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Original Article

Impact of Topical Antiglaucoma Medications on Tear Film Stability and Tear Secretion in Glaucoma Patients

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ABSTRACT

Background: Topical antiglaucoma medications are widely used to lower intraocular pressure, but chronic exposure to their active components and preservatives can adversely affect the ocular surface and tear film. Objective: To study the effect of topical antiglaucoma medications on tear film stability and tear secretion in glaucoma patients. **Methods**: A hospital-based prospective observational study was conducted in the Department of Ophthalmology, Andhra Medical College, Visakhapatnam, from January 2021 to October 2021, involving 88 eyes of 46 newly diagnosed glaucoma patients aged 20–60 years. The Ocular Surface Disease Index (OSDI) questionnaire, Schirmer 1 test, tear film break-up time (TBUT), and the Oxford ocular surface staining system were used to assess the ocular surface and tear film before starting topical antiglaucoma therapy and at 1, 3, and 6 months thereafter. Data were analysed using repeated measures ANOVA (SPSS version 25); $p < 0.05$ was considered statistically significant. **Results**: Mean OSDI scores increased progressively in all treatment groups, with the greatest change seen with Timolol and Brimonidine + Timolol ($p = 0.0001$). Mean TBUT declined progressively in all groups, reaching statistical significance with Bimatoprost, Travoprost, and Travoprost + Timolol ($p = 0.0001$). Mean Schirmer I values also declined in all groups, significantly so with Timolol, Brimonidine + Timolol, and Travoprost + Timolol. Oxford staining grades worsened over the follow-up period, with grade 3–4 staining most frequent in the combination-therapy groups at 6 months. **Conclusion**: Long-term use of topical antiglaucoma medications is associated with progressive deterioration of tear film stability and tear secretion, and this effect is more pronounced with combination therapy than with monotherapy. Regular ocular surface assessment should be incorporated into the routine follow-up of glaucoma patients receiving chronic topical therapy.

Keywords: *Glaucoma; Ocular surface disease; Dry eye; Tear film break-up time; Schirmer test; Ocular Surface Disease Index; Topical antiglaucoma medications.*

INTRODUCTION

Glaucoma is a progressive multifactorial optic neuropathy which is frequently associated with raised intraocular pressure (IOP). There is characteristic loss of optic nerve fibers presenting as classical optic nerve head features and correlating visual field changes.[1] The condition is more common in older individuals.[2] Glaucoma is the second leading cause of blindness worldwide.[3] The most widely prescribed therapy for glaucoma is pharmacological management with topical intraocular-pressure-lowering medications.[4] The purpose of treating glaucoma is to maintain the patient's visual function and related quality of life. Quality of life is decreased in patients with bilateral advanced glaucoma, and can also be affected by side effects of treatment.[5] However, chronic use of topical intraocular-pressure-lowering drugs and their preservatives is known to cause significant changes on the ocular surface.[6]

Ocular surface disease (OSD) is a multifactorial disorder of the tear film, eyelids, cornea, and conjunctiva. It is characterized by inadequate tear quality, an unstable tear film, and ocular surface breakdown, all of which may lead to visual interference.[7] Given this background, the present study was undertaken to evaluate the effect of topical antiglaucoma medications on tear film stability and tear secretion in glaucoma patients.

Aim and Objective

To study the effect of topical antiglaucoma medications on tear film stability and secretion in glaucoma patients.

MATERIALS AND METHODS

Study Parameter	Details
Study Design	Hospital-based prospective observational study
Study Period	January 2021 to October 2021
Study Setting	Department of Ophthalmology, Andhra Medical College, Visakhapatnam
Study Population	Patients diagnosed with glaucoma attending the Department of Ophthalmology
Sample Size	88 eyes of 46 glaucoma patients

Inclusion Criteria

1. Newly diagnosed glaucoma patients
2. Age 20–60 years (both males and females)
3. Patients willing to provide written informed consent

Exclusion Criteria

1. Active ocular inflammation or allergy
2. Lid margin disease
3. History of ocular trauma
4. Previous symptoms of dry eye or prior treatment for dry eye disease
5. Previous glaucoma surgery
6. Contact lens wearers
7. History of refractive surgery within the previous 12 months
8. Systemic diseases associated with dry eye (e.g., diabetes mellitus)
9. Use of systemic medications known to induce dry eye
10. Age > 60 years
11. Use of any topical ocular medication other than antiglaucoma drugs
12. Patients with secondary glaucoma

Tear film assessment was performed in all patients before starting topical medications, using the following:

- OSDI questionnaire
- Schirmer 1 test (S1T)
- Tear film break-up time (TBUT)
- Oxford ocular surface staining system

Ocular Surface Disease Index (OSDI) Questionnaire

This is a 12-item questionnaire designed to give a rapid assessment of symptoms of ocular irritation consistent with dry eye disease (DED) and their impact on vision-related functioning. Each symptom is given an individual score, and the total score is calculated taking into account the number of questions answered and the cumulative scores.[8] The OSDI score ranges from 0 to 100, with higher scores representing greater disability; for this reason, this questionnaire was employed in the present study.

Test for Tear Secretion – Schirmer's Test

This test provides a measure of tear production per unit time and is the most common technique for the assessment of tear secretion, first described in 1903.

Schirmer's 1 test is done with or without topical anesthesia to measure basic, combined, and reflex (total) secretion, respectively. It is performed using a no. 41 Whatman filter paper strip, 35 mm long and 5 mm wide, with a notch at 5 mm from one end to mark the position of the lid fold that helps hook the paper onto the lower lid. The strip is placed at the junction of the middle and lateral one-third of the lower lid. With the patient's eyes open in a dimly lit room, looking straight

ahead and blinking normally, both eyes are tested simultaneously, taking care not to touch the cornea. After 5 minutes, the strip is removed and the wetted length is measured from the fold.

Pathological values: Borderline dry eye – <10 mm/5 min; Hyposecretive dry eye – <5 mm/5 min.

Measurement of Tear Film Stability – Tear Film Break-Up Time (TBUT)

A fluorescein strip, moistened slightly with balanced salt solution or a similar ocular irrigant, is touched against the inferior tarsal conjunctiva, and the patient is asked to blink several times to distribute the dye across the tear film. The examiner then asks the patient to look straight ahead without blinking while the cornea is observed through the slit lamp using diffuse illumination with a cobalt blue filter. The time between the last blink and the appearance of the first randomly distributed dry spot in the fluorescein film is noted in seconds; a TBUT of 10 seconds or more is considered normal, while a TBUT of less than 10 seconds indicates the presence of dry eye.

Dry eye severity grading (DEWS report) based on TBUT: Level 1 – variable; Level 2 – <10 seconds; Level 3 – ≤5 seconds; Level 4 – ≤2 seconds.

Oxford Ocular Surface Staining System

Conjunctival and corneal staining with a dye was graded using the Oxford scheme, with grades 0–1 indicating normal findings and grades >1 indicating dry eye.

Statistical Analysis

Data were analysed using Microsoft Excel and SPSS version 25. Repeated measures ANOVA was used for statistical analysis. Results were expressed as means and percentages. A p-value of < 0.05 was considered statistically significant.

RESULTS

Table 1: Patient Profile (n = 46)

Characteristic	Frequency (n = 46)	Percentage (%)
Age distribution (years)		
30–40 years	5	10.8
41–50 years	21	45.7
51–60 years	20	43.5
Gender		
Male	21	45.7
Female	25	54.3
Laterality		
Unilateral	4	10.9
Bilateral	42	89.1

A total of 46 glaucoma patients were included in the study. The majority of patients belonged to the 41–50 years age group (21; 45.7%), followed by the 51–60 years age group (20; 43.5%), while only 5 patients (10.8%) were aged 30–40 years. There was a slight female predominance, with 25 females (54.3%) and 21 males (45.7%). Most patients had bilateral glaucoma (42; 89.1%), whereas only 4 patients (10.9%) had unilateral involvement.

Figure 1: Distribution of Cases Based on the Drug Used

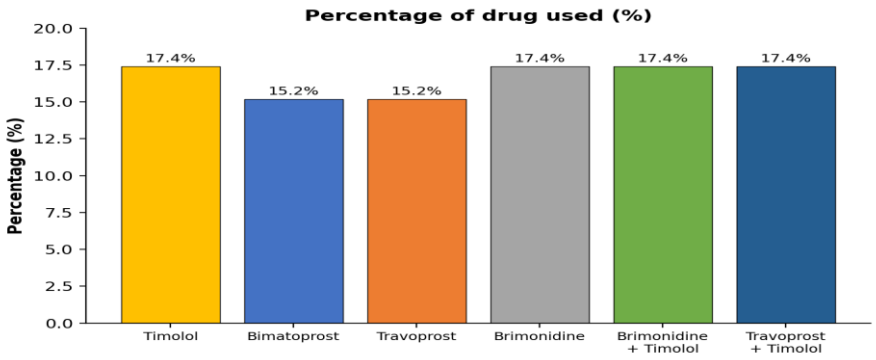

Table 2: Mean OSDI Score Before and After Medication

Drug name	Before medication	After 1 month	After 3 months	After 6 months	P-value
Timolol	4.80 ± 2.31	5.47 ± 1.81	9.13 ± 1.36	18.27 ± 2.55	0.0001 (significant)
Bimatoprost	5.93 ± 3.17	9.14 ± 2.66	10.79 ± 2.55	13.43 ± 2.68	0.051
Travoprost	6.29 ± 3.63	8.71 ± 1.73	10.57 ± 1.56	14.0 ± 1.71	0.057
Brimonidine	4.4 ± 2.95	8.47 ± 1.55	13.27 ± 3.19	16.07 ± 3.85	0.05
Brimonidine + Timolol	6.93 ± 4.15	13.27 ± 3.67	19.2 ± 1.94	22.27 ± 2.25	0.0001 (significant)
Travoprost + Timolol	9.2 ± 2.93	14.47 ± 3.85	18.53 ± 1.99	20.6 ± 1.92	0.05

Mean OSDI scores increased over time in all treatment groups, indicating worsening dry eye symptoms following topical antiglaucoma therapy. The greatest increase was observed with Brimonidine + Timolol and Timolol monotherapy, both showing statistically significant changes ($p = 0.0001$). The other treatment groups also demonstrated increased OSDI scores during follow-up, although the differences were not statistically significant or were of borderline significance ($p = 0.05–0.057$).

Table 3: Mean TBUT Before and After Medication

Drug name	Before medication	After 1 month	After 3 months	After 6 months	P-value
Timolol	16.0 ± 0.0001	16.6 ± 2.1	15.6 ± 1.96	13.2 ± 1.78	0.061
Bimatoprost	17.5 ± 2.35	15.07 ± 1.54	12.07 ± 1.27	9.5 ± 1.51	0.0001 (significant)
Travoprost	17.57 ± 2.98	15.64 ± 2.47	12.71 ± 2.16	10.14 ± 1.88	0.0001 (significant)
Brimonidine	19.8 ± 2.18	18.47 ± 1.69	15.8 ± 1.27	13.13 ± 0.92	0.055
Brimonidine + Timolol	19.47 ± 2.17	16.13 ± 1.06	13.2 ± 1.37	12.07 ± 1.16	0.05
Travoprost + Timolol	18.13 ± 2.75	14.6 ± 1.88	12.67 ± 1.92	9.87 ± 1.51	0.0001 (significant)

Mean TBUT decreased progressively over 6 months in all treatment groups, indicating reduced tear film stability. A statistically significant reduction was observed with Bimatoprost, Travoprost, and Travoprost + Timolol ($p = 0.0001$). Decreases in the Timolol, Brimonidine, and Brimonidine + Timolol groups were not statistically significant or were of borderline significance ($p = 0.05–0.061$).

Table 4: Mean Schirmer 1 Before and After Medication

Drug name	Before medication	After 1 month	After 3 months	After 6 months	P-value
Timolol	24.93 ± 4.95	22.73 ± 3.92	20.67 ± 3.89	19.4 ± 3.76	0.04 (significant)
Bimatoprost	21.71 ± 2.16	18.86 ± 1.99	17.0 ± 1.71	16.64 ± 1.82	0.58
Travoprost	21.5 ± 4.15	20.43 ± 3.45	17.64 ± 3.23	16.93 ± 2.37	0.062
Brimonidine	21.47 ± 3.07	19.53 ± 2.69	17.13 ± 2.39	16.73 ± 2.43	0.051
Brimonidine + Timolol	22.47 ± 3.31	20.47 ± 2.5	17.93 ± 1.28	15.27 ± 0.96	0.0001 (significant)
Travoprost + Timolol	21.13 ± 1.89	19.07 ± 1.83	16.93 ± 1.83	15.2 ± 1.27	0.0001 (significant)

The highest mean Schirmer I value before treatment was observed in the Timolol group (24.93 ± 4.95), while the lowest was in the Travoprost + Timolol group (21.13 ± 1.89). At 6 months, the highest mean value was in the Timolol group (19.40 ± 3.76), and the lowest was in the Travoprost + Timolol group (15.20 ± 1.27). The lowest p-value (0.0001) was observed in the Brimonidine + Timolol and Travoprost + Timolol groups, while the highest p-value was observed in the Bimatoprost group (0.58).

Table 5: Oxford Scheme Corneal and Conjunctival Staining Before and After Medication

Drug	Time Point	Score 0	Score 1	Score 2	Score 3	Score 4
Timolol	Before treatment	10 (66.7%)	5 (33.3%)	–	–	–
	After 1 month	0	9 (60.0%)	5 (33.3%)	1 (6.7%)	–
	After 3 months	–	3 (20.0%)	9 (60.0%)	3 (20.0%)	–
	After 6 months	–	0	3 (20.0%)	7 (46.7%)	5 (33.3%)
Bimatoprost	Before treatment	10 (71.4%)	4 (28.6%)	–	–	–
	After 1 month	2 (14.3%)	12 (85.7%)	0	0	–
	After 3 months	–	8 (57.1%)	6 (42.9%)	0	–
	After 6 months	–	4 (28.6%)	7 (50.0%)	3 (21.4%)	0
Travoprost	Before treatment	9 (64.3%)	5 (35.7%)	–	–	–
	After 1 month	0	13 (92.9%)	1 (7.1%)	0	–
	After 3 months	–	9 (64.3%)	4 (28.6%)	1 (7.1%)	–
	After 6 months	–	2 (14.3%)	9 (64.3%)	3 (21.4%)	0
Brimonidine	Before treatment	9 (60.0%)	6 (40.0%)	–	–	–
	After 1 month	0	10 (100%)	0	0	–
	After 3 months	–	10 (66.7%)	5 (33.3%)	0	–
	After 6 months	–	1 (6.7%)	9 (60.0%)	5 (33.3%)	0
Brimonidine + Timolol	Before treatment	10 (66.7%)	5 (33.3%)	–	–	–
	After 1 month	0	10 (66.7%)	5 (33.3%)	0	–
	After 3 months	–	5 (33.3%)	6 (40.0%)	4 (26.7%)	–
	After 6 months	–	0	8 (53.3%)	4 (26.7%)	3 (20.0%)
Travoprost + Timolol	Before treatment	10 (66.7%)	5 (33.3%)	–	–	–
	After 1 month	0	9 (60.0%)	6 (40.0%)	0	–
	After 3 months	–	2 (13.3%)	8 (53.3%)	5 (33.3%)	–
	After 6 months	–	0	5 (33.3%)	5 (33.3%)	5 (33.3%)

Before treatment, score 0 ranged from 60.0% to 71.4%, while score 1 ranged from 28.6% to 40.0% across all drug groups. At 1 month, score 1 was the most common finding (60.0%–100%). At 3 months, score 2 ranged from 28.6% to 60.0%, and score 3 ranged from 0% to 33.3%. At 6 months, score 3 ranged from 21.4% to 46.7%, while score 4 ranged from 0% to 33.3%, with the highest frequency observed in the Travoprost + Timolol group (33.3%).

DISCUSSION

Demographic Characteristics

In the present study, the majority of patients were aged 41–50 years (45.7%), followed by 51–60 years (43.5%). Females (54.3%) slightly outnumbered males (45.7%), and bilateral glaucoma was observed in 89.1% of patients. A similar age distribution was reported by George et al.[9] in the Chennai Glaucoma Study, where the prevalence of glaucoma increased with advancing age. Dandona et al.[10] also reported that glaucoma is more common in middle-aged and elderly Indian populations.

OSDI Score

The mean OSDI score increased progressively in all treatment groups, with the highest score observed in the Brimonidine + Timolol group at 6 months. These findings are comparable with those of Jain et al.[11], who reported significantly higher OSDI scores among glaucoma patients receiving topical antiglaucoma medications than healthy controls. Uusitalo et al.[12] also observed worsening ocular surface symptoms with prolonged topical therapy.

Tear Film Break-Up Time (TBUT)

A progressive reduction in TBUT was observed in all treatment groups over the 6-month follow-up. Similar findings were reported by Srinivasan et al.[13], who found significantly reduced TBUT in patients receiving long-term topical antiglaucoma therapy. Aptel et al.[14] also demonstrated that chronic use of topical glaucoma medications is associated with reduced tear film stability.

Schirmer I Test

The mean Schirmer I values declined progressively during follow-up in all treatment groups. Similar findings were reported by Kumar et al.[15], who observed significantly lower Schirmer test values in patients receiving chronic topical antiglaucoma medications. Stewart et al.[16] also demonstrated a reduction in tear secretion associated with long-term glaucoma therapy.

Oxford Ocular Surface Staining

Before treatment, most eyes had Oxford staining scores of 0 or 1, while higher grades became increasingly frequent during follow-up. Similar observations were reported by Arici et al.[17], who found significantly increased fluorescein and lissamine green staining in patients receiving preserved antiglaucoma medications. Baudouin et al.[18] also demonstrated progressive ocular surface epithelial damage with long-term topical glaucoma therapy.

CONCLUSION

The present study demonstrated that topical antiglaucoma medications adversely affected the ocular surface and tear film over a 6-month follow-up period. Progressive worsening was observed across all ocular surface parameters, including increased Ocular Surface Disease Index (OSDI) scores, reduced tear film break-up time (TBUT), decreased Schirmer I test values, and higher Oxford ocular surface staining scores. These findings indicate deterioration in both tear film stability and tear secretion following long-term topical antiglaucoma therapy. Combination therapy was associated with greater ocular surface changes than monotherapy, suggesting that the use of multiple topical medications may increase the risk of ocular surface disease.

Among the treatment groups, combination therapies, particularly Brimonidine + Timolol and Travoprost + Timolol, showed greater deterioration in tear film parameters and ocular surface staining during follow-up. These changes may negatively affect patient comfort, treatment adherence, and quality of life. Therefore, regular assessment of the ocular surface using OSDI, TBUT, Schirmer I test, and Oxford staining should be incorporated into the routine evaluation of glaucoma patients receiving long-term topical therapy.

Early identification and appropriate management of ocular surface changes may help reduce treatment-related complications, improve patient compliance, and optimize long-term outcomes in glaucoma management. Further studies with larger sample sizes and longer follow-up are recommended to validate these findings.

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