

PREVALENCE OF DRY EYE SYNDROME AMONG GLAUCOMA PATIENTS ON TOPICAL ANTI-GLAUCOMA MEDICATIONS IN A TERTIARY CARE CENTRE- AN OBSERVATIONAL STUDY

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Received : 04/01/2024
Received in revised form : 03/02/2024
Accepted : 18/02/2024

Keywords:

Glaucoma, dry eye, OSDI, Schirmer's test, TBUT, goblet cell, prevalence, antiglaucoma agents.

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DOI: 10.47009/jamp.2024.6.1.423

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 2126-2129



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Abstract

Background: Glaucoma is the leading cause of irreversible blindness worldwide. The mainstay of management is lowering of intraocular pressure by topical anti-glaucoma medications. The need for long term therapy with these drugs can cause many chronic side effects, of which dry eye and ocular surface disorder are the major concern. The aim and objective are to assess the prevalence of dry eye among primary and secondary open angle glaucoma patients taking chronic anti glaucoma medications. To study different factors involved in dry eye formation such as duration of medication and number of drugs. **Materials and Methods:** About 100 glaucoma patients of age more than 18 years with primary and secondary open angle glaucoma (SOAG) on anti-glaucoma medications with no other pre-existing ocular diseases, attending Ophthalmology OPD from March 2021 to March 2022 were included in the study. After brief history and detailed clinical examination, they were made to fill OSDI questionnaire. The patients were assessed for dry eye using Schirmer's test, Tear film break up time (TBUT) and conjunctival impression cytology. **Result:** Among 100 glaucoma patients, 65% of them were using single drug topical anti-glaucoma medication and 30% were using combination of 2 drugs. 65% had dry eye according to OSDI (ocular surface disease index), 45% and 48% had dry eye according to Schirmer's test and TBUT respectively. Impression cytology showed 40% of the patients had less than 50 goblet cell/HPF and 34% had metaplastic changes. There is positive correlation between duration of drug usage and OSDI. The goblet cell density decreases and metaplasia increases with increasing duration of topical anti glaucoma drug usage. Also, the result of OSDI questionnaire was correlating significantly with other non-invasive tests like Schirmer's test, TBUT and impression cytology. **Conclusion:** Ocular surface changes, dry eyes and tear film instability are seen in significant number of patients on topical anti- glaucoma medications with a prevalence of 65%. The prevalence increases with the duration of medication. The prevalence of dry eye among POAG patients was found to be 62.7 % and that among SOAG was 72%. There was correlation between OSDI, Schirmer's test and TBUT results. So periodic subjective and objective assessments of the ocular surface for individuals with glaucoma undergoing prolonged treatment is recommended.

INTRODUCTION

Dry eye is a major tear deficiency disorder that affects millions of people in the world.^[1] According to the International Dry Eye Workshop (DEWS) 2007, dry eye is defined as a multi - factorial tear film and ocular surface disorder that results in visual disturbance, eye discomfort and often ocular surface damage which is characterized by tear film

hyperosmolarity and ocular surface inflammation.^[2] Glaucoma is the leading cause of irreversible blindness with a global prevalence of 3.5% among age group of 40 to 80 years.^[3] The mainstay of treatment for primary open angle glaucoma is lowering of intra-ocular pressure by topical antiglaucoma medications such as Beta blockers, Alpha agonists, Carbonic anhydrase inhibitors and prostaglandin analogues. Since long term treatment is

needed in such patients, chronic side effects are a major concern, which can be caused by either the drug itself or its preservatives. These preservatives are the usual cause of ocular surface disturbances caused by the topical medications.^[4,5] The major side effects are ocular surface changes such as reduced tear secretion, reduced tear film break up time and conjunctival epithelial changes.^[6] This study was carried out to assess the prevalence of dry eye in patients using chronic anti glaucoma medications using Ocular Surface Disease Index (OSDI) and to assess the integrity of tear film by simple noninvasive methods such as Schirmer's test, Tear film break up time, Tear meniscometry, ocular surface staining and conjunctival impression cytology.

MATERIALS AND METHODS

This is a hospital based cross sectional observational study conducted in the department of Ophthalmology in Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur from march 2021 to march 2022. About 100 glaucoma patients of age group more than 18 years with primary and secondary open angle glaucoma on anti-glaucoma medications were included in the study. Patients with Primary and secondary angle closure glaucoma, post-trabeculectomy status, on topical eye drops, patients with pre -existing ocular diseases like dry eye, disorder of lids were excluded from the study. All patients underwent detailed history and clinical examination including slit lamp and fundus examination. They were asked to fill the OSDI Questionnaire. It consists of 12 questions which gives rapid assessment of symptoms of ocular irritation that is consistent with dry eye. These 12 questions were subdivided into 3 sets. The first set of questions was regarding ocular symptoms of dry eye. The second set was regarding the ocular symptoms while watching TV or reading book. The third set contained questions regarding ocular symptoms caused by environmental factors. It is a likert type scale grading from 0 to 4. Then a formula is used to calculate the total score. If the OSDI score is 0 to 12, it is considered as normal ocular surface. Then each patient was subjected to dry eye assessment procedures, which includes Tear film breakup test (TBUT), Schirmer's test, ocular surface staining and conjunctival Impression Cytology. TBUT is the interval between the last blink and the appearance of first dry spot on the cornea. The time assessment was recorded in seconds. An average of three recordings was taken. TBUT of less than 10 seconds is taken as suspicious of dry eye. In schirmer's test value of less than 10 mm of wetting after 5 minutes without anaesthesia is suspicious of dry eye. The commonly used dyes in testing ocular surface staining are Fluorescein, Lissamine green and Rose Bengal. 1% fluorescein strip is applied to the tear film and viewed through a slit lamp after 2 minutes using cobalt blue filter. The stain will be taken up in the area of disrupted epithelium.^[7] After conjunctival

impression cytology, smear was graded based on the presence or absence of inflammatory cells, goblet cell density and squamous metaplasia [Figure 1-2]. The statistical analysis is done by using IBM SPSS software. P value of less than 0.05 will be considered statistically significant.

RESULTS

The average mean age group in years was 57.5 (20 to 80 years). Among 100 glaucoma patients, 66% were male and 34% were female. 75% of patients had primary open glaucoma and 25% had secondary open angle glaucoma. 65% patients were on single anti-glaucoma medications, 30% were on combination of two drugs and 5% were on 3 drug regimen. 96% of the anti-glaucoma drug had BAK as preservative. Out of 100 patients, 13% have used drug for less than one year and 87% have used for more than a year. Assessment by OSDI questionnaire showed dry eye in 65% of patients, among which 29% had mild dry eye, 17% had moderate dry eye, 19% had severe dry eye. Only 35% patients had no symptoms of dry eye. There is no relationship between age, gender, number of drugs and OSDI score. Increase in duration of drug usage increases OSDI score.^[8] Among 100 patients, schirmer's test is abnormal in 45% patients and normal in 55% patients. TBUT is normal in 52% of patients and abnormal in 48% of patients. There is significant relationship between Schirmer's test, TBUT and OSDI score. Impression cytology examination revealed goblet cell density of more than 50 cells/high power field (HPF) in 60% of patients, whereas 40% had less than 50 cells/HPF. 64% of patients had no inflammatory cells, but 36% had inflammatory cells. Squamous metaplasia was present in 34% patients, remaining 66% did not have metaplastic changes. Increase in duration of drug usage is associated with decrease in goblet cell density and increase in squamous metaplasia. There is significant relationship between goblet cell density and OSDI score. The ocular surface disease severity increased with increase in duration of treatment and increase in number of topical antiglaucoma drugs.

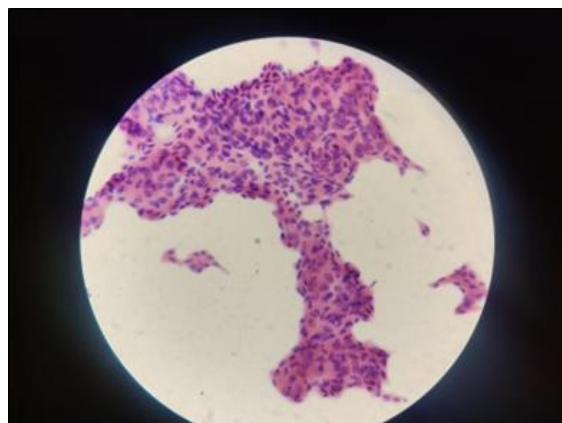


Figure 1: showing Normal Conjunctival Impression smear with plenty of goblet cells in a patient having no dry eye symptoms (PAS)

Table 1: shows Ocular Surface Disease Index - Severity.

S. No	Result	N	%
1	No dry eye	35	35.0
2	Mild	29	29.0
3	Moderate	17	17.0
4	severe	19	19.0
	Total	100	100.0

Table 2: shows Conjunctival Impression Cytology- Goblet Cell Density

S. No	Result	N	%
1	<15 CELLS/HPF	4	4.0
2	15-49 CELLS/HPF	36	36.0
3	50-75 CELLS/HPF	29	29.0
4	>75 CELLS/HPF	31	31.0
	Total	100	100.0

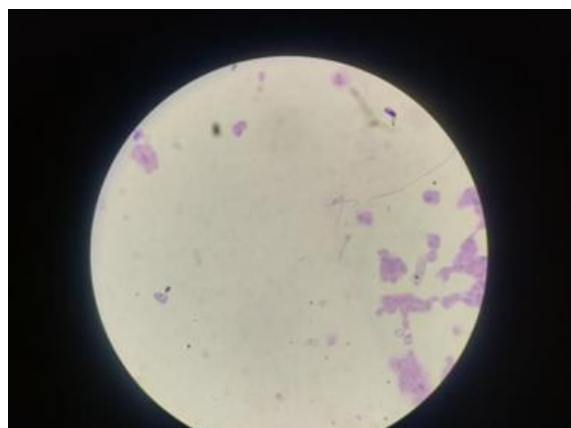


Figure 2: showing Conjunctival impression smear showing depletion in goblet cell density (PAS)

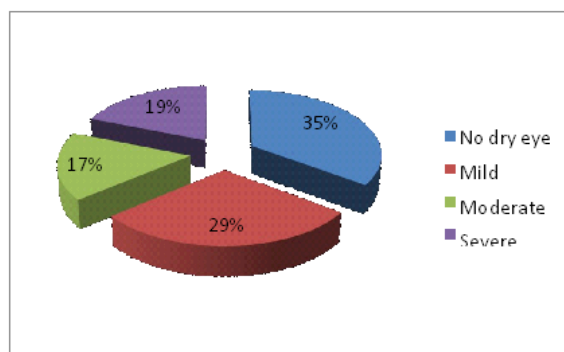


Chart 1: shows OSDI – Severity

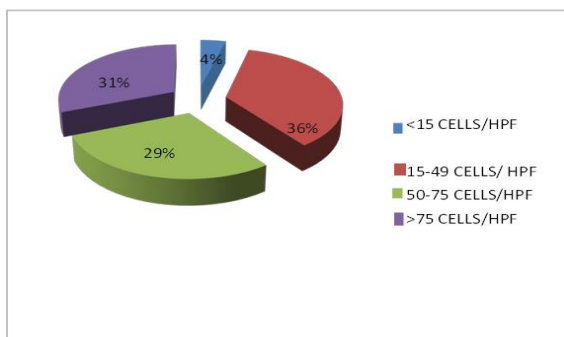


Chart 2: shows Goblet Cell Density

DISCUSSION

Glaucoma is the third leading cause of irreversible blindness across the globe. In India, around 12

million people had glaucoma and 1.5 million were estimated to be blind due to glaucoma. Glaucoma is a chronic disease which causes permanent damage to the optic nerve and visual field changes resulting in irreversible blindness. Increase in intraocular pressure is an important risk factor for disease progression. Medical management with anti-glaucoma drugs is the mainstay of treatment to prevent the progression of disease in early stages. Since anti glaucoma drugs has to be used for a long period of time, chronic side effects are a major concern. The most common side effects includes ocular surface changes and reduced tear secretion resulting in dry eyes apart from causing irritation, stinging, redness and blepharoconjunctivitis. These ocular side effects were caused either by drug itself or its preservatives. In a study, conducted by M Zemba et al on ocular surface in glaucoma patients, they found out that 63% of glaucoma patients had Dry Eye Syndrome as a result of long-term therapy that affected the integrity of tear film and the ocular surface.^[9] There is a lack of widely accepted criteria for the diagnosis of dry eye. The OSDI questionnaire is used as a screening survey for assessing symptoms and their impact on visual functions. It can also discriminate between normal, mild, moderate and severe ocular surface disease [Table 1] [Chart 1]. This test is found to have sensitivity and specificity in distinguishing patients with OSDI from normal subjects. Clinical evaluation of tear film is done using objective tests such as Schirmer's test, Tear film break-up time and Conjunctival impression cytology. To test tear film break up time (TBUT), an impregnated 1% sterile fluorescein strip moistened with 0.5% topical proparacaine was instilled into the lower fornix and asked to blink several times. Then the tear film was examined under cobalt blue filter in a slit lamp with a broad beam. Black spots or lines appear in the fluorescein-stained tear film after an interval indicating the formation of dry areas. TBUT is the interval between the last blink and the appearance of first dry spot on the cornea. The time assessment was recorded in seconds. An average of three recordings is taken. TBUT of less than 10 seconds is taken as suspicious of dry eye.

Schirmer's Test (II) involves measuring the amount of wetting of No.41 Whatman filter paper with

dimensions 5mm x 35mm. It was kept folded 5mm from one end and inserted at the junction of middle and outer third of lower fornix. Care should be taken not to touch the cornea or lashes. The patient was asked to gently close the eyes. The filter paper was removed after 5 minutes and the amount of wetting from the fold was measured. Less than 10 mm of wetting after 5 minutes without anaesthesia is considered abnormal.

Conjunctival Impression Cytology is useful in detecting early metaplastic changes before clinical manifestation.^[10] To perform Conjunctival Impression Cytology, a 5x5 mm of sterile nitrocellulose acetate filter paper was gently placed in the temporal bulbar conjunctival and corneal surface. It is kept pressed firmly for 5 seconds and then the filter paper was gently peeled off and transferred to glass slides. The slide was fixed immediately by putting it in a coplin jar which contained 1:1 mixture of absolute alcohol and ether. Then it was subjected to Periodic Acid Schiff stain, Papanicolau stain and H & E Stain. Then the smears were studied by an expert pathologist.

It was graded into presence or absence of inflammatory cells, goblet cell density of >75/HPF, 50-75/HPF, 15-50/HPF, <15/HPF and mild, moderate and severe squamous metaplasia [Table 2] [Chart 2]. There is a correlation between OSDI, Schirmer's test and TBUT results. It is thus possible that the chronic use of topical antiglaucoma drugs can lead to dry eye disease.

CONCLUSION

In our study, the prevalence of dry eye among patients using topical antiglaucoma medications was found to be 65% based on OSDI. The prevalence of dry eye among POAG patients was found to be 62.7% and that among SOAG was 72% based on OSDI. Ocular surface changes, reduced tear secretion and tear film instability were seen in significant number of patients on topical anti glaucoma medications. The usage of topical anti glaucoma medications can lead to ocular surface disease in

glaucoma patients and its prevalence increases with duration of medication. The causes might be the preservatives used, the medication itself or both. There was correlation between OSDI, Schirmer's test and TBUT results. It is possible that the chronic use of topical antiglaucoma drugs can lead to dry eye disease. This study provides an insight into the tear film disturbances that can arise and recommends periodic subjective and objective assessments of the ocular surface for individuals with glaucoma undergoing prolonged treatment.

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