

## Effect of Topical Antiglaucoma Drugs on Tear Film in Human Eyes

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### Abstract:

**Objective(s):** Evaluate the effect of topical antiglaucoma drugs on tear film and determine the time taken to develop symptoms and or signs of dry eye in diagnosed open angle glaucoma patients by Schirmer's test I, Schirmer's test II, Tear film break up time.

**Method(s):** This prospective study was carried out in 60 patients attending Ophthalmology outdoor with newly diagnosed patients of primary open angle glaucoma by using Schirmer's test I, Schirmer's test II, Tear film break up time. These 60 cases were divided into 2 groups:- Group I: 30 cases were given 0.5% timolol drops twice a day and Group II: 30 cases were given 0.005% latanoprost drops once a day.

**Result(s):** The tear film changes were greater in patients treated with timolol than with latanoprost. There were 11(36.7%) patients in timolol group and 3(10%) patients in latanoprost group which had developed dry eye at the end of the study period.

**Conclusion(s):** Thus it is concluded that tear film changes are seen in significant number of patients of primary open angle glaucoma at the end of 90<sup>th</sup> days follow up with both topical antiglaucoma drugs timolol and latanoprost therapy more so with timolol. These changes in the tear film were directly related to the duration of treatment.

**Keywords:** Antiglaucoma drugs, Primary open angle glaucoma, Schirmer's test I, Schirmer's test II, Tear film break up time, Dry eye.

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### I. Introduction

Glaucoma can be defined as a multifactorial optic neuropathy<sup>1</sup> with a characteristic loss of optic nerve fibres presenting as classical optic nerve head features<sup>2</sup> and correlating visual field changes.<sup>3,4</sup> The intraocular pressure was considered to be the sole factor in the causation of glaucoma<sup>5</sup>, the role of intraocular pressure in the current definition is only one of the multiple factors responsible for the disease.<sup>6,7</sup> Primary open angle glaucoma is the second most common cause of blindness all over the world. The lowering of the IOP could be achieved either by topical use of antiglaucoma drugs or surgery.<sup>8</sup> The topically applied antiglaucoma drugs have to cross the cornea and conjunctiva to reach their sites of action.<sup>9</sup> Intraocular pressure, funduscopy, gonioscopy and visual field analysis are the other investigative procedures to ascertain glaucomatous status.<sup>10</sup> Tear film breakup time can be defined as interval between a complete blink and appearance of first randomly distributed dry spot. The tear film break up time averages between 25-30 seconds.<sup>11</sup> But country like India due to topical climate and majority of population working in fields thus exposed to dry and arid climatic condition tear breakup time 10 seconds or more is considered normal.<sup>12</sup> Dry eye and ocular surface damage are the major concerns related to this chronic, sight-threatening disease since they may have an impact on all those parameters that affect the success of glaucoma treatment. Schirmer's test -1 was done using 5 mm by 35 mm whatman's filter paper #41 without prior instillation of topical anaesthetic drops, A reading of less than 10 mm was regarded as abnormal and indicative of dry eye. . Schirmer's test-2 topical anesthetic was instilled into the conjunctiva and after 5 minutes, the excess fluid was dried with a filter paper.

### II. Methods

The sixty freshly diagnosed cases were randomly selected in outpatient Department of Ophthalmology, Govt Medical College, Amritsar from January 2011 to August 2012. The nature of study was explained to the patient and an informed written consent was obtained from each selected case prior to inclusion in the study alongwith approval from ethical committee. The tear film tests were noted before commencing antiglaucoma drugs (Beta-blockers, Prostaglandin derivatives) and after 7<sup>th</sup>, 45<sup>th</sup> and 90<sup>th</sup> day of treatment. All measurements were recorded at the same hour of the day in order to avoid the diurnal variations. Detailed history and meticulous examination was carried out in each case which was included systemic as well as local examination. The diagnosis was confirmed by Schiotz tonometry, gonioscopy, visual fields recording and fundus

examination. All subjects were subjected to routine eye examination with slit lamp. The patients were divided into two groups of 30 each.

Group A was put on commercially available preparation of timolol maleate 0.5% twice daily dose. Group B was put on 0.005% latanoprost eye drops once at bed time. All patients were followed up for a period of three months. Visual acuity and intra ocular pressure (IOP) were recorded every followed up. Schirmer's test I, II and tear film break up time were also carried out every follow up.

### III. Results

In this study the youngest case was 35 years old and the oldest case was 75 years old. In timolol drug group mean age was 55.40 years and in latanoprost drug group was 54.17 years. The mean age of distribution of the cases under study was 54.78 years. Out of 60 patients there were 30 (50%) male and 30 (50%) females. The initial mean intraocular pressure in the affected eye of cases Group I and Group II was 27.70 mm of Hg and 29.57 mm of Hg respectively.

The mean values of Schirmer's test I initially was 18.67 mm and at the end of study was 10.40 mm in group and in group II initially mean value was 18.13mm and at the end of study was 12.87mm.

**TABLE: I Showing intra group mean value changes of Schirmer's test I in both groups (in mm):-**

Time	Timolol			Latanoprost		
	Mean ± SD	Mean change	P value	Mean ± SD	Mean change	P value
Day 1	18.67±2.139	-	-	18.13±2.726	-	-
Day 7	16.40±1.499	2.267± 1.363	<0.001**	17.00±2.816	1.133±1.167	<0.001**
Day 45	11.93±2.377	6.633±1.818	<0.001**	13.13±2.501	5.000±2.393	<0.001**
Day 90	10.40±3.122	7.867±2.330	<0.001**	12.87±2.726	5.267±2.303	<0.001**

**TABLE: II Showing intra group mean value changes of Schirmer's test II in both groups:-**

Time	Timolol			Latanoprost		
	Mean ± SD	Mean change	P value	Mean ± SD	Mean change	P value
Day 1	12.53±1.871	-	-	14.33±1.688	-	-
Day 7	10.83±1.859	1.70±1.236	<0.001**	12.03±2.173	2.300±1.264	<0.001**
Day 45	08.37±2.109	4.167±1.877	<0.001**	9.37±2.125	4.967±1.542	<0.001**
Day 90	07.10±2.551	5.433±2.096	<0.001**	8.60±2.207	5.733±1.701	<0.001**

**\*\* p < 0.001; Highly Significant**

Above table showed intra group comparison in between different time interval in Schirmer's test II in both drug groups. The mean value was 12.53 ±1.871mm on day one and 10.83 ±1.859 mm on day 7 i.e. mean change was significant 1.70±1.236 mm. Thereafter the mean changes of Schirmer's test readings further changed to 4.167±1.877 mm and 5.433±2.096 mm on 45<sup>th</sup> and 90<sup>th</sup> day respectively and were also highly significant. Similarly in latanoprost drug group mean change was highly significant on the 7<sup>th</sup> day as it was 2.300±1.264 mm. In the subsequent follow up days the mean values further changed to 4.967±1.542 mm and 5.733±1.701mm respectively and were also highly significant.

**TABLE: III Comparison of mean value of tear break up time between the two groups:-**

Time	Timolol	Latanoprost	P value
	Mean ± SD	Mean ± SD	
Day 1	18.80 ±2.265	18.93 ± 2.212	0.818 <sup>NS</sup>
Day 7	17.07 ±2.420	17.20±2.448	0.677 <sup>NS</sup>
Day 45	12.67±2.510	13.83±2.914	0.102 <sup>NS</sup>
Day 90	11.47±3.224	13.10±2.940	0.045*

**NS: p > 0.05; Not Significant, \* p < 0.05; Significant**

In the tear film break up time comparison of mean value between timolol drug group and latanoprost drug group and the p value on 1<sup>st</sup> day, 7<sup>th</sup> day and 45<sup>th</sup> day were 0.818, 0.677 and 0.102 respectively and were not significant but on 90<sup>th</sup> day it was 0.045 which was significant.

**TABLE: IV Comparison of incidence of dry eye in the two groups:-**

Time		Timolol (out of 30)	Latanoprost (out of 30)	Total	P value
1 <sup>st</sup> day	Present	None	None	None	-
7 <sup>th</sup> day	Present	None	None	None	-
45 <sup>th</sup> day	Present	4 (13.33%)	1(3.33%)	5(8.3%)	0.161 <sup>NS</sup>
90 <sup>th</sup> day	Present	11(36.67%)	3 (10.0%)	14(23.3%)	0.015*

**NS: p > 0.05; Not Significant; \* p < 0.05; Significant**

On 1<sup>st</sup> and 7<sup>th</sup> day all cases in both drug groups were normal none had dry eye. On 45<sup>th</sup> day 4 cases of timolol and 1 case of latanoprost had developed dry eye. While on the 90<sup>th</sup> day 11(36.67%) cases of timolol and 3(10.0%) cases of latanoprost had dry eye i.e. a total of 14 (23.3%) cases were diagnosed to have dry eye at the end of the study.

#### IV. Discussion

In our study the age distribution of the selected primary open angle glaucoma patients varied from 35 to 75 years. The mean age of distribution of cases of both the groups under study was 54.78 years. Tuck MW, Crick RP reported that the major incidence of primary open angle glaucoma was seen in age group  $\geq 55$  years of age.<sup>13</sup> In the present study, out of 60 cases, 30(50%) were males and 30(50%) were females. A similar study conducted by Mitchell observed there was no significant difference in distribution of sex.<sup>13</sup>

The mean values of Schirmer’s test I initially was 18.67 mm and at the end of study was 10.40 mm in group I and in group II initially mean value was 18.13 mm and at the end of study was 12.87mm. Schirmer’s test II mean value change differences in group I on the follow up days were  $1.70 \pm 1.236$ mm,  $4.167 \pm 1.877$ mm and  $5.433 \pm 2.096$  mm and were highly significant. In the group II in all the visits the mean differences were  $2.300 \pm 1.264$ mm,  $4.967 \pm 1.542$ mm and  $5.733 \pm 1.701$ mm which were also highly significant. A similar study by John Sonntag showed slight decrease in results of Schirmer’s test while studying efficacy and side effects of timolol in 78 patients, mean values of Schirmer’s test initially was 13.7 mm and at the end of 4 months study was 12.6mm.<sup>14</sup>

Intra group comparison in tear film break up time in both drug groups was also highly significant. In group I the mean value was  $18.80 \pm 2.265$  sec on day one and  $17.07 \pm 2.420$  sec on day 7 i.e mean change was  $1.733 \pm 2.033$  sec. Thereafter the mean changes in the readings had a difference of  $6.133 \pm 2.285$  sec and  $7.333 \pm 2.928$  sec on 45<sup>th</sup> and 90<sup>th</sup> day respectively. Similarly in group II mean changes on the 7<sup>th</sup>, 45<sup>th</sup> and 90<sup>th</sup> day were  $1.600 \pm 1.47$ ,  $5.100 \pm 2.369$  sec and  $5.833 \pm 2.451$  sec. Bonomi et al in a study of 45 days on timolol reported a significant decrease of Schirmer’s test I and II, tear break up time and tear lysozyme after one week; thereafter remaining constant for the whole period of observation.<sup>15</sup> Results matched with our study. In the present study on 1<sup>st</sup> and 7<sup>th</sup> day all cases showed tear film break up time reading  $> 10$  sec in both groups but on 45<sup>th</sup> day there were four (13.3%) cases with  $< 10$  sec and on 90<sup>th</sup> day there were eleven (36.7%) cases with  $< 10$  sec reading in group I and in group II on 45<sup>th</sup> there was only one (3.3%) case and on 90<sup>th</sup> day there were three (10.0%) cases  $< 10$  sec. In the two groups the p value was 0.16 on the 45<sup>th</sup> day which was not significant while on the 90<sup>th</sup> day the p value was (0.015) which was significant. Kamath et al observed the tear film break up time 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 break up time 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 break up time of less than 10 seconds. A total of 23 (26%) out of 88 patients showed reduced tear film break up time at the end of one year and 36% of these belonged to timolol group.<sup>16</sup>

In the present study on 1<sup>st</sup> and 7<sup>th</sup> day all cases in both drug groups were in normal or above the dry eye range readings. On 45<sup>th</sup> day 4 cases of timolol drug group and 1 case of latanoprost drug group had developed dry eye. On 90<sup>th</sup> day 11(36.67%) cases of timolol drug group out of 30 and 3(10.0%) cases of latanoprost were diagnosed as dry eye cases out of 30 cases. Total 14(23.3%) cases were diagnosed to have developed dry eye out of 60 cases.

Similarly Kamath et al observed altered Schirmer’s test value in 40% of patients and reduced tear film break up time values in 26%, at the end of one year. In latanoprost, altered Schirmer’s test value was seen in 9% of patients and reduced tear film break up time values in 18%, at the end of one year. These changes were more in patients treated with timolol.<sup>16</sup> Although Schwartz et al reported in a study over 1 year, 4.3% of latanoprost and 4.5% of travoprost-Z patients were identified with dry eye.<sup>17</sup>

## V. Conclusion

Study was conducted to evaluate the effects of topical antiglaucoma drugs (0.5% timolol and 0.005% latanoprost) on the tear film. The mean age of the patients was 54.78 years in both groups. Schirmer's test I, II and tear film break up time were the parameters to assess the tear film changes. The observations were noted, analyzed and intra and inter group comparisons were done on 1<sup>st</sup>, 7<sup>th</sup>, 45<sup>th</sup> and 90<sup>th</sup> day in both the groups. The inter group comparison of Schirmer's test I, II and tear film break up time of timolol drug group and latanoprost drug group on 1<sup>st</sup> and 7<sup>th</sup> day however showed the tests in the normal range but on the 45<sup>th</sup> day 4 patients in timolol group and 1 patient in latanoprost group showed readings <10mm, <6mm and <10sec respectively however which was not significant. On the 90<sup>th</sup> day 11 cases in the timolol group and 3 cases in latanoprost group showed abnormal readings in all the three parameters and were significant. The tear film changes were greater in patients treated with timolol than with latanoprost. There were 11(36.7%) patients in timolol group and 3(10%) patients in latanoprost group which had developed dry eye at the end of the study period. Tear film changes are seen in significant number of patients of primary open angle glaucoma at the end of 90<sup>th</sup> days follow up with both topical antiglaucoma drugs timolol and latanoprost therapy more so with timolol. These changes in the tear film were directly related to the duration of treatment.

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