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EVALUATION OF TEAR FILM STATUS IN PATIENTS USING ANTI-GLAUCOMA MEDICATION

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ABSTRACT

Aim: The purpose of this study was to determine the prevalence of ocular surface disease symptoms and the state of the tear film among patients with glaucoma who are receiving topical intraocular pressure lowering therapy.

Methods: The Prospective observational cohort study was conducted in a Tertiary Hospital and Research Centre in Western Maharashtra from September 2020 to October 2022. 78 Patients

(156 eyes) attending Ophthalmology OPD in a Tertiary Hospital and Research Centre in Western Maharashtra were included in the study.

Results: Majority of the patients in our study were males (67.9%), while 32.1% were females. Majority of the patients were in the 35-45 age group followed by >55 age group. The mean Intraocular pressure in the right and left eye was 27.4 mm Hg before the medication. The mean Schirmer 1 test scores in the right and left eye were 16.8 mm before the medication. The mean Schirmer 2 test scores in the right and left eye were 15.7 mm & 15.5 mm, respectively, before the medication. All patients had normal TBUT time in both right and left eye (>10 seconds). All patients had intact corneal sensation in right and left eye. Post-medication, the schirmer 1 was reduced in 66.7% of the patients, increased in 11.5% and remained same in 21.8% of the patients in right eye and left eye. Post-medication, the schirmer 2 was reduced in 66.7% of the patients, increased in 11.5% and remained same in 21.8% of the patients in right eye and left eye. TBUT was found abnormal among 7.7% of the patients in either eye, at 6 months after the anti-glaucoma medications.

Conclusion: Anti-glaucoma medication (E/D Timolol 0.5%) twice a day for a period of 6 months had significantly reduced TBUT, Schirmer-1 and Schirmer-2 among the glaucoma patients in our settings. Reduced corneal sensitivity has been noted in few patients. Anti-glaucoma medication had led to dry eye symptoms with severity ranging from moderate to severe in majority of the patients.

Keywords: dry eye, glaucoma, ocular surface disease, topical

INTRODUCTION

Primary open angle glaucoma (POAG) is a progressive neurodegeneration of retinal ganglion cells (RCGs) and their axons characterized by a specific pattern of visual field and optic nerve head damage.[1,2] Clinical trials confirmed the importance of intraocular pressure (IOP) in the development and progression of open-angle glaucoma, even if evidence suggests the existence of ocular and systemic factors, in addition to IOP, that can be responsible of this development and progression. IOP is still the only risk factor that we can effectively treat with medical and surgical therapy.[3,4]

Tear film deficiencies are among the most common eye problems[5]: epidemiologic studies have reported that more than 6% of the population over the age of 40 suffer from dry eye, with the prevalence increasing to 15% of the population over the age of 65.[6-8] Using a prevalence of 6% and the 2000 census data, there are an estimated 7.1 million people in the US over the age of 40 who experience dry eye symptoms. Most studies have found an increasing prevalence with age and some studies have shown a greater prevalence of dry eye among women.[6,8,9]

A set of progressive optic neuropathies called glaucoma are defined by alterations in the optic nerve head brought on by the degradation of retinal ganglion cells and retinal nerve fibre layers.[10] Glaucoma is linked to damage to the optic nerve caused by high intraocular pressure (IOP), which causes the death of retinal ganglion cells.[11] Glaucoma is the primary cause of permanent blindness globally and is linked to a lower quality of life.[12]

For glaucomatous patients, who frequently utilise topical medication for many years, medical therapy is typically the primary line of treatment.[10] The majority of glaucoma patients who have been diagnosed benefit from therapy with drugs that reduce intraocular pressure (IOP) in order to reach target levels during the early stages of the illness. IOP-lowering drugs may aggravate ocular surface disease (OSD), by themselves or in part as a result of the preservatives they contain.4 The use of topical medications over an extended period of time may result in ocular pain, instability in the tear films, inflammation of the conjunctival surface, fibrosis in the sub-conjunctiva, apoptosis of the epithelium, deterioration of the surface of the cornea, and an increased likelihood of failure following glaucoma surgery in the future.[13,14]

Studies have revealed that preservative-free timolol and carteolol eye drops are less harmful to the ocular surface, indicating that preservatives are primarily to blame for the negative effects of beta-blocker eye drops.[15] Albeit, past studies show that over 60 percent of glaucoma patients receiving medical treatment reported having OSD symptoms. This substantial overlap between the two disorders raises the possibility of a therapeutic interaction between them.[14,16] A frequent side effect of using eye drop solutions containing preservatives is the worsening of already dry eye.[15] The effect of dry eye on a glaucoma patient's everyday life, particularly the feelings of pain, is a crucial factor to take into account in the follow-up. Hence, it is of vital importance to assess the effect of the IOP lowering medication and the use of preservatives among the glaucoma patients on the ocular surface diseases and tear characteristics.

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The purpose of this study was to determine the prevalence of ocular surface disease symptoms and the state of the tear film among patients with glaucoma who are receiving topical intraocular pressure lowering therapy.

Materials and METHODS

The Prospective observational cohort study was conducted in a Tertiary Hospital and Research Centre in Western Maharashtra from September 2020 to October 2022. 78 Patients (156 eyes) attending Ophthalmology OPD in a Tertiary Hospital and Research Centre in Western Maharashtra were included in the study.

Assuming that 72% of the glaucoma patients are developing dry eye after using antiglaucoma medication, with a confidence interval of 95% and acceptable difference of 12%, minimum sample size is calculated to be 78 patients (156 eyes) Software used is WINPEPI method.

INCLUSION CRITERIA:

- All patients newly diagnosed with glaucoma and started on Topical Anti-Glaucoma medication. (E/D TIMOLOL 0.5%)

EXCLUSION CRITERIA:

- Dry eye due to any other cause.
- Patients with any infectious or inflammatory ocular conditions
- Patients with ocular trauma within 6months
- Patients with advanced glaucoma disease
- Patients with secondary glaucoma

The ethics committee approved this prospective observational cohort study, which was carried out at a tertiary care facility over the course of September 2020 to October 2022. Written as well as informed consent was taken from all the patients who has participated in this study. History of the patient included demographic details including age, sex, area of residence, occupation, history of presenting illness, past history, any systemic illness

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Complete ophthalmic examination was done on all the patients participated in the study

- Snellen's visual acuity
- Slit lamp bio microscopy for Anterior segment examination
- Pupillary reflex assessment
- Slit lamp bio microscopy with +90D for optic nerve head evaluation to check for glaucomatous disc changes
- Intra ocular pressure is measured using Goldmann applanation tonometer

After clinical diagnosis was made based on history and clinical ophthalmic examination additional investigations were done to support the diagnosis

- Visual fields were recorded using Automated perimetry
- Optical coherence tomography to look for neuro retinal thickness, RNFL, Ganglion cell layer.

Further following tests were done to determine the tear film status of all the patients

- Tearfilm breakup time (TBUT) (>10 seconds)
- Schirmer-1(>10mm after 5 minutes)
- Schirmer-2(>15mm after 2 minutes)
- Corneal sensations (intact, brisk, reduced)

All the above mentioned tests for tear film status were done before starting the patient on anti-glaucoma medication (e/d Timolol 0.5%).

Patient were followed up every 2 monthly for 6 months for IOP monitoring.

TBUT, schirmer-1, schirmer-2, values are noted at starting of the anti-glaucoma medication and after completion of the 6 months of the treatment.

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In addition to the above mentioned tests dry eye questionnaire (OSDI) has been given to all the patients after using the anti-glaucoma medication (e/d Timolol 0.5%) at the end of 6 months. 12-item questionnaire, questionnaire has 3 subscales: ocular symptoms, vision-related function, and environmental triggers (normal, mild, moderate, severe).

RESULTS

Table 1: Demographic details

Gender	**N%**
Male	53 (67.9%)
Female	25 (32.1%)
Age groups	
35-45	38 (48.73%)
46-55	18 (23.07%)
>55	22 (28.20%)

Majority of the patients in our study were males (67.9%), while 32.1% were females. Majority of the patients were in the 35-45 age group followed by >55 age group.

Table 2: Pre-medication status

IOP (mm Hg)	**Mean**	**SD**	**Median**	**IQR**
Right	27.4	4.7	26.0	24,30
Left	27.4	2.8	26.0	26,30

The mean Intraocular pressure in the right and left eye was 27.4 mm Hg before the medication.

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Table 3: Schirmer-1 & 2, TBUT before medication

Schirmer-1 (mm) **Normal >10mm**	**Mean**	**SD**	**Median**	**IQR**
Right	16.8	3.8	15.0	15,20
Left	16.8	3.8	15.0	15,20
Schirmer-2 (mm) **Normal >15mm**				
Right	15.7	3.9	15.0	14,20
Left	15.5	3.6	15.0	14,20

	TBUT Normal (>10 seconds)	
Eye	No of patients	Percentage (%)
Right	78	100
Left	78	100

The mean Schirmer 1 test scores in the right and left eye were 16.8 mm before the medication. The mean Schirmer 2 test scores in the right and left eye were 15.7 mm & 15.5 mm, respectively, before the medication. All patients had normal TBUT time in both right and left eye (>10 seconds). All patients had intact corneal sensation in right and left eye.

Table 4: Schirmer-1 & 2, TBUT and Corneal sensations post medication

Schirmer 1 (mm)	**Mean**	**SD**	**Median**	**IQR**
Right	13.5	2.72	14.0	10,15

Left	13.5	2.72	14.0	10,15
Schirmer 2 (mm)				
Right	11.7	3.00	12.0	10,15
Left	11.7	3.00	12.0	10,15
TBUT	**Normal (>10 seconds)**		**Abnormal**	
	No of patients	Percentage	No of patients	Percentage
Right	72	92.3	6	7.7
Left	72	92.3	6	7.7
Corneal sensation	**Both eyes**			
	Frequency	**Percentage**		
Intact	66	84.6		
Brisk	4	5.1		
Reduced	8	10.3		

Post-medication, the schirmer 1 was reduced in 66.7% of the patients, increased in 11.5% and remained same in 21.8% of the patients in right eye and left eye. Post-medication, the schirmer 2 was reduced in 66.7% of the patients, increased in 11.5% and remained same in 21.8% of the patients in right eye and left eye. TBUT was found abnormal among 7.7% of the patients in either eye, at 6 months after the anti-glaucoma medications. Schirmer 1 scores was significantly reduced post medication in both right ($p<0.001$) and left eyes ($p<0.001$) Schirmer 2 scores was significantly reduced post medication in both right ($p<0.001$) and left eyes ($p<0.001$). Corneal sensation was found to be intact in 84.6%, brisk in 5.1% and reduced in 10.3% of the both eye, at 6 months after the anti-glaucoma medications.

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Table 5: Ocular surface disease index (OSDI) Scores

OSDI Scores	**Percentage**
Normal (0-12)	11.5%
Mild (13-22)	26.9%
Moderate (23-32)	43.6%
Severe (33-100)	17.9%

Normal ocular surface disease index (OSDI) is noted in 11.5% of the patients, mild OSDI is noted in 26.9% of the patients, moderate OSDI is noted in 43.6% of the patients, severe OSDI is noted in 17.9% of the patients.

DISCUSSION

Intraocular pressure (IOP) is the only modifiable in patients with glaucoma, treatment with IOP‐lowering topical medication has been essential to prevent the worsening of glaucomatous damage.[17,18] In the present study, majority of the patients were males (67.9%). Most of the previous studies also included majority of males as the study participants.[19,20]

Duration of the anti-glaucoma medication has also been shown to increase the risk of dry eye disease.[21] The medication used in the present study was Timolol (monotherapy) for six months duration. Wong et al included patients taking different variety of anti-glaucoma medications as monotherapy as well as combination therapy. (Prostaglandin analogues, Timolol, Dorzolamide etc.,) for a mean duration of 5.3 years.[19] Ghosh et al reported that patients were using the medications for mean duration of 7.9 years.[18] Patients in Cvenkel et al were taking the anti-glaucoma medication for a median duration of 6 months.[22]

The mean Schirmer 1 test scores of the patients in our study were 16.8 before the medication. In contrast, previous studies reported lower Schirmer test values. Cvenkel et al reported lower median Schirmer value of 10 in the control group without medication.[22] Baffa et al observed a Schirmer test of 9.2 for the normal patients who did not take anti-glaucoma medications.[20]

Post Medication, TBUT was found abnormal among 7.7% of the patients in either eye in our study, which was higher than the pre-medication rate. Ghosh et al reported much higher abnormal TBUT of 57.3% in the medication group, which was significantly higher than controls.[18] Similarly, Wong et al, Baffa et al and Cvenkel et al reported that eyes treated with anti-glaucoma medications had a significantly shorter TBUT than the normal eyes/control patients.[20,22] Kurna et al noted that there was no significant difference in terms of TBUT between various groups of anti-glaucoma medication and yet they also found beta-blockers had produced relatively more damage in the ocular surface. Increasing number of eyes drops per day also had detrimental effect on the TBUT.[23]

Post-Medication, the mean Schirmer 1 test scores was 13.5 in our study, and it was significantly reduced in comparison to the pre-medication values. Similarly, the mean Schirmer 2 test scores was 11.7 and also had significant reduction from pre-medication values. This signifies a reduction in the tear secretion post-medications in our glaucoma patients. Kurna et al noted that there was significant difference in terms of Schirmer I test between various groups of anti-glaucoma medication.[23] While Cvenkel et al reported Schirmer test value of 10 in the treated group, it was not significantly different from the control group.[22] Schirmer 1 was normal in all patients in our study but it's reduced when compared to the pre-medication values, while Schirmer 2 test was found abnormal among 14.1% of the patients in either eye. Similarly, 13% of the patients in Ghosh et al reported abnormal values.[18]

Preservative usage in the anti-glaucoma medication has shown to worsen the deleterious tear film changes in the glaucoma patients. Kobia-Acquah et al reported 3.5 times more odds of dry eye disease when preservatives are used in the anti-glaucoma medication.[24] Goldberg et al reported that when benzalkonium chloride free medication was used, it led to reduction in the dry eye symptoms.[25] Using such preservatives in medications on a regular basis has the potential to cause or exacerbate underlying OSD.[21].

Among the patients in our study, corneal sensation was found to be intact in 74.4%, brisk in 15.4% and reduced in 10.3% of the right eye. Terai et al reported a significant reduction of corneal sensation in patients taking timolol after 5 minutes.[21]

Ghosh et al reported that 15.3% reported dryness, 11.7% had gritty/sandy feel, 5% had burning feeling, 14% had sticky feeling, 23.7% had teary eyes and 22.7% had redness. Burning feeling, and sticky were found to be significantly higher prevalent among the glaucoma medication group than controls, thus implying a significant association.

The severity of the dry eye symptoms was evaluated by means of OSDI questionnaire in our patients and majority of them were found to have moderate severity after 6 months of treatment (43.6%), followed by mild (26.9%) symptoms. Wong et al and Cvenkel et al also evaluated the dry eye symptoms by means of OSDI score.[19,22] In contrast, Lee et al found that medicated group was at 5 times more risk of developing severed dry eye manifestations.[26] However, we didn't have a parallel comparison group, hence we could not assess significance of association between anti-glaucoma medication and the adverse events observed in our study.

CONCLUSION

Anti-glaucoma medication (E/D Timolol 0.5%) twice a day for a period of 6 months had significantly reduced TBUT, Schirmer-1 and Schirmer-2 among the glaucoma patients in our settings. Reduced corneal sensitivity has been noted in few patients. Anti-glaucoma medication had led to dry eye symptoms with severity ranging from moderate to severe in majority of the patients. The patients under anti-glaucoma medication must be routinely assessed for their tear film changes and managed accordingly. Multi-centric studies must be conducted to verify and apply our findings to other settings. Dose-response analysis, in terms of the effect of the number of drops per day on the tear film status and dry eye symptoms needs to be evaluated in the further studies. In future prospective, parallel groups comparison study including anti-glaucoma medications other than timolol, with & without preservatives must be conducted to evaluate the effect of these aspects on the tear film status of glaucoma patients in our settings.

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