Original Article

# Ocular Surface Changes in Primary Open Angle Glaucoma with Long Term Topical Anti Glaucoma Medication

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**Abstract**

**Background: Topical life long anti glaucoma medication forms the mainstay of treatment of primary open angle glaucoma. Their long term usage can cause changes in conjunctival epithelium.**

**Methods: Hundred cases of primary open angle glaucoma were divided into four groups of 25 patients each. Each group was put on Timolol, Pilocarpine, Brimonidine and Latanoprost respectively. Ocular surface changes were monitored using Schirmer's test, tear film break up time (BUT) and conjunctival impression cytology.**

**Result: Altered Schirmer's test value was seen in 40% of patients and reduced tear film BUT values in 26%, at the end of one year. These changes were more in patients treated with timolol. Changes in conjunctival cytology such as decrease in goblet cell density, squamous metaplasia and presence of inflammatory cells were seen in significant number of patients at the end of one year treatment. There was direct relation of duration of treatment to various ocular surface changes.**

**Conclusion: Ocular surface changes are seen in significant number of patients of primary open angle glaucoma at the end of one year follow up with topical anti glaucoma therapy. Conjunctival impression cytology is a non invasive technique to monitor these changes.**

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**Key Words : Primary open angle glaucoma; Ocular surface changes; Goblet cell density; Squamous metaplasia**

## Introduction

Primary open angle glaucoma is the second most common cause of blindness all over the world. The exact patho physiology of optic nerve damage in glaucoma is not clearly understood but there is enough evidence to believe that raised intra ocular pressure (IOP) has direct relation to extent of optic nerve damage. Out of the various causative factors, IOP is the only modifiable factor in primary open angle glaucoma. Hence control of intra ocular pressure remains the mainstay of therapy for glaucoma. In the last two decades a range of newer topical medications have been introduced such as beta blockers, topical carbonic anhydrase inhibitors, prostaglandin analogues and alpha adrenergic agonist for management of glaucoma. Glaucoma therapy is life long and topical agents used over long time, are likely to cause changes in ocular surface particularly reduction in tear secretion, changes in tear film break up time (BUT) and changes in conjunctival epithelium.

This study was carried out to analyze the effects of four commonly used anti glaucoma drugs i.e timolol, pilocarpine, brimonidine and latanoprost on ocular surface by a simple non invasive technique of conjunctival impression cytology and to correlate them with IOP controlling effect of the drugs.

## Material and Methods

Hundred new cases of primary open angle glaucoma reporting to the eye out patient department were included in the study. The diagnosis was confirmed by aplanation tonometry, gonioscopy, visual fields recording and fundus examination. Patients on long-term topical medication like artificial tear drops/disodium cromoglycate drops, those with primary or secondary ocular surface disorders like conjunctival xerosis, trachoma, chemical burns, intra or extra ocular surgery and lagophthalmos/ lid deformities were excluded.

The patients were divided into four groups of 25 each. Group A was put on commercially available preparation of timolol maleate 0.5% twice daily dose. Group B was put on 2% pilocarpine nitrate eye drops four times a day, Group C on 0.2% brimonidine tartarate eye drops thrice daily dose and Group D on 0.005% latanoprost eye drops once at bed time. All patients were followed up for a period of one year. Visual acuity and intra ocular tension (IOT) were recorded monthly. Schirmer's test and tear film break up time were carried out once in three months. Visual field recording was done by automated perimetry using 24-2 programme of Humphry visual field analyzer initially and at six monthly intervals. Conjunctival impression smear was taken at three monthly intervals. The technique was to apply 1x1 cm strip of cellulose

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**Table 1**

**Schirmer's test results**

| Drug Group | Number of patients | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 0 month | | | 6 months | | | 12 months | | |
| | >15 mm | 10-15 mm | <10 mm | >15mm | 10-15mm | <10mm | >15mm | 10-15mm | <10 mm |
| Timolol (n=21) | 21 | 0 | 0 | 19 | 2 | 0 | 6 | 7 | 8 (38%) |
| Pilocarpine (n=22) | 21 | 1 | 0 | 20 | 2 | 0 | 14 | 5 | 3 (13%) |
| Brimonidine (n=22) | 21 | 1 | 0 | 21 | 1 | 0 | 17 | 3 | 2 (9%) |
| Latanoprost (n=23) | 23 | 0 | 0 | 22 | 1 | 0 | 16 | 5 | 2 (9%) |

acetate filter paper to upper temporal bulbar conjunctiva of each eye and keep it pressed firmly for five seconds. Each strip was transferred on to glass slides and fixed immediately using 1:1 mixture of absolute alcohol and ether. One of the smears thus fixed was subjected to Papanicolau stain and the other to Periodic Acid Schiff stain. The stained smears were studied and graded by an experienced pathologist (blind observer) into Goblet cells density of >75/HPF, 50-75/HPF, 15-50/HPF, <15/HPF; mild,moderate and severe squamous metaplasia and presence or absence of inflammatory cells.

## Results

Out of 100 patients, four were lost to follow up. In another eight patients intra ocular pressure was not controlled and they were put on two-drug therapy and excluded from the study. A total of 88 patients completed the study. The group included 42 males and 46 females with a mean age of 53 years.

Timolol exhibited 34%, pilocarpine 32%, brimonidine 30% and latanoprost 32% reduction in baseline IOP at one month follow up. IOP lowering effect of all the drugs was consistent throughout the study. There was no deterioration of visual fields in all the 88 subjects.

Schirmer's test value was more than 15 mm in all except two (2.3%) patients where it was between 10-15 mm. At the end of the six months two patients of timolol group and one patient of pilocarpine group showed Schirmer's Test value between 6 to 10mm. At the end of one year, eight (38%) patients of timolol group, three(13%) patients from pilocarpine, and two (9%) each from brimonidine and latanoprost group showed Schirmer's Test value of less than 10 mm. In total out of 88 patients who completed the study, 35 ( 40%) patients had Schirmer's test value of less than 15mm at the end of one year as against two (2.6%) at the outset. Out of these 15 (42%) patients had Schirmer's test value of less than 10 mm and 53% of these belonged to timolol group (Table 1).

The tear film BUT was more than 10 seconds in all patients at the beginning of the study. The values remained same at the end of the first quarter. At the end of the six months three (14%) patients of timolol group, two (9%) patients of pilocarpine group and one (4.5%) each from brimonidine and latanoprost group showed tear film BUT of less than 10 seconds. At the end of one year nine (43%) patients of timolol group, six (27%) patients of pilocarpine group and four (18%) each from brimonidine and latanoprost group showed tear film BUTof less than 10 seconds. None required tear substitute as they were asymptomatic. A total of 23 (26%) out of 88 patients showed reduced tear film BUT at the end of one year

**Table 2**

**Number of patients with tear film break up time <10 sec**

| Drug Group | Number of patients | | | |
|---|---|---|---|---|
| | 0 month | 3 months | 6 months | 12 months |
| Timolol group (n=21) | 0 | 0 | 3 | 9 (43%) |
| Pilocarpine group (n=22) | 0 | 0 | 2 | 6 (27%) |
| Brimonidine group (n=22) | 0 | 0 | 1 | 4 (18%) |
| Latanoprost group (n= 23) | 0 | 0 | 1 | 4 (18%) |

**Table 3**

**Number of patients with goblet cell density of <50 cells /HPF**

| Study Group | Number of patients | | | |
|---|---|---|---|---|
| | 0 month | 3 months | 6 months | 12 months |
| Timolol group (n=21) | 0 | 1 | 6 | 12 (57%) |
| Pilocarpine group (n=22) | 1 | 1 | 4 | 7 (32%) |
| Brimonidine group (n=22) | 1 | 1 | 2 | 5 (23%) |
| Latanoprost group (n=23) | 0 | 1 | 2 | 4 (17%) |

and 36% of these belonged to timolol group (Table 2).

Conjunctival impression smears at the beginning of the study showed presence of goblet cell density of more than 75 cells /HPF in 76 (86%) out of 88 patients, cell density of 50-75 cells per /HPF in 10 (11%) patients and cell density of 15-50 cells / HPF in two (2.2%) patients. At the end of six months goblet cell density between 15-50 cells /HPF was seen in six (28%) patients from timolol group, four (18%) of pilocarpine and two (9%) each of brimonidine and latanoprost group. At the end of one year goblet cell density between 15-50 cells / HPF was seen in 12 (57%) patients from timolol group, seven (32%) of pilocarpine group, five (23%) of brimonidine and four (17%) of latanoprost group. A total 28 (32%) patients showed moderate loss of goblet cell at end of one year treatment (Table 3, Figs 1, 2).

Presence of inflammatory cells was seen in eight (9%) patients out of 88 patients at the beginning of study. At the end of six months, four(19%) patients from timolol group, six (27%) of pilocarpine group, eight (36%) of brimonidine and four(17%) of latanoprost group showed the presence of inflammatory cells. At the end of one year , six (27%) patients