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Original Research Article

Overall Standard of Living in Glaucoma Patients with Dry Eye Syndrome

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Abstract

Background: The multifactorial condition of the tear and ocular surface known as dry eye syndrome (DES) can manifest as symptoms of pain, blurred vision, and unstable tear films.

Methods: 61 patients were enrolled in this observational cross-sectional study at a clinical practise. Depending on how many glaucoma drops the patients received each day, they were split into three groups (G1=1 drop/day, G2=2 drops/day, G3=3 drops/day). A control group of 20 subjects was also selected (G0). Along with a thorough ocular examination that included tear function and ocular surface state (OSDI). Punctate keratitis and a reduced break-up time were used to define DES. The Kruskal-Wallis analysis of variance, Mann-Whitney U tests, the $\chi 2$ and Fisher test, as well as the comparison of median values between groups, were all used in the statistical study (to verify significant differences).

Results: In comparison to 11 percent of G1 patients and 5 percent of G0 patients, DES was present in a total of 40% of G3 patients and 39% of G2 patients (p=0.01). (NEI-VFQ 25 total mean, GSS total mean, and symptoms average: p=0.0085, p=0.006, and p=0.03, respectively) QOL was considerably impacted and changed. OSDI identified variations by group: A moderate OSDI was evident in 26% of G2 and 15% of G3, while a severe OSDI was detected in 15% of G3 and 8.7% of G2 (p>0.05).

Conclusions: DES is more frequently found in patients with topically treated glaucoma than in a comparable control group (p=0.01). The patient's QOL suffers because of the presence of DES. Regular evaluations of glaucoma patients' ocular surface health are necessary to ensure the prompt identification and treatment of any pathologic symptoms on the ocular surface.

Keywords: Glaucoma therapy, Ocular surface, Quality of life, NEI-VFQ questionnaire, Ocular Surface Disease Index, Glaucoma Symptom Scale

Introduction

Since medical treatment is seen to be an efficient method of treating glaucoma in its first stage, the majority of glaucoma patients are treated for extended periods of time with eyedrops to lower intraocular pressure [1]. It is typical for drugs or their preservatives to cause ocular surface problems. The recognised ocular negative effects of preservatives outweigh the advantages of lowering microbial contamination and preventing the active ingredient's breakdown [2].

An extrinsic cause of increased tear evaporation that results in a toxic reaction

from the ocular surface is the extended use of topical medications that have been maintained. The most widely used preservative in ocular solutions, particularly in antiglaucoma medications, is benzalkonium chloride (BAK); it has a well-known dose-dependent toxicity [3, 4, 5]. Conjunctiva-derived and corneal cells were used in in vitro experiments to establish its cellular toxicity [6, 7].

The effect of dry eye on a glaucoma patient's day-to-day activities, particularly discomfort-related symptoms, is a crucial factor to take into account in the follow-up. Recent research has produced instruments for quantifying the symptoms of dry eye as described by patients, including the Dry Eye Questionnaire, the McMonnies Questionnaire, and the Ocular Surface Disease Index (OSDI) [8-19]. A few glaucoma patient-specific surveys have been created, such the Glaucoma Symptom Scale (GSS) and the Treatment Satisfaction Survey for Intraocular Pressure (TSSIOP) [20]. [21]. The break-up time, Schirmer test, rose bengal staining, tear film osmolarity assessment, lysozyme and lactoferrin assays, impression cytology, conjunctival biopsy, and fluorescein dilution tests are among the objective methods used to diagnose dry eye syndrome (DES) [22].

The objectives of this study were to 1) confirm the use of DES in glaucomatous patients based on the number of instillations per day and 2) compare the effects of DES on these patients' quality of life to that of controls using the generic (25-item National Eye Institute Visual Function Questionnaire [NEI-VFQ 25]) [23], glaucoma-specific (GSS), and ocular surface-specific (OSDI) questionnaires. No prior research has, to our knowledge, addressed these problems. MEDLINE was used in an automated search, but no references to these were discovered. [24,25]

Methods

61 patients with primary open-angle glaucoma or ocular hypertension participated in a cross-sectional study, along with 20 control people (G0). All participants were chosen from one of the authors' practise (G.C.M.R.). In order to remove prejudice brought on by patients' perceptions of discomfort, patients were chosen in succession. Depending on how many glaucoma drops they received each day, they were placed into three groups: G1 patients were treated with prostaglandin derivative, G2 patients with beta-blockers, G3 patients with association prostaglandin derivative and fixed combination timolol/dorzolamide. G3 patients were treated three or more times daily. Before participating in the study, each subject provided informed consent. The following were the patient inclusion requirements: Age of 18 years or older, a diagnosis of primary open-angle glaucoma or ocular hypertension, a history of at least 12 months of the same topical treatment (with preservative), and a best-corrected visual acuity of 0.7 in the affected eye are all requirements. Age of 18 years or older, the absence of ocular pathology or therapy, and a best-corrected visual acuity of 0.7 in the worse eye were the inclusion criteria for controls. Systemic (like rheumatoid arthritis) or ocular (like rosacea, infectious disease) diseases, the presence of an absolute central visual field defect, known allergies or hypersensitivity to the drugs used, and filtering or other ocular surgery within the previous six months were the exclusion criteria for both groups.

The presence of a glaucomatous optic nerve head (ONH), as determined by a skilled fundus examination, at least three reliable Humphrey 24-2 full threshold visual field tests performed on various days, and a glaucoma hemifield test (GHT) that was outside of normal ranges were all necessary for the diagnosis of glaucoma.

IOP > 21 mmHg on at least two occasions, a normal feature of ONH, and Humphrey 24- 2 complete threshold GHT within

normal bounds were all necessary for ocular hypertension.

All individuals underwent comprehensive evaluations of the anterior segment, measurements of the intraocular pressure, evaluations of the optic nerve and visual fields, as well as some of the tear function tests and ocular surface health checks detailed below. The cornea was stained with fluorescein to detect the existence of corneal surface injury. More than one fluorescein dot covering the corneal surface was considered to be evidence of corneal staining. The area and density of the lesion were used as characteristics to score superficial punctate keratitis [26,27], but it was only graded as present or absent for statistical purposes.

Utilizing a slit lamp microscope with white light and a reference standard hyperemia photographic chart, the conjunctival hyperemia was graded from 0 (no visible vessel dilatation) to 3 (diffuse vessel dilation), with the possibility of half-unit increments, before intraocular measurements and the administration of anaesthetic and fluorescein. To reduce the variability of these evaluations, the same observer conducted the fluorescein staining, the BUT, and the hyperemia assessment. The presence of BUT 10 seconds and superficial punctate keratitis was used to determine whether or not any of the patients had a dry eye disease. Ocular hyperemia was noted but not included in statistical analysis due to the possibility that prostaglandin derivatives could result in this conjunctival adverse effect [28].

Because the projected range of function loss owing to dry eye in this study was small, functioning (visual field, function-related quality of life) was not taken into consideration (all selected patients had best-corrected visual acuity of 0.7 in the worst eye).

Results

20 controls and a total of 61 patients participated in this study. The patients were all white. Age and gender among recruited groups were comparable (p=0.29 and 0.12, respectively) (Table 1). Patients under treatment generally had a low schooling level versus control group (G0 vs G1: p=0.015; G0 vs G2: p=0.004; G0 vs G3: p=0.04). G1 and G3 patients had been on topical therapy for more years than patients from the other groups.

Table 1: Demographic data of patients

	G0	G1	G2	G3	p
Sex, %					
Female	49	70	67	45	
Male	49	29	32	56	0.291*
Age, yr, median (IQR)	65(55-71)	65(60-70)	70(61-72)	69(64-75)	0.1190†
School level, yr, median (IQR)	9(7-12)	6(4-7)	4(4-4)	4(4-4)	0.0058†‡
Years from diagnosis, median (IQR)	1(1-5)	4(3-8)	3(1-4)	4(1-6)	0.0085†‡

*Chi square, †Kruskal-Wallis test, ‡Significant

About systemic comorbidities, different rates of diabetes were recorded among the four groups: 50% of G3 versus 10%, 26%, and 27% of G0, G2, and G1, respectively (chi-square p=0.046) with a statistically significant difference between G3 and G0 (Fisher exact test p=0.014). Signs of dry eye were similar among all groups, despite gender and age differences.

The most changed corneal parameter among all individuals whose eyes were investigated was punctate keratitis. In comparison to G1 (33.3 percent, 12 percent, and 29.4, respectively) and G0, G2 and G3 showed higher rates of punctate keratitis

(43.5 and 50 percent), hyperemia (9.3 and 15 percent), and lacrimal film instability (54.5 and 60 percent) (15 percent, 5 percent, 40 percent).

Some group differences were noted by OSDI, although they were not statistically significant (Table 2). In sum, 89 percent of G1 patients and 80 percent of G0 patients had normal to mild OSDI, while 15 percent of G3 patients and 8.7 percent of G2 patients had moderate to severe OSDI.

Table 2: Ocular surface disease index grading

	G0	G1	G2	G3
Normal	65.0	66. 7	47.8	50.0
Mild	15.0	22.2	17.4	20.0
Moderate	15.0	5. 6	26.1	15.0
Severe	5.0	5.6	8.7	15.0

Data are in %. Chi-square = 0.7899.

Discussion

A chronic condition, glaucoma is frequently managed with topical medications. Unfortunately, persistent use of the majority of IOPlowering drugs is linked to several harmful side effects, including ocular inflammation, allergies, and dry eye. The preservative BAK, which harms conjunctival and ocular epithelial cells, has been linked to this toxicity. An article published recently [11] on a rabbit dry eye model caused by topical BAK showed that BAK damages the cornea and conjunctiva, reduces tear basal production, results in goblet cell loss, and impairs MUC5AC. According to recent studies [29–33], 1) using only preservative-free eyedrops significantly reduces the symptoms of ocular surface alteration in glaucoma patients, and 2) using alternatively preserved glaucoma medications has less of an adverse effect on the ocular surface than using medications with high BAK levels. Only timolol, levobunolol, and carteolol are now accessible in Italy without a preservative, hence all of the patients chosen for and analysed in the present study were receiving preserved topical treatment. Our data unambiguously demonstrated the dose-dependent toxicity of BAK [4, 5]. G1 and G3 patients did not differ in terms of the number of years they had received topical medication, but rather in terms of the amount of drops they had received. Studies were undertaken by Thygesen et al in 2000 [34] and Costagliola et al in 2001 [35] to assess prostaglandin analogues in the ocular surface. These investigations found that topical timolol was less safe for ocular surface function than prostaglandin analogues. Our findings support this assertion because DES was more common in patients receiving topical timolol bid (G2) as opposed to prostaglandin analogues (G1).

Although the effects of prevalent age-related (12, 13) or hormone-regulated [36] keratitis sicca could not be completely eliminated, all groups were similarly affected since there was no statistically significant difference in age or gender between the three groups. The large percentage of diabetic patients who participated in our trial constituted a drawback. Diabetes alone has the potential to cause an ocular surface disorder; by diminishing corneal sensitivity and aiding in the loss of trophic substances produced from nerves, diabetes reduces tear production [3, 37, 38]. Squamous metaplasia, goblet cell loss, and a disturbance of tear production and quality are the hallmarks of the ocular surface alterations. A correlation between impression cytologic analysis, peripheral neuropathy, inadequate diabetic control, length of diabetes, and decreased corneal

sensitivity was found [39-42]. The difference between registered DES in the G1 and G2 groups, despite a similar prevalence of diabetes (26 percent and 27 percent, respectively), should be primarily related to BAK toxicity rather than diabetic consequences because all of the diabetic patients in our study displayed very good metabolic control, and only one subject with retinopathy received focal argon laser treatment.

The NEI-VFQ 25's effectiveness and test-retest repeatability were evaluated in dry eye patients by Nichols et al [43] The repeatability of the overall score and subscale scores was moderate to high, and patients with dry eye had lower OP subscale scores than published normative data. This means that the worst DES, the worst OP, and the worst total mean VFQ values were recorded in our results for G3 patients, or participants with more frequent DES. Even while dry eye symptoms were not severe enough to have a statistically significant impact on the OP subscale of the NEI-VFQ ($p=0.25$), they were adequate to show ocular discomfort when assessed using the GSS questionnaire's symptoms scale. [44-46]

Conclusion

Each glaucoma patient should get a thorough eye examination, including an assessment of the ocular surface, both before beginning a topical medication and during follow-up visits. The tests used to determine whether dry eye is present are quick, uncomplicated, and very simple. In these individuals, early detection of DES may help to keep the patients' quality of life from changing. Prospective randomised clinical trials should be conducted to examine the long-term impact of glaucoma treatment on the emergence of a DES and the repercussions for QOL.

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