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Original Research Article

OCULAR SURFACE CHANGES IN GLAUCOMA PATIENTS ON LONG-TERM ANTI-GLAUCOMA MEDICATIONS V/S NORMAL PATIENTS.

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ABSTRAC

Background: Glaucoma is one of the leading causes of blindness in India. In cases of glaucoma increased intraocular pressure (IOP) is the primary modifiable risk factor. Ocular surface disease (OSD) in these patients results from impaired tear film function and long-term use of antiglaucoma medications. This effect is significant in medications containing benzalkonium chloride (BAK) as a preservative. BAK, though cost-effective, can cause allergic reactions, inflammation, and epithelial damage. Alternative preservatives like Purite® and SofziaTM help mitigate these effects. Reducing the number of medications or using preservative-free options can alleviate OSD and improve patient outcomes.

Materials and Methods: An Analytical cross-sectional study to compare the prevalence of ocular surface disease in 61 glaucoma patients and 61 non-glaucoma patients on long-term topical anti-glaucoma medications. The study parameters evaluated include the Ocular surface disease index questionnaire (OSDI) and using the Schirmer 1 test and Tear break-up time (TBUT), ocular surface staining score (OSS) with fluorescein and lissamine green.

Results: The prevalence of dry eye disease among glaucoma cases was significantly high at 60.7% compared to 19.7% in the non- glaucoma patients ($p<0.01$). A marginal tear break-up time (TBUT) was observed in 60.7% of glaucoma patients. Mild to moderate tear deficiency on Schirmer's test was observed in 60.7% of glaucoma patients, while mild to moderate ocular surface disease severity on OSDI was seen in 54.1% (mild) and 6.6%(moderate) of glaucoma patients. Abnormal Ocular surface staining score is seen in 45.9% of glaucoma patients.

Conclusion: The presence of dry eye disease in this population is associated with the duration of glaucoma, the number of drugs and the presence of Benzalkonium chloride (BAK) as a preservative in anti-glaucoma drugs. Screening can detect dry eye in glaucoma patients early thus decreasing disease severity and increasing drug compliance.

Keywords: Ocular surface disease, Glaucoma, OSDI, OSS, TBUT, BAK, Schirmer.

INTRODUCTION

Glaucoma is an optic neuropathy with a multi-factorial aetiology; the increased intraocular pressure (IOP) is the only risk factor we can acton and is thought to play the main role in pathogenesis.[1] India contributes to the highest (23.5%) regional burden of global blindness due to glaucoma.[2]

Ocular surface disease (OSD) and glaucoma are frequent co-morbidities in geriatric patients.[3] The ocular surface which consists of subepithelial fibrous tissue beneath the corneal and conjunctival

epithelium, is essential for the eye's structural integrity and optical acuity. To facilitate the proper functioning of the ocular surface cells, it is imperative that a stable tear film adequately protects them while the eye is open. Impairment of this function causes OSD, also known as dry eye disease, which is a complex ocular surface disorder caused by multiple factors. Higher expression of HLA-DR on conjunctival epithelial cells indicates that applying antiglaucoma drops to the eye for at least three months results in considerable subclinical inflammation.[4]

Due to cost-effectiveness, the preservative benzalkonium chloride (BAK) is present in most topical antiglaucoma drugs, especially in government settings. It reduces the chance of an eye infection by preventing microbiological growth in the drug. The benefits of using preservatives include longer drug shelf life, less biodegradation, and lower microbiological contamination.[5]

Among the most frequent side effects are local allergic reactions, abnormal tear film formation, prolonged conjunctival inflammation, corneal epitheliopathy, punctate epitheliopathy, disruption of epithelial function, persistent inflammatory infiltration, expression of inflammatory markers, delayed wound healing, and squamous metaplasia.[6,7] To avoid the harmful effects of BAK and other preservatives in multidose preparations, Purite® and SofziaTM are substitute ophthalmic preservatives.

It is crucial to ascertain the severity of the illness, the patient's tolerance to preservatives, and the patient's overall therapy objectives, as antiglaucoma side effects are a severe concern. As an additive or alternative treatment, we can decrease the number of medications used, utilise a fixed combination of medications, and add non-BAK-preserved, preservative-free, or oral medication to lessen the severity of ocular surface disease.[8,9]

MATERIALS AND METHODS

This was an analytical cross-sectional study. Patients with glaucoma (n=61) formed the study group; age and gender-matched normal patients who were not on topical medications were included. Informed consent was obtained from all participants. Eligible participants in the study group were individuals aged 18 years or more with POAG and had been exclusively on one or more topical antiglaucoma medications for at least 6 months before enrolment. The normal patients group was age and sex-matched individuals who had not been on any topical medication in the preceding 2 months. Individuals with antecedent corneal or conjunctival surgery, topical corticosteroid or contact lens wear, and/or current use of dry eye therapeutic agents and history of any systemic illness causing dry eye were excluded from the study. Approval was obtained from the hospital's Ethical Review Committee.

Eligible consenting participants were evaluated for signs of Ocular surface disease (OSD) using a triad of objective tests in the following order: fluorescein tear breakup time(FTBUT), Schirmer I test (without anaesthesia),and ocular surface staining with fluorescein and lissamine green.

Schirmer Itest was performed by meticulously applying a graduated Whatman 41 filter (Schirmer strip) to the inferior fornix for 5 minutes, with the rounded end bent at the zero mark. A diagnosis of ocular surface disease (OSD) using the Schirmer I test was made when the solvent line on the Schirmer strip advanced less than 10 mm.[10]

The fluorescein tear breakup time (FTBUT) was measured by moistening a sterile fluorescein strip containing 1 mg of dye with three drops of preservative-free 0.9% saline using a tuberculin syringe and needle. After about 10 seconds, the excess fluid was shaken off, and the strip's wetend was carefully placed on the lower fornix to avoid triggering reflex tearing. The time from the last complete blink to the initial appearance of a tear film breakup (micelle formation) was recorded with a digital stopwatch, and the average of three consecutive measurements was taken for each eye.[11]

Ocular surface staining was assessed using the SICCA Ocular Surface Staining Score, which involved the sequential application of fluorescein and lissamine green dyes for corneal and conjunctival staining, respectively. The lissamine green dye was applied using sterile strips containing 1.5 mg of the dye.[12]

OSDI is generally a questionnaire containing 12 questions divided into three groups: Symptoms of the eye, Vision-related functions, Environmental factors OSDI scoring is based on a 0- 100 scale, with the highest score representing greater disability. The OSDI questionnaire is graded on a scale from 0 to 4, where 0 indicates none of the time; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time.

Continuous data, such as the Schirmer's test results, Tear Break-Up Time (TBUT), and Ocular Surface Disease Index (OSDI) scores, will be presented as mean ± standard deviation (SD). Categorical data, including the prevalence of dry eye disease (DED) and abnormal ocular surface staining scores, will be expressed as frequencies and percentages. For the comparison of continuous variables between the two groups, the unpaired t-test will be applied. The Chi-square test will be used to analyze categorical variables. A p-value of less than 0.05 will be considered statistically significant, indicating a meaningful difference between the glaucoma and non-glaucoma groups in terms of ocular surface parameters.

RESULTS

The analysis of the demographic data between both the groups showed that both groups consisted of 61 eyes each. In terms of gender distribution, the anti-

glaucoma group had a higher proportion of males (39 males, 22 females), while the non-glaucomatous group had a more balanced gender ratio (31 males, 30 females). The mean age in the anti-glaucoma group was slightly higher at 58.11 years (±11.36), compared to 55.46 years (±13.48) in the non-glaucomatous group. However, the difference in mean age of both the groups was not statistically significant (P=0.2427). [Table 1]

All the mean ocular surface parameters like tear break-up time, Schirmer's, Ocular surface disease index and ocular surface staining with fluorescein and lissamine green were significantly higher in cases of glaucoma than controls (p<0.01). [Figure 1]

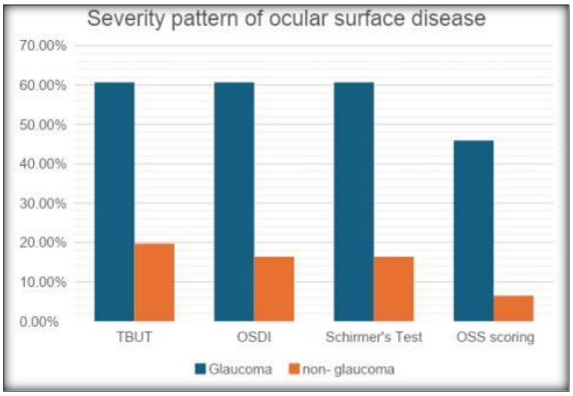

Figure 1: Severity pattern of ocular surface disease

No association of dry eye disease (DED) was observed with increasing age in the present study (p-0.07). No association of dry eye disease was observed with any specific gender in the present study (p-0.093). Incidence of OSD was observed as 57.1% in cases on one anti-glaucoma drugs as compared to 63% and 66.7% in cases on two and three drugs respectively (p – 0.086). The prevalence of OSD among glaucoma cases was significantly high at 60.7% as compared to 19.7% in the non-glaucoma population (p<0.01). [Table 2]

The comparison between glaucoma and non-glaucoma patients revealed significant differences in tear film stability, Schirmer's test, ocular staining score and ocular surface disease index. Glaucoma patients showed a higher prevalence of mild to moderate impairment in tear break-up time (p < 0.01) and ocular surface disease (p < 0.01), while non-glaucoma patients mostly had normal results. Similar trends were seen in Schirmer's test, where glaucoma patients exhibited more signs of mild dry eye (p < 0.01), and in the ocular staining score, which showed more abnormalities in the glaucoma group (p < 0.0001). All differences were statistically significant, indicating worse ocular surface conditions in glaucoma patients. [Table 3]

The incidence of dry eye disease was significantly associated with duration of glaucoma. The incidence of OSD was 55.6% in cases with less than 5 years duration, 57.7% in cases with 5 to 7 years and 70.6% in cases with more than 7 years of glaucoma (p<0.01). A significant association was observed between presence of OSD among glaucoma patients and presence of Benzalkonium chloride (BAK) as a preservative in anti-glaucoma drugs. All 37 cases of dry eye disease (DED) observed in present study were having BAK as preservative in their drugs (p<0.01). The incidence of OSD was 57.1% in patients with one anti-glaucoma drug compared to 63% and 66.7% in cases on two and three drugs respectively. [Figure 2]

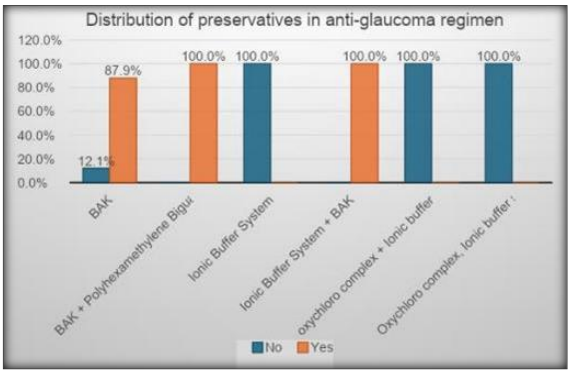

Figure 2: Distribution of preservatives in anti-glaucoma regimen

Table 1: Demographic Details of The studied cases

Demographic data	Anti-glaucoma therapy group	Non- glaucomatous patient
No. of eyes	61	61
Gender (M/F)	39/22	31/30
Mean age (Mean±SD)	58.11±11.36	55.46±13.48
P = 0.2427 (Not significant) 95% CI =-7.1189 to 1.8189		

Table 2: Comparison of Dry Eye Disease (DED) in studied groups

Dry eye disease (DED)	Group		Total
	Anti-glaucoma therapy group	Non- glaucomatous patient	
No	24	49	73
	39.30%	80.30%	59.80%
Yes	37	12	49
	60.70%	19.70%	40.20%
Total	61	61	122
	100.00%	100.00%	100.00%
p- value <0.01			

Table 3: Tear film stability, Schirmer's test, ocular staining score and ocular surface disease index

	Glaucoma (%)	Non -Glaucoma patients	*p*
Tear Break-Up Time			
Normal	39.30%	80.30%	<0.01
Mild- Moderate	60.70%	19.70%	<0.01
Severe	0.00%	0.00%	-
Ocular Surface Disease Index			
Normal	39.30%	83.60%	<0.01
Mild	54.10%	16.40%	<0.01
Moderate	6.60%	0.00%	<0.01
Severe	0.00%	0.00%	<0.01
Schirmer's Test			
Normal (>=10 mm)	39.30%	83.60%	<0.01
Mild (7-9 mm)	54.10%	16.40%	<0.01
Moderate (5-6 mm)	6.60%	0.00%	<0.01
Severe <5	0.00%	0.00%	<0.01
Ocular Staining Score			
Normal (<3)	54.10%	93.40%	<0.0001
Abnormal (≥3)	45.90%	6.50%	<0.0001

DISCUSSION

In the present study, the prevalence of dry eye disease among glaucoma cases was significantly high at 60.7% compared to 19.7% in the non-glaucoma population (p<0.01). A marginal decrease in tear break-up time (Table No. 3) was observed in 60.7% of glaucoma cases and significantly less in the non-glaucoma population, 19.7% (p<0.01). Similarly, Awe OO,[13] in their study found FTBUT in POAG patients vs controls to be 83.5% vs 57.3%, p<0.001, respectively. Pai Vijaya et al,[14] found TBUT values of glaucoma vs controls to be 67.1% vs 47.8%, which was similar to our study.

In our study, mild to moderate tear deficiency on Schirmer's I test was observed in 60.7% of glaucoma patients (p<0.01) and 16.4% of non-glaucoma patients. In their study, Saini M et al,[15] observed mean Schirmer values in glaucoma patients of 7.63±2.64 and in controls of 12.86 ±1.93. In Pai Vijaya's et al,[14] study, Schirmer I decreased by 84%, which was much greater than in ours. Similarly, the Awe OO13 study showed Schirmer I in the glaucoma group at 30.1% vs the control group at 17.5% (p=0.033). In our study, mild to moderate ocular surface disease severity on OSDI was seen in 54.1% and 6.6% of glaucoma cases, as compared to 16.4% and 0% in non-glaucoma controls (p<0.01). Pai Vijaya et al,[14] observed that the prevalence of OSD was significantly higher in the study group (72.4%) compared to controls (44.6%) using the OSDI questionnaire. OSD is present in approximately 15% of the general elderly population and is reported in 48% to 59% of patients treated with topical anti-glaucoma medications.

Our study showed abnormal ocular surface staining scores in 45.9% of glaucoma patients vs 6.5% of non-glaucomatous patients. Awe OO et al,[13] observed ocular surface staining in glaucoma vs controls (62.1% vs. 31.1%; P < 0.001). Pai Vijaya H,[14] observed Lissamine green staining was positive in 36.2% of patients in the study group and 31.8% of controls. The incidence of dry eye disease was observed as 57.1% in cases on one anti-glaucoma drug, as compared to 63% and 66.7% in cases on two and three drugs, respectively, which was not significant (p = 0.086). In a similar study, Awe OO,[13] found that the prevalence of ocular surface disease (OSD) based on all three objective tests (FTBUT, Schirmer, and OSDI) was not significantly influenced by the number of medications used. However, the prevalence of OSD was consistently higher in patients using medications compared to the control group, regardless of the number of topical medications. Specifically, the Schirmer test showed a prevalence of 8%, 18%, and 5% in patients using one, two, and three medications, respectively.

The limitations of our study are its cross-sectional design and relatively small number of subjects, who were examined at different times of the day and year. As in our study, a significant association was observed between the presence of dry eye disease among glaucoma patients and the presence of Benzalkonium chloride (BAK) as a preservative in anti-glaucoma drugs. All 37 glaucoma cases of DED observed in the present study were using drugs containing BAK as a preservative (p<0.01). The other 24 patients who had not developed DED were on an ionic buffer system, oxychloride complex as well as ionic buffer system, and 4 patients on BAK. To study the effects of multiple drugs or combinations of drugs in glaucoma patients, a larger sample size or longer follow-up is required to establish the prevalence of ocular surface disease and the toxicity of preservatives used in anti-glaucoma medications.

CONCLUSION

This study demonstrates a significantly higher prevalence of ocular surface disease (OSD) in glaucoma patients on long-term topical antiglaucoma medications compared to non-glaucoma patients. The severity of OSD was associated with the duration of glaucoma and the number of medications used, particularly those containing benzalkonium chloride (BAK) as a preservative. Early detection through screening and the use of preservative-free or

alternative formulations like Purite® and SofziaTM can help reduce the burden of OSD. Optimizing treatment strategies may improve patient compliance and overall outcomes.

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