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 two 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 90th 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.

I. Introduction
Glaucoma can be defined as a multifactorial optic neuropathy1 with a characteristic loss of optic nerve fibres presenting as classical optic nerve head features2 and correlating visual field changes.3,4 The intraocular pressure was considered to be the sole factor in the causation of glaucoma5, the role of intraocular pressure in the current definition is only one of the multiple factors responsible for the disease.6,7 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.8 The topically applied antiglaucoma drugs have to cross the cornea and conjunctiva to reach their sites of action.9 Intraocular pressure, fundoscopy, gonioscopy and visual field analysis are the other investigative procedures to ascertain glaucomatous status.10 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.11 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.12 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 7th, 45th and 90th 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
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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 bedtime. All patients were followed up for a period of three months. Visual acuity and intraocular 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%) males 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.

Table I: Showing intra group mean value changes of Schirmer’s test I in both groups (in mm):

<table>
<thead>
<tr>
<th>Time</th>
<th>Timolol</th>
<th>Latanoprost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>18.67±2.139</td>
<td>18.13±2.726</td>
</tr>
<tr>
<td>Day 7</td>
<td>16.40±1.499</td>
<td>17.00±2.816</td>
</tr>
<tr>
<td>Day 45</td>
<td>11.93±2.777</td>
<td>13.13±2.501</td>
</tr>
<tr>
<td>Day 90</td>
<td>10.40±3.122</td>
<td>12.87±2.726</td>
</tr>
</tbody>
</table>

** 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 18.67±2.139 mm on day one and 12.53±1.871 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 45th and 90th day respectively and were also highly significant. Similarly in latanoprost drug group mean change was highly significant on the 7th 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±1.701 mm respectively and were also highly significant.

Table II: Showing intra group mean value changes of Schirmer’s test II in both groups:

<table>
<thead>
<tr>
<th>Time</th>
<th>Timolol</th>
<th>Latanoprost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>12.53±1.871</td>
<td>14.33±1.688</td>
</tr>
<tr>
<td>Day 7</td>
<td>10.83±1.859</td>
<td>12.03±2.173</td>
</tr>
<tr>
<td>Day 45</td>
<td>08.37±2.109</td>
<td>9.37±2.125</td>
</tr>
<tr>
<td>Day 90</td>
<td>07.10±2.551</td>
<td>8.60±2.207</td>
</tr>
</tbody>
</table>

** p < 0.001; Highly Significant

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 1st day, 7th day and 45th day were 0.818, 0.677 and 0.102 respectively and were not significant but on 90th day it was 0.045 which was significant.
TABLE: IV Comparison of incidence of dry eye in the two groups:

<table>
<thead>
<tr>
<th>Time</th>
<th>Timolol (out of 30)</th>
<th>Latanoprost (out of 30)</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st day</td>
<td>Present</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>7th day</td>
<td>Present</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>45th day</td>
<td>Present</td>
<td>4 (13.33%)</td>
<td>1 (3.33%)</td>
<td>5 (8.3%)</td>
</tr>
<tr>
<td>90th day</td>
<td>Present</td>
<td>11 (36.67%)</td>
<td>3 (10.0%)</td>
<td>14 (23.3%)</td>
</tr>
</tbody>
</table>

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

On 1st and 7th day all cases in both drug groups were normal none had dry eye. On 45th day 4 cases of timolol and 1 case of latanoprost had developed dry eye. While on the 90th 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 >=55 years of age. 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.

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 12.87 mm. Schirmer’s test II mean value change differences in group I on the follow up days were 1.70±1.236 mm, 4.17±1.877 mm and 5.43±2.096 mm and were highly significant. In the group II in all the visits the mean differences were 2.30±1.264 mm, 4.96±1.342 mm and 5.73±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 pilocarpine. Mean values of Schirmer’s test initially was 13.7 mm and at the end of 4 months study was 12.6 mm.

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±2.265 sec on day one and 17.07±2.420 sec on day 7 i.e mean change was 1.733±0.233 sec. Thereafter the mean changes in the readings had a difference of 6.133±2.285 sec and 7.333±2.928 sec on 45th and 90th day respectively. Similarly in group II mean changes on the 7th, 45th and 90th day were 1.600±1.47, 5.100±2.369 sec and 5.833±2.451 sec. In our study the age distribution of cases of both the groups under study was 54.78 years.

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In the present study on 1st and 7th day all cases in both drug groups were in normal or above the dry eye range readings. On 45th day 4 cases of timolol drug group and 1 case of latanoprost drug group had developed dry eye. On 90th 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. 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.

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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 1st, 7th, 45th and 90th 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 1st and 7th day however showed the tests in the normal range but on the 45th day 4 patients in timolol group and 1 patient in latanoprost group showed readings <10mm, <6mm and <10sec respectively which was not significant. On the 90th 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 90th 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.

Reference