle glaucoma among 139 eyes was analyzed as Latanoprost was effective in reducing CCT of 104 (75%) eyes and in 35(25%) eyes, there was no change in CCT (as shown in Table 4).

Stratification of efficacy of Latanoprost in causing CCT reduction with involvement of eye was analyzed as in 104 effective cases of latanoprost therapy, 42 patients had right eye affected, 42 patients had left eye

Table 5: Efficacy and Stratification with Gender (n = 139 eyes).

Efficacy	Gender		Total
	Male	Female	
Yes	56(40%)	48(35%)	104(75%)
No	20(15%)	15(10%)	35(25%)
Total	76(55%)	63(45%)	**139(100%)**

Chi square test was applied in which p value was 0.047

Table 6: Efficacy and Stratification with Age Distribution (n = 125 patients).

Efficacy	Age distribution				Total
	20 – 30 years	31 – 40 years	41 – 50 years	51 – 60 years	
Yes	1 (1%)	5 (4%)	19 (15%)	69 (55%)	94 (75%)
No	1 (1%)	1 (1%)	13 (10%)	16 (13%)	31 (25%)
Total	2 (2%)	6 (5%)	32 (25%)	85 (68%)	125 (100%)

Chi square test was applied in which p value was 0.021

affected and 20 patients had both eyes affected (As shown in Table 4).

Stratification of efficacy of Latanoprost causing reduction of CCT with gender distribution was analyzed as in 104 effective cases of latanoprost, 56 eyes belonged to males, and 48 eyes belonged to females (As shown in Table 5).

Stratification of efficacy of Latanoprost causing reduction of CCT with age distribution was analyzed as in 94 effective cases of latanoprost (104 eyes), 1 patient was in age rage 20 – 30 years, 5 patients were in age rage 31 – 40 years, 19 patients were in age rage 41 – 50 years and 69 patients were in age rage 51 – 60 years (As shown in Table 6).

DISCUSSION

Open angle glaucoma is silent killer of vision. It is slowly progressive and remains asymptomatic until it is very advanced and severe and irreversible damage has usually occurred in one or both eyes. It is the second leading cause of blindness worldwide.[12]

There are a number of risk factors for glaucoma but currently IOP is the only modifiable risk factor that can be used to prevent progressive optic neuropathy. The Early – Manifest Glaucoma Treatment Study showed that IOP reduction by at least 25% reduced disease progression from 62 to 45% in the treated group compared to an untreated group.[13,14]

To prevent glaucoma progression and to preserve vision, mean intraocular pressure should be decreased to a patient dependent target pressure. The target pressure depends on a number of factors, including age of patient, baseline IOP at which the damage occurred, structural damage (status of optic disc and RNFL), functional damage (assessed on perimetry) and the presence of additional risk factors for glaucomatous damage.[15]

The aim of glaucoma management is to preserve the visual functions and quality of life of the individual. Our objective should be not just to treat the intraocular pressure (IOP), but to treat the patient as a whole so as to provide maximum benefit with minimal side effects.

Medical treatment is the mainstay of glaucoma management, particularly of open angle glaucoma. A number of intraocular pressure-lowering agents are available which act either by decreasing aqueous secretion or by enhancing the aqueous outflow. The goal of medical treatment is to obtain 24 – hour IOP control with the minimum concentration and number of medications, as well as minimal local and systemic side effects.[16]

Latanoprost was well tolerated at all concentrations, with no differences between doses groups with respect any of the adverse events, including conjunctival hyperemia. There were two reports of iris darkening and 11 reports of eyelash growth, but there was no dose association for either of these events. Both are well recognized side effects of prostaglandin analog therapy.[17]

After a single topical dose of latanoprost 0.005%, IOP reduction is maximal within 8 to 12 hours and IOP remains below pretreatment level for at least 24 hours. In 24-hour IOP measurements, latanoprost administered once a day in the evening induces a constant IOP reduction, although the hypotensive effect seems to be greatest during the day.[16,17]

In patients with glaucoma or ocular hypertension (IOP ≥ 21), a number of studies, between 1 and 12 months' treatment, report a reduced IOP level, from 22% to 39%.[18]

Our study shows that topical 0.005% Latanoprost eye drops reduces the central corneal thickness as the mean CCT was observed (538 ± 1.87 µm vs. 534 ± 2.1 2 µm) in 75% eyes in 8 weeks follow up. Similar results were found in other studies as Hatanaka M *et al in a* controlled trial have shown that Latanoprost 0.005% showed reduction of 0.86% in CCT from a baseline level of 548.57 µm ± 32.4 to 543.88 µm ± 35.6 after 8 weeks of use.[17] Xhong. Y, *et al* reported a decrease in CCT of 15.73 ± 3.25µm following latanoprost monotherapy.[19] A statistically significant reduction in the mean CCT was observed in the latanoprost group (535.5 ± 37.9 µm vs. 530.1 ± 36.4 µm) in 77.10% eyes 24 months following initiation of therapy by a similar study conducted by Kim HJ and Cho BJ.[19] Another study conducted by Sen E, et al[21] revealed a 1.9 ± 2.4% reduction in CCT from a mean baseline CCT value of 559.5 ± 35.3 µm, 12 months following latanoprost therapy.

A meta – analysis of randomized clinical trials widely estimated the IOP reduction achieved by the most frequently prescribed glaucoma drugs and a placebo and pointed out that prostaglandin analogs are the most effective group for lowering IOP by mono therapy in primary open angle glaucoma (POAG) or ocular hypertensive patients, with a relative change of −31% (at peak) and −28% (at trough) for latanoprost.

After a long-term treatment, since latanoprost has no clinically significant effect on the permeability of the blood–aqueous barrier, IOP will return to pretreatment levels within a few weeks, indicating that latanoprost is safe for long-term treatments.

CONCLUSION

Our study concludes that topical 0.005% Latanoprost eye drops reduces the central corneal thickness as the mean CCT was observed (538 ± 1.87 µm vs. 534 ± 2.12 µm) in 75% eyes in 8 weeks follow up, so latanoprost therapy requires careful monitoring while treating patients with primary open angle glaucoma. However this reduction in CCT was not ≥ 25 µm from base line readingwhich is not significant enough and hence did not have an effect on IOP reading using the Goldman Applanation tonometer.

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