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Original Research Article

The relationship between glaucoma and dry eye illness as well as the function of preservatives in glaucoma drugs

Marianus Deepak Lakra, Puspa Kumari*, Sarojini Murmu

Department of Eye, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

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***Correspondence:**
Puspa Kumari,
E-mail: kumaripushpa603@gmail.com

ABSTRACT

Background: The aim of the study was to evaluate the incidence of xerophthalmia in individuals with glaucoma by administering a topical regimen of antiglaucoma medication containing timolol and dorzolamide and to determine the frequency of ocular surface abnormalities among individuals with glaucoma who are undergoing treatment with topical antiglaucoma medications.
Methods: The study included a total of 75 participants of both genders. A total of 50 ocular units from 25 subjects under medication with two or more antiglaucoma agents for a period of six months were subjected to examination.
Results: The study compared tear breakage time, Schirmer's test-1, and corneal staining score between the glaucoma cases and control groups. The mean values for tear breakage time were 9.44±2.76 seconds and 11.8±1.88 sec in the glaucoma and control group respectively (p=0.001). The mean values for Schirmer's test-1 were 7.63±2.64 mm and 12.86±1.93 mm in the glaucoma and control group respectively (p=0.001). The mean values for corneal staining score were 5.7±2.33 and 1.1±0.58 in the glaucoma and control group (p=0.001) respectively.
Conclusions: The prevalence of ocular surface disease and dry eye is higher among individuals undergoing antiglaucoma therapy. The application of glaucoma medication in the form of topical treatment has been associated with the development of dry eye syndrome and has been observed to affect the stability of the tear film.

Keywords: Topical medications, Glaucoma, Ocular surface disease, Dry eye frequency, Antiglaucoma therapy

INTRODUCTION

Glaucoma is a progressive optic neuropathy that may not always be associated with elevated intraocular pressure (IOP). The predominant therapeutic approach for individuals with glaucoma is pharmacotherapy, which entails the administration of topical IOP reducing medications.[1-3]

The primary mode of therapy in developed countries with a higher incidence of glaucoma is the use of topical medications that lower intraocular pressure. Beta-adrenergic receptor antagonists and prostaglandin analogues (PGAs) are the recommended primary pharmacological agents. In order to manage IOP, certain individuals opt for a range of topical pharmacological interventions to address their glaucoma.[4,5]

The optimisation of patient exposure to elevated preservative dosages can be achieved through the implementation of polypharmacy and frequent administration. The application of topical medications for the purpose of lowering IOP may result in adverse effects on the conjunctival, corneal, and trabecular meshwork due to the presence of preservatives.[6,7]

Glaucoma is the second leading cause of blindness globally. In the initial stages of glaucoma, a significant

proportion of patients receive therapeutic benefits from medication aimed at reducing IOP to the desired level.

Ocular surface disease is a frequently encountered complication in individuals receiving prolonged therapy for glaucoma. One plausible hypothesis for this adverse impact is the existence of chemical substances that function as preservatives in the pharmaceutical formulation. The ocular surface may experience deleterious effects that can potentially reduce the quality of life.[9,10] Benzoalkonium chloride is a frequently used preservative in pharmaceuticals that exhibits antimicrobial properties, thereby inhibiting the growth of microorganisms in medicinal products. The use of cationic surfactants by conservators induces microbial cell death by modifying the lipids present in cell membranes and cytoplasmic constituents.[11] The lipidolytic properties of benzalkonium chloride extend to the lipids present in the lacquer coating, which undergo solubilization upon exposure to BAK.[12] Lipids present in tears play a crucial role in preserving the structural integrity of the tear film and regulating the rate of evaporation. A major aetiology of xerophthalmia is lacrimal gland dysfunction. The aetiology of glaucoma, a prevalent ocular pathology, can be attributed to a notable manifestation of dry eye syndrome.[13,14] The International dry eye workshop's identification of anti-glycemic medications as a contributing factor to the phenomenon of dry eye evaporation.[15,16]

Previous studies have explored the effects of topical anti-glycemic agents on lacrimal function in human subjects. The Schirmer test and the tear break-up time (TBUT) test are two commonly employed diagnostic tests in the field of ophthalmology. Tear film osmolarity (TFO) is an additional metric utilised in the evaluation of dry eye syndrome pertaining to the tear film. Studies have shown that the determination of tear film osmolarity is a precise and superior diagnostic modality for dry eye syndrome compared to other testing methods. When compared to other clinical procedures, tear film osmolarity measurements exhibit a coefficient of 0.55, rendering them as the most reliable indicator of the severity of dry eye syndrome.[17]

Glaucoma, an ocular neuropathy, can lead to irreversible blindness and visual field defects. According to the WHO, glaucoma ranks as the third most prevalent cause of blindness globally. Based on statistical estimates, the global prevalence of glaucoma is expected to increase to 79.6 million cases by the year 2020, representing a significant rise from the 60.5 million cases reported in 2010. Females (59%) and individuals of Asian ancestry (49%) exhibit a higher propensity for developing glaucoma compared to other racial groups. Primary open angle glaucoma (POAG) is the most common form of glaucoma. It is caused by trabecular obstruction, which impedes the outflow of aqueous humour and results in elevated IOP. Elevated IOP remains a notable predisposing element for the onset and progression of glaucoma. The objective of pharmacotherapy, which serves as the primary modality of intervention, is to maintain the IOP within the physiological range.

The co-occurrence of glaucoma and dry eye syndrome can potentially impede the efficacy of treatment and exacerbate the progression of both conditions. Ocular surface disease resulting in dry eye symptoms can lead to patient discomfort and reduced compliance, ultimately compromising the therapeutic efficacy. It is established that extended exposure to the preservatives present in ocular medications may lead to persistent ocular irritation and reduced efficacy of glaucoma surgical interventions. The identification and treatment of dry eye is crucial in enhancing adherence and the efficacy of glaucoma therapy. This study will delve into the medical treatment of glaucoma, the pathogenesis of dry eye, and the management strategies for glaucoma patients with dry eye.

Dry eye syndrome is characterised by an increase in the osmolarity of the tear film in affected individuals. Furthermore, this results in an increase in the osmolarity of the epithelial cells of the ocular surface. Cellular hyperosmolarity induces a series of proinflammatory cytokines. Presently, tear cytokine overexpression is clinically manifested by hyperemia, shallow point keratites, and ocular discomfort.[18] Studies have shown that individuals undergoing treatment with topical medication for glaucoma exhibit elevated levels of tear film osmolarity. However, these Triplex-forming oligonucleotide (TFO) values were not compared in the previous experiments with a cohort of normative subjects as a reference group. Labbe et al conducted cross-sectional studies to assess the impact of preserved topical anti-glaucoma medications on trabecular facility outflow (TFO).[19] On the other hand, Januleviciene et al examined the changes in TFO when patients transitioned from preserved anti-glaucoma treatment to preservative-free versions.[20] This research aims to examine the prevalence of dry eye syndrome among glaucoma patients who are treated with topical glaucoma medications.

METHODS

Between July 1 and December 31, 2020, a total of 75 subjects were enrolled in a descriptive and observational investigation conducted at the Rajendra Institute of Medical Sciences, Ranchi. Following the acquisition of informed written consent, the patient's demographic data, encompassing age, gender, and body mass index, was documented. Patients presenting with rosacea and blepharitis conditions were excluded from the study, along with individuals who did not furnish written informed consent. The study population comprised individuals between the ages of 20 and 75 years. This research involved the inclusion of patients who exhibited symptoms of paresthesia, pruritus, maceration, and inflammation as a result of prolonged use of topical antiglaucoma medications, specifically the combination of timolol and dorzolamide, for a duration exceeding 12 months. The

assessment of the prevalence of dry eye disease was conducted using the Basal Schrimer's test and the tear film break-up time test, which are standard diagnostic tools for determining the severity of the condition, ranging from mild to moderate and severe cases. The statistical software package SPSS version 22 was utilised to perform analysis on the complete dataset.

RESULTS

The study sample consisted of 90 participants, of which 30 (40%) were male and 60 (60%) were female. The study population exhibited a mean age of 48.67±12.44 years and a mean body mass index (BMI) of 25.14±6.33 kg/m^2. Among the cohort of 75 patients, 36 (48%) presented with symptoms of burning and stinging, while 16 (21.33%) reported itching, 12 (16%) reported dampness and irritation, and 11 (14.67%) reported dry eye sensation (Table 1). According to tear film break-up time test, 21 (21.33%) patients had mild dry eye, 25 (33.3%) had moderate, 13 (17.33%) had severe and 16 (21.33%) cases had no dry eye syndrome (Table 2). According to Basal Schrimer's test 15 (20%) patients was normal while 18 (24%) cases had mild dry eye syndrome, 29 (38.67%) had moderate and 13 (17.33%) had severe (Table 3).

Table 1: Baseline details and symptoms of enrolled cases (n=75)

Variables	N	%
Mean BMI (kg/m^2)	25.14±6.33	
Mean age (years)	48.67±12.44	
Gender		
Female	46	61.33
Male	29	38.67
Symptoms		
Itching	16	21.33
Itching, burning and stinging	36	48
Dry eye sensation	11	14.67
Watering and irritation	12	16

Table 2: Frequency of dry eye syndrome after tear film break-up time test (n=75).

Tear film break-up time test	N	%
Moderate	25	33.3
Mild	21	28
Normal	16	21.33
Severe	13	17.33

Table 3: Frequency of dry eye syndrome after Basal Schrimer's test (n=75).

Basal Schrimer's test	N	%
Moderate	29	38.67
Mild	18	24
Normal	15	20
Severe	13	17.33

DISCUSSION

Although topical antiglaucoma medications are commonly used as the primary treatment for glaucoma, they may result in ocular surface complications in the setting of prolonged and persistent ocular diseases such as glaucoma.[21,22] The deleterious impact of preservatives on ocular solutions is a subject of ongoing medical investigation.[23,24] Prolonged use of topical medications may result in ocular surface disease, including dry eye syndrome, subconjunctival fibrosis, epithelial apoptosis, and cellular loss.

The study cohort comprised individuals aged 20 to 75 years, with a mean age of 48.68±12.43 years and a mean BMI of 25.15±6.32 kg/m^2. The study population comprised of 80 cases, out of which 35 (40%) were male and 45 (60%) were female. Our findings were consistent with the results reported in the study conducted by Kovaevi et al.[25] The study comprised of a sample size of 60 patients, with 28 (46%) male and 32 (54%) female participants. The age range of the patients was between 45 to 70 years, with a median age of 54.5 years.[26]

Within the scope of this investigation, 36 patients (49.32%) reported experiencing itching and sensations, while 12 patients (14.68%) reported experiencing incontinence and inflammation. Additionally, 11 patients (15.8%) reported experiencing symptoms of xerophthalmia. Pisella et al. reported the presence of ocular symptoms such as burning and stinging (36%), foreign body sensation (27%), dry eye sensation (23%), and tearing (20.1%).[27] In the year 2001, a study found that 17% of participants reported experiencing symptoms of dry eyes and pruritus of the eyelids. The results of our inquiry corroborate the aforementioned statements. The efficacy of the drug and the patient's quality of life have been affected by the elevated incidence of dry eye syndrome symptoms and signs in individuals with glaucoma.

As per the results obtained from the tear film break-up time test, it was observed that out of the total number of patients, 21 (26.76%) exhibited mild dry eyes, 25 (34.65%) exhibited moderate dry eyes, 13 (18.66%) exhibited severe dry eyes, and 16 (20.1%) did not exhibit any symptoms of dry eye syndrome. As per the results of the Basal Schirmer test, a significant proportion of the patient cohort exhibited symptoms of dry eye disease. Specifically, 13 patients (16.1%) were diagnosed with severe dry eye disease, 29 patients (39.9%) exhibited moderate symptoms, and 18 patients (18.89%) presented with mild dry eye syndrome. The results were consistent with the findings of the previous study. As per the findings of a study conducted by Manusaini et al in the medical and academic domain, it has been observed that a total of 66 patients who were prescribed anti-glucidal medication were included in the study.[28] Of these, 17 eyes (34%) exhibited dryness at levels 2 or 3. A further investigation conducted by Leung and colleagues. The study findings

indicate that 29% of the subjects did not manifest the clinical manifestations of xerophthalmia. A study found that 27% of glaucoma patients exhibited mild to moderate ocular surface disease, while 35% of patients had a significant tear deficiency. This suggests a potential correlation between glaucoma and ocular surface disease.[29]

Glaucoma is a prevalent ocular disorder that ranks second in the list of leading causes of visual impairment. It exerts a chronic influence on an individual's quality of life. Discontinuation of prescribed medications is not feasible due to the manifestation of adverse effects, including xerophthalmia. Compliance with treatment regimens for dry eye disease is a subject of debate due to its association with the condition. Timely identification and simultaneous management may result in a better prognosis.

CONCLUSION

The application of glaucoma medication topically has been associated with the development of dry eye syndrome and has been observed to affect the stability of the tear film. Non-adherence to treatment regimen and ocular surface disease are common issues encountered in patients diagnosed with glaucoma who are prescribed antiglaucoma medications. Our research findings indicate that individuals undergoing antiglaucoma therapy are more susceptible to ocular surface disease and dry eye. The presence of preservatives in pharmaceuticals and a prolonged duration of therapy were the primary factors that contributed to the outcome.

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