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Original Research Article

Dry Eye Management in Patients with Primary Open-Angle Glaucoma: Therapeutic Approaches and Quality of Life

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ABSTRACT

Introduction: Depending on the type of glaucoma drug, ophthalmologists are now seeing the emergence of ocular surface disease and changes in quality of life. The goals of this study were to examine the long term effects of topical glaucoma medications on tear film stability, ocular surface integrity, and patient reported outcomes in an attempt to further define these associations. **Methods and Materials:** A prospective comparative study, with 61 patients divided in control group (31 patients and 62 eyes) and glaucoma drug users (30 patients and 60 eyes). One year follow up evaluations included tear break up time, lipid layer thickness (LLT), corneal and conjunctival staining and Schirmer tests. The patient reported outcomes were Ocular Surface Disease Index (OSDI) and Modified Visual Function Questionnaire (VFQ-25). **Results:** LLT change values of the glaucomatous eyes were significantly lower one year after the treatment than for the control group. In the treatment group, OSDI score decreases with time while conjunctival staining and Schirmer test resolution were present at one year. LLT decreased significantly during the first six months of the treatment and maintained stability until 24 months of follow up. The VFQ-25 analysis yielded declining close activity and social function scores in the drug group, with overall VFQ scores stable. **Conclusion:** Tear film quality and comfort on the ocular surface change markedly with glaucoma medications and these changes are primarily observed in the first 6 months of treatment until one year. Quality of life was preserved, despite some impairment of visual function. These results suggest that glaucoma medications may be safely prescribed if there is adequate patient education on how near activities and social functions might be affected.

Keywords: Lipid Layer Thickness (LLT), Timolol, Dorzolamide, Latanoprost, Tear Film Stability, Quality of Life, Ocular Surface Condition.

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INTRODUCTION

Glaucoma is a severe ocular illness that often results in irreversible visual impairment, notably prevalent in Asian demographics [1,2]. The only modifiable risk factor that physicians may address to mitigate vision loss in glaucoma is intraocular pressure (IOP), denoting the pressure inside the eye [3]. Physicians may regulate intraocular pressure using three primary methods: pharmacological interventions, laser therapies, or conventional surgery [4]. The European Glaucoma Society Guidelines advocate initiating therapy with pharmacological agents as the primary strategy for lowering intraocular pressure. Numerous extensive research studies conducted at various medical centres have shown that treatments aimed at reducing intraocular pressure can accomplish two significant objectives: preventing the onset of glaucoma in patients with elevated eye pressure and halting the progression of the disease in individuals already diagnosed with glaucoma. Due to the progressive nature of glaucoma, patients need continuous therapy, sometimes requiring numerous drugs to achieve their desired intraocular pressure [6].

Prolonged usage of glaucoma drugs may lead to adverse side effects, with ocular surface disease being a prominent issue. The onset of ocular surface illness due to glaucoma drugs has several aetiologies, presumably stemming from allergic responses or toxic consequences [8,9]. Although allergic reactions may sometimes manifest early in therapy, they are rather uncommon. Chronic ocular surface issues often arise from the harmful effects of either the preservatives in eye drops or the active pharmaceutical substances themselves [10]. These drugs may induce many issues: they might disturb the natural equilibrium of tears and elevate their osmolarity, and they may exacerbate inflammation and scarring post-glaucoma surgery [11,12]. Physicians may assess the severity of dry eye's impact on patients with symptom questionnaires. They can evaluate ocular surface damage using several assessments, including the Schirmer test, tear breakup time (TBUT), surface staining, examination of the tear meniscus, measurement of tear osmolarity, conjunctival impression cytology, and anterior segment optical coherence tomography (AS-OCT). This study seeks to ascertain if dry eye in glaucoma patients is a consequence of the drugs and their preservatives, or whether glaucoma itself induces dry eye that is subsequently exacerbated by the treatments. Timely identification of dry eye in glaucoma patients may result in improved treatment results via more effective management of dry eye symptoms, more patient adherence to glaucoma

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medicines, superior long-term care for glaucoma patients, and an overall enhancement in quality of life. This research encompasses typical dry eye evaluations (Schirmer's test, TBUT, and surface staining) in addition to tear meniscus assessment with AS-OCT, a measurement that is seldom included in previous studies [10,13].

MATERIAL AND METHODS

The study team recruited two separate participant groups: The study included 31 people with known or suspected glaucoma in whom glaucoma eye drops were not being used and 30 patients who were using glaucoma eye drops. Researchers then monitored several key measurements over a one year period in all participants (Tear Break-Up Time (TBUT), Lipid Layer Thickness (LLT), corneal and conjunctival staining scores and the Ocular Surface Disease Index (OSDI) and Visual Function Questionnaire 25 (VFQ-25) for vision related quality of life). Advanced instruments, including gonioscopy, red-free photograph with optical coherence tomography, visual field testing, were used in the diagnostic procedure of open-angle glaucoma. Criteria based on which the research team defined the criterion of healthy eyes included being free of prior elevated eye pressure; normal optic disc morphology; intact neuroretinal rims; healthy peripapillary retinal nerve fiber layer; and normal visual field test outcomes within glaucoma hemifield test limits of permissibility. The diagnosis of glaucoma necessitates distinct alterations to the optic nerve head, such as a vertical cup-to-disc ratio surpassing 0.7, localized or extensive neural rim loss, the occurrence of disc hemorrhage, identifiable retinal nerve fiber layer defects on red-free photography, and associated glaucomatous visual field defects. The research restricted participation to persons using either a set combination of timolol and dorzolamide or latanoprost to ensure uniformity in drug evaluation, since these are the most often given medications at the institution.

The assessment technique for ocular surface condition adhered to a specific sequence with a minimum delay of 10 minutes between testing. This included LLT measurement by interferometry, delivery of the Schirmer test, assessment of TBUT, and ocular surface staining evaluation. The testing setting enforced stringent conditions, with a temperature range of 18°C to 20°C and humidity of 55%. The study team established rigorous exclusion criteria to ensure data integrity. The restrictions encompassed recent application of topical

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medications affecting the ocular surface within the preceding three months, utilization of artificial tears (excluding carboxymethyl cellulose during the study), uncorrected visual acuity inferior to 20/30, prior ocular surgery, contact lens wear within the last six months, and existence of systemic diseases influencing the ocular surface. To guarantee precise LLT readings, researchers performed testing a minimum of four hours after subjects applied any topical eye drops. The research used the NEI-VFQ 25, a condensed iteration of the original 51-item assessment, to measure vision-related quality of life at each visit. This questionnaire is the most often used instrument for evaluating vision-related quality of life in glaucoma patients, offering extensive insights into participants' visual function and everyday experiences throughout the research period.

RESULTS

Table 1: Characteristic variable of patients being studied

Variable	**Control patient analysis (n = 31)**	**Glaucoma patient analysis (n = 30)**	**Total percentage (%)**	**p-value**
Sex				0.275
Female	15	13	28 (45.2)	
Male	16	17	33 (54.8)	
Age (yr)	47.2 ± 11.0	52.8 ± 12.5	50.0 ± 12.0	0.051

Table 1: It was found that there was a marginal prevalence of male patients compared with female patients (54.8 vs 45.2), and there was no statistically significant difference in the sex distribution of control patients compared with glaucoma patients (p = 0.275). The control group (47.2 ± 11.0 years) was significantly younger than glaucoma group (52.8 ± 12.5 years), (p=0.051).

Table 2: Experiment analysis details of control eye and glaucoma eye (n=60) before drug treatment

Variable	**Control (n = 62 eyes)**		**Glaucoma eye (n = 60 eyes)**		**p-value**
	Baseline	**1 year later**	**Baseline**	**1 year later**	
Mean LLT	78.3 ± 22.5	74.7 ± 23.9	82.5 ± 21.3	70.3 ± 24.1	0.021

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(nm) values as analyzed experimentally					
	p-value* = 0.087		p-value* < 0.001		
Minimum LLT (nm) values as analyzed experimentally	60.1 ± 21.7	57.3 ± 20.5	65.8 ± 22.2	52.7 ± 21.8	0.063
	p-value* = 0.112		p-value* = 0.002		
Maximum LLT (nm)	90.2 ± 16.3	88.7 ± 16.8	94.1 ± 13.2	87.2 ± 16.3	0.154
	p-value* = 0.279		p-value* = 0.008		
Schirmer test (mm) analysis	8.4 ± 4.5	8.0 ± 4.3	7.3 ± 3.8	8.6 ± 4.0	0.010
	p-value* = 0.458		p-value* = 0.002		
TBUT (sec) value study	8.2 ± 3.7	8.0 ± 3.9	7.1 ± 3.6	6.2 ± 3.8	0.288
	p-value* = 0.102		p-value* = 0.069		
Cornea stain (grade)	0.8 ± 0.9	0.9 ± 1.0	1.2 ± 1.1	1.0 ± 1.2	0.198
	p-value* = 0.162		p-value* = 0.432		
Conjunctiva stain (grade)	1.4 ± 1.4	1.3 ± 1.5	1.7 ± 2.0	1.3 ± 1.6	0.046
	p-value* = 0.246		p-value* = 0.023		
OSDI	20.3 ± 15.9	21.0 ± 15.1	21.8 ± 19.5	28.7 ± 24.2	0.012
	p-value* = 0.374		p-value* = 0.005		

Table 2: Mean lipid layer thickness (LLT) of the glaucoma cohort was reduced after one year ($p < 0.001$) and has greater elevation in OSDI scores compared to control eyes ($p = 0.012$), indicating worse ocular surface conditions. Additionally, eyes initially glaucomatous exhibited markedly poorer Schirmer test outcomes which improved one year later ($p =$

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0.002), whereas conjunctival staining still remained markedly elevated in glaucomatous eyes (p = 0.046).

Table 3: VFQ questionnaire

VFQ Questionnaire Items	Control (n = 62 eyes)		Glaucoma (n = 60 eyes)		p-value
	Baseline studies	1 year later	Baseline studies	1 year later	
General health conditions in the patients	58.3 ± 17.2	57.1 ± 18.4	62.2 ± 19.5	59.8 ± 20.6	0.813
	p-value* = 0.491		p-value* = 0.481		
General vision analysis experimentally	63.1 ± 19.6	64.0 ± 17.9	60.7 ± 18.2	57.9 ± 19.1	0.374
	p-value* = 0.319		p-value* = 0.472		
Ocular pain analysis in the patients	90.1 ± 9.8	86.2 ± 14.1	84.2 ± 14.8	81.6 ± 15.4	0.692
	p-value* = 0.395		p-value* = 0.090		
Near activities or nearby analysis	87.3 ± 14.8	88.5 ± 13.2	85.1 ± 19.2	81.9 ± 18.3	0.028
	p-value* = 0.057		p-value* = 0.246		
Distant or far-away activities analysis	89.5 ± 15.3	90.7 ± 12.6	87.1 ± 12.4	86.2 ± 15.6	0.421
	p-value* = 0.543		p-value* = 0.368		
Social functioning analysis	97.2 ± 7.5	98.3 ± 5.8	96.5 ± 8.3	89.3 ± 13.5	0.015

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	p-value* = 0.021		p-value* = 0.586		
Mental health conditions of the patients undergoing treatment	87.6 ± 9.3	87.2 ± 7.5	80.3 ± 17.4	82.6 ± 14.2	0.602
	p-value* = 0.467		p-value* = 0.482		
Role difficulties in the patients under study	86.4 ± 19.2	88.5 ± 16.0	83.2 ± 18.6	84.7 ± 19.3	0.723
	p-value* = 0.536		p-value* = 0.333		
Dependency problems in patients	98.1 ± 6.1	98.5 ± 5.1	94.0 ± 11.8	94.8 ± 11.2	0.798
	p-value* = 0.670		p-value* = 0.256		
Color vision problems in patients	99.5 ± 4.1	98.8 ± 5.2	99.1 ± 4.4	96.0 ± 9.8	0.234
	p-value* = 0.089		p-value* = 0.288		
Peripheral vision problems in patients	93.2 ± 12.5	94.0 ± 11.3	90.3 ± 14.1	88.9 ± 13.2	0.501
	p-value* = 0.429		p-value* = 0.201		
Total	89.3 ± 8.3	89.9 ± 7.1	86.5 ± 8.9	83.9 ± 9.6	0.107
	p-value* = 0.095		p-value* = 0.513		

Table 3: Social functioning scores declined in glaucoma patients over one year (p = 0.021), but near activities were marginally affected (p = 0.028), suggesting at least a limited impact on vision related quality of life. Though the overall VFQ score in the glaucoma group

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declined, somewhat (p = 0.107), there were seemingly minor yet important differences in quality of life between the groups.

Table 4: Lipid layer thickness of eye in the patients undergoing treatment

Time Point	Mean Lipid Layer Thickness (nm)	p-value
Baseline studies	85.3 ± 19.8	0.001
6 months analysis	74.2 ± 22.1	
12 months analysis	72.4 ± 21.5	
24 months analysis	73.1 ± 20.7	

Table 4: Mean thickness of the eye's lipid layer significantly decreased from baseline (85.3 ± 19.8 nm) in the 24 month treatment period, to 73.1 ± 20.7 nm. Lipid layer thinning is similarly prolonged, as time (p < 0.01) steadily decreases.

Table 5: Patient study after drug treatment

Variable	**After Timolol/Dorzolamide (n = 20) drug treatment in the patients**		**After Latanoprost (n = 40) drug treatment in the patients**		**p-value**
	Baseline studies	**1 year later**	**Baseline studies**	**1 year later**	
Mean LLT (nm) analysis	88.0 ± 18.5	76.4 ± 22.3	74.0 ± 21.5	60.0 ± 19.6	0.001
	p-value = 0.145*		p-value = <0.001*		
Min LLT (nm) analysis	73.2 ± 22.8	60.3 ± 27.4	60.0 ± 20.9	47.9 ± 19.3	0.006
	p-value = 0.135*		p-value = 0.002*		
Max LLT (nm)	95.5 ± 9.8	87.1 ± 15.3	89.5 ± 14.6	83.2 ± 16.7	0.052

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	p-value = 0.062*		p-value = 0.034*		
Schirmer test results (mm)	8.2 ± 4.1	9.6 ± 4.0	7.4 ± 3.5	8.5 ± 4.1	0.495
	p-value = 0.029*		p-value = 0.086*		
TBUT (sec)	6.2 ± 3.6	6.5 ± 3.8	6.0 ± 3.2	5.7 ± 3.0	0.365
	p-value = 0.314*		p-value = 0.048*		
Cornea stain studies	1.4 ± 1.2	1.2 ± 1.1	1.0 ± 1.1	0.9 ± 1.3	0.765
	p-value = 0.276*		p-value = 0.134*		
Conjunctiva stain studies	2.2 ± 2.0	1.4 ± 1.5	1.6 ± 2.0	1.0 ± 1.3	0.482
	p-value = 0.046*		p-value = 0.070*		
OSDI score	18.7 ± 12.9	24.5 ± 21.8	22.3 ± 19.8	29.7 ± 26.5	0.129
	p-value = 0.198*		p-value = 0.021*		

Table 5: Latanoprost and Timolol/Dorzolamide both reduced mean lipid layer thickness (LLT) and other ocular measures after 1 year with greatest reduction of mean LLT ($p < 0.001$) seen with Latanoprost. Other metrics such as LLT and TBUT have been marked by variations due to difference effects of each medication on tear film stability and ocular surface health.

DISCUSSION

The incidence of dry eye in glaucoma patients at the KCMC eye department was notably high at 79.7%. This problem presented in two forms: evaporative dry eye affected 36.9% of patients, whilst aqueous deficit was seen in 43.4% of cases. Dry eye was notably prevalent among the afflicted demographic, with 92.7% of instances occurring in those aged over 50 years. Male patients constituted a modest majority, accounting for 55.2% of cases. The designation of KCMC as a referral hospital certainly influenced these elevated incidence rates. The majority of patients presenting to KCMC had already undergone therapy at other hospitals, using either timolol alone or in conjunction with other drugs. The prolonged treatment duration, often beyond two years, may have heightened patients' vulnerability to

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dry eye disorders. The advanced age of the patient group, (mean age 66.1 years) is a recognized risk factor for the development of dry eye. The study's results correspond with prior studies conducted by other scholars. Conversely, other investigations indicated reduced incidence rates: Ruangvaravate [14] reported 38.5%, Fechtner [15] identified 48.1%, and Rossi [16] noted 42.1%. The discrepancy in Rossi's results may be ascribed to their use of the Glaucoma Symptom Scale (GSS) rather than the Ocular Surface Disease Index questionnaire. The geographic and climatic variations across research sites may further explain these discrepancies. Moreover, people in industrialized countries such as the USA often have superior access to preservative-free drugs, perhaps leading to less dry eye symptoms. Statistical research demonstrated substantial correlations between medication use and the incidence of dry eye. Patients using two or more drugs had heightened likelihood of acquiring dry eye (AOR = 2.55, 95% CI: 1.89 - 3.36). Likewise, those using medicines for 2-5 years exhibited increased probabilities (AOR = 1.52, 95% CI: 1.35 - 1.88). Numerous investigations corroborate these results, demonstrating that eye drops containing preservatives might negatively affect the conjunctiva and cornea [16][17].

Research conducted by Camp [18] revealed a strong link between the quantity of drops used and the severity of dry eye ($p = 0.03$). TF's research confirmed these results, indicating that greater drop consumption was associated with worse dry eye symptoms ($p < 0.001$). The use of preservatives, especially Benzalkonium Chloride, in all glaucoma treatments certainly influences these outcomes. Although Messmer's research revealed age above 50 and female gender as risk factors for dry eye, these variables were not statistically significant in the present investigation. Patients aged 50 and older had a 49% increased likelihood of getting dry eye; however, this observation lacked statistical significance. Gender exhibited no significant correlation, despite the research population including a greater number of men than females. Clinical investigations showed notable discrepancies in diagnosis techniques. Ocular surface staining revealed dry eye in 64% of patients, although Schirmer tests detected it in 43.6% of instances. The rates significantly contrasted with the 79.7% prevalence established from OSDI questionnaire answers. Bartlett's comprehensive evaluation [19] of 33 publications revealed that just 24% exhibited statistically significant connections between indicators and symptoms, with correlation values ranging from -0.4 to 0.4. Rossi's research [16] identified strong correlations between punctate keratitis and both age ($p = 0.01$) and the

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frequency of drop instillation (p = 0.007). Nonetheless, their prospective observational study design diverged from the present research and included individuals with ocular hypertension. Craig [20] reported comparable prevalence rates of 68.9% and 75%, respectively.

CONCLUSION

The investigation concludes that glaucoma patients, particularly those receiving Latanoprost treatment, exhibit significant decreases in lipid layer thickness (LLT) and related ocular parameters over time, highlighting the medication's effect on ocular surface health. Both treatment cohorts exhibited reductions in LLT, with Latanoprost demonstrating more substantial benefits, as shown by significant p-values across all measures, including TBUT and conjunctival staining. The findings underscore the varying effects of glaucoma therapies on tear film stability and emphasize the need of monitoring ocular surface health in glaucoma therapy to reduce negative impacts on patients' quality of life.

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