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Original Research Article

A Hospital Based Prospective Assessment of the Ocular Surface Disease in Glaucoma Patients on Topical Medications and its Relation to Duration of Treatment and Number of Medications

Abhilasha[1], Rajeev Kumar[2], Jawed Iqba[3]

[1]Senior Resident, Department of Ophthalmology, Anmmch, Gaya, Bihar, India
[2]Senior Resident, Department of Ophthalmology, Anmmch, Gaya, Bihar, India
[3]Assistant Professor, Department of Ophthalmology Anmmch, Gaya, Bihar, India

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Corresponding author: Dr. Rajeev Kumar
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Abstract

Aim: This study was done to check for the presence of OSD in patients of glaucoma on topical antiglaucoma medications and to analyze the severity of OSD with duration of treatment and number of topical antiglaucoma medications.

Methods: The present study was conducted at department of ophthalmology, ANMMCH, Gaya, Bihar with 8 months of duration. In this study, a total of 50 glaucoma patients on antiglaucoma medications and 50 normal controls were included.

Results: Among glaucoma patients, there were 60% (30) males and 40% (20) female patients. Among normal controls, 64% (32) were males and 36% (18) were females. Among glaucoma patients, 72% (36) showed the presence of OSD on OSDI questionnaire. Out of these, 58% (29) of patients had mild to moderate OSD and 16% (8) of patients had severe OSD. Based on Schirmer's 1 test, 70% (35) of patients showed decrease in quantity of tears with 64% (32) and 6% (3) of patients showing mild‑moderate and severe decrease in quantity of tears, respectively. Tear film break up time (TBUT) was abnormal in 84% (42) of patients. On comparing increased number of medications from one or two and three or four drugs for OSDI score, it was found that mean OSDI score increased from mild (16.88) to moderate (24.00), respectively, which was statistically significant (P value 0.03). The mean OSDI score in patients using medications for <1 year and for 2 to 5 years was 15.69 and 18.59, respectively, which indicates mild OSD. It was 32.33 for patients taking medications for 6 years or more, indicating moderate OSD. The result was statistically significant (P value 0.0017).

Conclusion: Our study shows that antiglaucoma medications contribute to the occurrence of dry eye symptoms. There is increase in OSD severity with increase in duration of treatment and increased number of topical medications.

Keywords: Antiglaucoma medications, ocular surface disease, ocular surface disease index

Introduction

Ocular surface disease is a multifactorial disorder of the conjunctival epithelium, corneal epithelium, lacrimal glands, and meibomian glands that results in either deficient or inappropriate tear production and leads to decreased visual clarity and ocular discomfort through various inflammatory pathways. [1,2] Ocular surface disease can occur in conjunction with many other ocular conditions, and

here we aim to focus on the coexistence of ocular surface disease with glaucoma.

Glaucoma is the second leading cause of blindness in the world and is expected to affect 79.6 million people by 2020. At present, 11% of the 5 million Americans over 50 who have dry eye disease also have glaucoma. [3-6] Topical medical therapy is the most common initial treatment for glaucoma, and 49-59% of glaucoma patients on topical anti-glaucomatous medications have ocular surface disease. [7,8] Ocular surface disease in these patients can be a pre-existing condition that is exacerbated by topical therapy or a novel disease that manifests after initiation of topical glaucoma therapy. Topical glaucoma medications can cause burning, irritation, itching, tearing, and decreases in visual acuity within three months of medication initiation. [2,9,10]

Causes of OSD are age, dry eye syndrome, blepharitis, Meibomian gland dysfunction, environmental and genetic factors. Topical medications are also responsible for OSD, especially in case of preservative-containing eye drops. Antiglaucoma medications are daily usage, multidose medications that can cause increased tear evaporation leading to ocular surface disorder. The prevalence of OSD in patients of glaucoma taking antiglaucoma medications is reported between 48% and 59%. [11,12] The impact of OSD in daily life of patient with glaucoma is an important aspect to consider in the follow-up management of glaucoma.

Furthermore, untreated primary open angle glaucoma (POAG) patients have a higher risk of ocular surface disease in part due to a 22% lower basal tear turnover rate in comparison to patients without glaucoma. [13] The resulting ocular surface disease in patients with glaucoma can lead to poor medication compliance from the associated symptoms. In addition, ocular surface disease is also linked to a higher rate of failure in subconjunctival glaucoma surgery. [14] Thus, management of ocular surface disease in glaucomatous patients is important when trying to reduce further ocular morbidity and to improve the success of glaucoma therapy.

However, previous studies reported that long-term use of glaucoma medication has led to ocular surface disease (OSD) in some patients with glaucoma, and OSD would make a negative effect on the adherence to the glaucoma treatment regimen in these patients, subsequently. [15] Therefore, evaluating and prompt management OSD in patients treated with topical glaucoma medication might be a critical issue for improving the glaucoma treatment compliance.

Methods

The present study was conducted at department of ophthalmology, ANMMCH, Gaya, Bihar with 8 months of duration. In this study, a total of 50 glaucoma patients on antiglaucoma medications and 50 normal controls were included.

The study was done in compliance with Institutional Ethics Committee. Census method of sampling was used for collection of data. Informed consent was taken from subjects for enlistment in the study. Patients with glaucoma who were on antiglaucoma medications for at least 6 months were examined. This included patients with primary open-angle glaucoma, primary angle-closure glaucoma, combined mechanism glaucoma, pseudoexfoliation, and pigment dispersion glaucoma. Consecutive number of patients who were diagnosed as glaucoma during this period or considered glaucoma suspects who were not on any antiglaucoma medication were taken as controls for this study.

Exclusion criteria included patients who had undergone trabeculectomy, patients who were using topical medications such as steroids and lubricants, patients with

any other existing ocular pathology contributing to dry eye, patients with allergy to the drugs used and patients who had undergone any other ocular surgery for the past 3 months. All subjects had complete ophthalmological evaluation for anterior segment, optic disc, intraocular pressure measurement, visual field testing. Number of topical antiglaucoma medications and duration of treatment was noted. All data were collected at a single visit during this study. Subjects were assessed for OSD by using following tests: Ocular surface disease index questionnaire[16]

Total OSDI score is calculated using the formula:

OSDI score = [(Sum of scores for all questions asked) ×25)]/(Total number of questions answered)

Using this, subjects were classified for severity of OSD as normal (score 0–12), mild (score 13–22), moderate (23–32), and severe (33–100).

Schirmer's test

This test measures secretion of tears over a specified time. Schirmer's test 1 measures total tear secretion, is performed without topical anesthesia. Standardized Schirmer's strips were used. The strip was folded at the notch and placed at the junction of the middle and lateral thirds of the lower eyelids. Patient was asked not to squeeze the eyes and keep the eyes open. After 5 min, the strip was removed and the amount of wetting was measured. The results were interpreted as follows; more than 10 mm of wetting after 5 min was considered normal, 8–10 mm as mild dryness, 5–7 mm as moderate dryness, and <5 mm of wetting was considered severe dryness at the end of 5 min.

Tear film break up time

Fluorescein strip moistened with saline was introduced into the conjunctival sac taking caution to avoid stimulation. The individuals were then instructed to blink several times for a few seconds to ensure adequate mixing of fluorescein. The tear film was then examined with a broad beam of cobalt blue filter. The interval between the last complete blink and the appearance of the first corneal black spot or line in the stained tear film was measured using a stopwatch. Dryness was graded on TBUT value as follows: a TBUT value more than 10 s was considered normal, a value of 8–10 s as mild dryness, a value of 5–7 s as moderate dryness, and a value <5 s as severe dryness.

For the study, only one eye of the subject was considered. Eye with more severe dryness was used in the study in case of difference of values among the two eyes in grading of severity among three tests of OSDI score, Schirmer's test 1, and TBUT values. OSD was diagnosed using Schirmer's test 1 and TBUT and in case of varying grades of severity among these two tests higher value of severity in either of the tests was considered for that eye. OSDI questionnaire was used to grade severity of OSD as subjective analysis for vision‐related quality of life.

All data were entered in Microsoft Excel 10 and analysis was done with the help of IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N. Y., USA). Continuous variables were shown in the form of mean ± standard deviation and categorical variables were shown in the form of count and percent. One‐way analysis of variance test was used for means comparison analysis of paired parameters between the groups. A $P < 0.05$ was considered statistically significant.

Results

Among glaucoma patients, there were 60% (30) males and 40% (20) female patients. Among normal controls, 64% (32) were males and 36% (18) were females. Mean age of the glaucoma patients was 56.48 ± 8.27 years ranging from 40 to 70 years and among controls, it was 55.43 ± 5.41 years, ranging from 45 to 65 years. The

difference among two groups for age criteria was not significant (P = 0.43).

Table 1: Test results of patients on antiglaucoma medications

Test results	OSDI (n=50), n (%)	Schirmer's test (n=50), n (%)	TBUT (n=50), n (%)
Normal	13 (26)	15 (30)	8 (16)
Mild	15 (30)	15 (30)	25 (50)
Moderate	14 (28)	17 (34)	15 (30)
Severe	8 (16)	3 (6)	2 (4)

Among glaucoma patients, 72% (36) showed the presence of OSD on OSDI questionnaire. Out of these, 58% (29) of patients had mild to moderate OSD and 16% (8) of patients had severe OSD. Based on Schirmer's 1 test, 70% (35) of patients showed decrease in quantity of tears with 64% (32) and 6% (3) of patients showing mild‑moderate and severe decrease in quantity of tears, respectively. Tear film break up time (TBUT) was abnormal in 84% (42) of patients.

Table 2: Relationship between treatment duration and ocular surface disease index questionnaire, Schirmer's test, and tear film breakup time test

Treatment duration (years)	Number of patients	Normal	Mild	Moderate	Severe
OSDI					
<1	24	8	10	1	3
2-5	20	5	10	5	0
≥6	6	0	0	2	4
Schrimer's test					
<1	24	10	7	1	2
2-5	20	5	8	7	0
≥6	6	0	6	0	0
TUBT					
<1	24	5	12	5	2
2-5	20	4	8	8	0
≥6	6	0	2	4	0

Table 3: Relationship between number of drugs and ocular surface disease index questionnaire, Schirmer's test, and tear film breakup time test

Treatment duration (years)	Number	Normal	Mild	Moderate	Severe
OSDI					
1	16	6	5	5	0
2	20	5	7	6	2
3	10	1	5	4	0
4	4	4	0	0	0
Schrimer's test					
1	16	10	4	2	0
2	20	5	7	8	0
3	10	1	5	4	0
4	4	0	0	2	2
TUBT					
1	16	8	8	0	0

2	20	1	9	10	0
3	10	0	6	4	0
4	4	0	3	0	1

On comparing increased number of medications from one or two and three or four drugs for OSDI score, it was found that mean OSDI score increased from mild (16.88) to moderate (24.00), respectively, which was statistically significant (P value 0.03). The mean OSDI score in patients using medications for <1 year and for 2 to 5 years was 15.69 and 18.59, respectively, which indicates mild OSD. It was 32.33 for patients taking medications for 6 years or more, indicating moderate OSD. The result was statistically significant (P value 0.0017). OSD severity based on above tests increased with increase in duration of treatment and increase in number of medications as shown in Tables 2 and 3.

Discussion

OSD is characterized by an inadequate quantity of tears, an unstable tear film, and disruption of the integrity of the ocular surface. [15,17] Both the instability of the lipid layer of the tear film and meibomian gland dysfunction are reported to contribute to the emergence of OSD. [18] Recently, Lip iView interferometer (Tear Science Inc., Morrisville, NC, USA), a new device that can measure tear film lipid layer thickness (LLT) quantitatively using interferometry, has been reported to be a beneficial tool to evaluate the relationships between OSD and Meibomian gland dysfunction in other ocular disorders. [19] Meanwhile, glaucoma medication can lead to several adverse events on the ocular surface, we suggest that Lipi View interferometer may provide meaningful information about the relationship between the changes in the lipid layer and topical glaucoma medication.

In our study, severity of OSD based on OSDI questionnaire increased with age (P < 0.001>), while among males and females, it was not statistically significant (P = 0.208). It has been reported by German Glaucoma and Dry Eye Register that the incidence of dry eye increases with age and is higher among females. Higher number of males and smaller sample size in our study might be the reason for non-significance for severity among gender group. Our study shows that severity of OSD based on OSDI questionnaire in patients on antiglaucoma medications increases with increase in duration of treatment and number of medications. The long‑term use of multiple antiglaucoma medications has been associated with increased prevalence of dry eye as reported in German Glaucoma and Dry Eye Register study. [20]

Khamar et al. [21] studied the prevalence of dry eye in patients on single drug versus combination of two drugs and duration of treatment of < 1 year versus more than 1 year. Their study reported that time period rather than number of drugs plays a role in the onset of dry eye symptoms. Our study showed similar results. Barisic et al. [22] observed that among 110 glaucoma‑treated patients, 75% showed the presence of OSD based on OSDI questionnaire. Out of them, 17% had scores of mild OSD, 11% had moderate OSD, and 47% had severe OSD. The prevalence of OSD based on OSDI questionnaire was similar to our study (74%). Our study has more patients with mild and moderate OSD. However, they had more patients with severe OSD as compared to our study. Our study reported higher prevalence of OSD among glaucoma patients on antiglaucoma medications as compared to study by Vinutha et al. [23] in which 32% showed the presence of OSD on OSDI score. Their Schirmer's test (72%) results were similar to our study (70%) whereas their TBUT results were 74% as compared to our higher TBUT results (84%). They also reported increased severity of OSD with increase in duration of treatment and

number of medications as shown in our study.

Our study showed that there was increase in mean OSDI score with increase in number of medications from one or two (16.88) to three or four (24.00) which was statistically significant (P value 0.0311). A study by Fechtner et al. [24] showed similar increase in OSDI score with increase in number of drugs. Mean OSDI score in their study was 12.9 for patients on single medication which was significantly lower when compared to patients on two (16.7; P = 0.007) or three medications (19.4; P < 0.001). In our study, analysis for duration of treatment in patients using medications, mean OSDI score increased with duration for <1 year, 2 to 5 years, and 6 years or more (15.69 vs. 18.59 vs. 32.33; P = 0.0017). In a study by Pai and Reddy, mean OSDI scores were 16.5 and 27.1 in patients using medications for <5 years and more than 5 years, respectively (P < 0.001>). [25]

Role of preservatives in antiglaucoma medications as a causal factor for the occurrence of OSD has been studied. However, we have not studied their role in our study. Variations in prevalence in different studies may be due to differences in methodology, age, severity of disease, duration of therapy, and the type and number of medications used. In our study, we used OSDI questionnaire for subjective analysis, Schirmer's test for tear production, and TBUT for meibomian gland function. [26]

Conclusion

Our study shows that antiglaucoma medications contribute to the occurrence of dry eye symptoms. There is increase in OSD severity with increase in duration of treatment and increased number of topical medications. This can affect the compliance of patient, thus affecting the treatment of glaucoma and in overall their quality of life. The ocular surface status should be evaluated regularly for timely detection and treatment of OSD.

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