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REVIEW

Glaucoma and ocular surface: Review

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Abstract

Glaucoma is the leading cause of blindness worldwide. Ocular surface disease (OSD) is commonly found with glaucoma and could be initiated or exacerbated by topical glaucoma treatments. The preservative agents are important in multidose drugs. The main etiological factor of OSD is preservative agents. OSD with normal and glaucomatous people are evaluated frequently with diagnostic testing including clinical examination and questionnaires to explain the visual function and quality of life. Glaucoma treatments can be related with toxicities to the ocular surface, usually because of the preservatives included in the eye drops; however, the incidence of toxicity can be decreased with the preservative-free medications, or decreased preservative medications, or treatment of dry eye disease. The aim of this review to evaluate the prevalence, causes, and treatment of OSD in glaucoma patients through curent literature, especially those on topical therapy.

Keywords: Dry eye; glaucoma; ocular surface disease; preservatives.

Glaucoma is a significant cause of blindness worldwide.[1] The prevalence of 2.65% in the population over 40, glaucoma is expected to increase in the present decades.[2] Different studies showed that the use of topical drugs may induce ocular surface impairments, and increase the potential risk of unsuccessful glaucoma surgery with visual loss. Ocular surface disease (OSD) is a common subject to come ophthalmology clinics.[3] OSD is estimated to be 15% among individuals aged 65 years or older.[1,4] Different factors are considered to affect the prevalence of OSD, such as age, sex, and race.[3] Glaucoma medications are one of the factors.[4-7] Glaucoma prevalence also increases aged 65 years or older.[8] Leung et al.[9] showed tear break-up time and tear quality was abnormal in 79 (78%) glaucoma patients and severe decrease in tear quality was found in at least 1 eye in 66 (65%). Using preservative-containing eyedrops increases the development of OSD.[4] The effect of benzalkonium chloride (BAK) on the ocular surface has been demonstrated in the different studies.[10] Preservatives have a detergent effect on the lipid layer of the tear film and can decrease the density of goblet cells in the conjunctival epithelium. The stability of the precorneal tear film could be decreased and deteriorate the ability to provide protection and trophic factors to the cornea.[4,5,8,11]

Initial treatment in glaucoma is medical therapy; patients need to use medication for life unless surgical treatment is required.[1,12,13] Most of the time, monotherapy tends to be insufficient in achieving the target intraocular pressure (IOP), and more than 50% of patients require multiple glaucoma medications.[14,15] In glaucoma patients, dry eye often develops when there is concomitant age-related aqueous tear deficiency or meibomian gland dysfunction

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alongside long-term use of topical ocular hypotensive medications.[6,16] Dry eye disease (DED) symptoms decrease patients' quality of life and reduce medication adherence. In the general population, OSD is observed in approximately 5–30% of individuals aged 50 and above, while in glaucoma patients, this rate is around 50–60%.[17]

Multidose topical eye drops require preservatives to extend their shelf life and prevent microbial contamination. However, in glaucoma patients, chronic medication use, particularly those containing preservatives, can lead to ocular surface problems over time.[18]

Most of the glaucoma medications which are being used today contain BAK in different concentrations.[19] It is preferred due to its strong antimicrobial activity, low antigenicity, and relative safety compared to mercury and other preservatives. However, because it is not selective, it can lead to cellular damage and inflammation in the conjunctiva and cornea in a dose- and time-dependent manner.[4,20] With age, there may be a decrease in tear production and narrowing of the canaliculi, making it difficult to remove BAK from the ocular surface and increasing its toxic effects. It is also known that glaucoma medications can cause blockage and atrophy of the meibomian glands. In glaucoma patients receiving medical treatment, dry eye symptoms such as burning, stinging, and foreign body sensation in the eyes, along with low Schirmer test results, reduced tear breakup time, punctate keratitis, and ocular surface staining are frequently observed.[7,20,21]

The medications used in glaucoma treatment are now recognized as an iatrogenic cause of dry eye. Hollo et al.[22] defined OSD related to glaucoma treatment as "the disruption of ocular surface homeostasis due to the toxic effects of chronic topical medications, leading to instability of the tear film, epithelial damage, and inflammation." In addition, the frequency of OSD increases with the severity of glaucoma, the number of ocular hypotensive medications, the presence of preservatives, frequency and duration of use, and the age of the patient.[21]

The Preservative Agents of the Medical Therapy

BAK, Purite® (Allergan Inc., Irvine, California, USA), Polyquaternum 1 as Polyquad® (PQ) (Alcon Research, Fort Worth, Texas, USA), SofZia® (Novartis AG, Basel, Switzerland) are the preservatives which are used commonly in antiglaucomatous therapy.[18] These are important for sterility in multidose eyedrops.[14]

Other preservatives have different effects including precipitate bacterial proteins and are active against Gram-positive bacteria, cross the bacterial lipid layer, and disrupt cells function.[23]

BAK is the most frequently used preservative and has toxic effects with a detergent activity, which dissolve bacterial walls and membranes, and damage the cytoplasmic contents.[10,24] BAK is a quaternary ammonium which cause loss of goblet cells, tear film instability, conjunctival apoptosis, destruction of the corneal epithelium barrier, and damage to other ocular tissues. The mechanisms of the BAK have not been understood, but possible mechanisms are the release of proinflammatory cytokines, apoptosis, oxidative stress, as well as the effect to the corneal epithelial barrier.[25] The decrease in conjunctival goblet cell density is accepted as an important parameter in assessing the OSD. [26] The conjunctival inflammation and reduced goblet cell density of dry eye are exacerbated by the use of preserved topical agents.[27]

Purite® is a stabilized oxychloro complex.[28] Glaucoma medications' adverse effects on the ocular surface are multifactorial, glaucoma medications which contain the higher levels of BAK resulted in greater corneal damage and conjunctival cell infiltration than treated with Purite. [29,30]

PQ is a polyquaternum.[31] Polyquaternum 1 is used in ophthalmology. Liang et al.[32] investigated the travoprost 0.004% ophthalmic solution with PQ, with the travoprost with BAK 0.004% ophthalmic solution and they found that advantage for the ocular surface of patients receiving chronic glaucoma treatment with PQ-preserved drugs. Studies showed that PQ, except in a high concentration of 0.5%, did not create important changes in the ocular surface compared to saline solution.

SofZia® is a preservative agent which has microbicidal effect with oxidative properties. This ionic buffer solution converts to nontoxic produts after contact to the ocular surface.[33] Aihara et al.[34] studied the travoprost with BAK or SofZia and they found that the group with SofZia travoprost 0.004% has lower keratoconjunctival epitheliopathy (p=0.036) and the intergroup difference was also significant (p=0.001).

Clinical Practice

The aim of treatment for glaucoma to prevent OSD.

1. Treatment of dry eye disease: First of all the DED must be treated before the glaucoma disease and medications. The lubricants without preservatives can be used. Tea tree oil preparations and hot compress for meibomian

gland dysfunction, topical steroid, immunomodulator drugs, oral macrolids, and omega 3 preparations could be use for treatment. Punctum plugs are useful for DED but preserves are also being for a long time on the ocular surface also. Punctum plugs may be more harmful in glaucoma patients by prolonging the preservan residence time on the ocular surface.

2. Decrease the number of drugs: The drugs which are monodose or fixed combinations could be using. In such patients, it is possible to use a fixed combination of glaucoma drugs, two IOP lowering agents combined in a single formulation.
3. The preservative-free (PF) agents commonly used are a significant advancement in glaucoma therapy, so this therapy is a good choice.
4. The drugs with the less toxic preservatives can be used.
5. Alternative drug systems
6. Other treatment methods: Selective laser trabeculoplasty (SLT), and minimal invasive glaucoma surgery are the other treatment options. LIGHT study showed that 74% of the patients who were treated with SLT did not need the glaucoma drugs.

Patients with glaucoma suffer OSD at a higher prevalence rate than patients without glaucoma. Table 1 summarizes the results on the studies about OSD and glaucoma.

There is an important problem that both topical glaucoma medications themselves and their added preservatives damage the meibomian glands, and the ocular surface. Preserved topical glaucoma drops appear to cause dysfunction and atrophy of the meibomian glands. Several studies have demonstrated that meibomian gland dropout. Asiedu et al.[35] indicates that worsening dry eye symptoms correlate with the duration of treatment with topical glaucoma medications. Long-term exposure to preservatives can harm the conjunctiva, cornea, and trabecular meshwork. The practice of polypharmacy and frequent dosing heightens patients' exposure to these preservatives. Preservatives and active ingredients in many topical glaucoma medications are linked to ocular surface discomfort. Three clinical signs of meibomian gland dysfunction are assessed: Lid margin abnormality score, meibum expressibility, and the degree of meibomian gland dropout.

Preservative-free glaucoma medications have minimal effect on corneal hysteresis (CH). Aydemir et al.[36] the active agents and preservatives in these drops may impact CH, which is more critical than central corneal thickness in the progression of glaucoma. Monitoring changes in CH in patients using these drops is essential. Glaucoma patients often require prolonged use of antiglaucomatous drops. PF formulations should be preferred to minimize adverse effects on treatment outcomes. Both preservatives and active agents can influence CH, making the variation in CH during long-term use of antiglaucomatous drops significant for disease progression and management. Boso et al.[37] evaluated the OSD index (OSDI) questionnaire, non-invasive objective assessments of the ocular surface, photographic documentation (Keratograph 5M), ocular surface staining with fluorescein and lissamine green, Schirmer test, and IOP measurements. OSD treatment involved eyelid hygiene twice daily, fluorometholone acetate 0.1%, PF lubricant every 2 h, fatty acid supplementation, and oral doxycycline at 100 mg daily, alongside glaucoma topical medications. They showed that the prevalence of OSD signs was high in glaucoma patients under medical treatment. Effective treatment can enhance ocular surface parameters and symptoms, improving compliance and IOP control.

Some studies showed that glaucoma medications can also affect the trabecular outflow structure. Dubrulle et al.[38] discussed the important factor for the ocular surface is the diffusion of inflammatory mediators into deeper tissues and the direct toxicity of medications to the trabecular meshwork. Other potential explanations can also be considered. This study demonstrated that addressing ocular surface irritation and inflammation could enhance IOP control in patients with medically uncontrolled glaucoma associated with OSD. Caring for the ocular surface inherently involves caring for the trabecular meshwork, which affects IOP. Thus, we believe that the management of these three aspects should be integrated.

DED and OSD can be described as disorders which are involving multiple interacting mechanisms. Dysfunction of the lacrimal functional unit can be the reason for DED by causing differences in the volume, composition, or clearance of the tear film. Two most important mechanisms are tear hyperosmolarity and tear film instability. Chen et al.[39] studied about the DED and glaucoma. They showed that the temporary plugs prove effective without complications, consideration for long-term or permanent punctal occlusion may be warranted. Zhang et al.[40] showed that glaucoma medications often cause ocular surface toxicity, primarily due to preservatives; however, this can be reduced through PF options, lower preservative formulations, or dry eye treatments. Results indicated that OSD in both normal and glaucomatous eyes was assessed through diagnostic testing, including clinical examinations and questionnaires evaluating visual

Table 1. Major studies evaluating the role of glaucoma in ocular surface disease development and progression

Study title	Participants and follow-up	Trial design	Materials and methods	Findings
Agnifili et al., 2020, Tear meniscus imaging by anterior segment-optical coherence tomography in medically controlled glaucoma[49]	24 patients with evaporative dry eye (EDE), and 30 healthy subjects (controls), were enrolled. Group 1 (14 eyes): β-blockers; group 2 (14 eyes): prostaglandin analogs; group 3 (28 eyes) ≥2 drugs.	Case–control, single-center, observational study	Ocular surface disease ındex (OSDI) questionnaire, tear film break-up time, corneal fluorescein staining, Schirmer Test I, and tear meniscus height (lower and upper: L-TMH, U-TMH) and area (L-TMA, U-TMA) using AS-OCT, were performed.	OSDI score was higher ($p<0.05$) in patients with EDE and in group 3 compared with groups 1, 2, and controls. No significant differences were found between group 3 and patients with EDE for all clinical parameters.
Portela et al., 2018, evaluation of ocular surface disease in patients with glaucoma: Clinical parameters, self-report assessment, and keratograph analysis[50]	A total of 30 glaucoma patients and 27 subjects with cataracts (control group)	Observational study	Tear break-up time (BUT), Ocular Surface Disease Index (OSDI) questionnaire, keratograph analysis including noninvasive BUT, meibography, tear meniscus height, National Eye Institute Visual Function Questionnaire (NEI VFQ)-25.	There was a significant difference in ocular surface diseases were worse in the glaucoma group ($p=0.009$). The glaucoma group had significantly worse scores on the OSDI questionnaire ($p=0.007$). For the keratograph assessment, the glaucoma group had significantly smaller tear meniscus height ($p=0.041$); worse bulbar redness ($p=0.021$); higher meibography grades ($p=0.001$); and worse noninvasive keratograph tear BUT ($p=0.023$). Patients with glaucoma had a worse quality of life ($p=0.039$).
Agnifili et al., 2018, meibomian gland features and conjunctival goblet cell density in glaucomatous patients controlled with prostaglandin/timolol fixed combinations: A case control, cross-sectional study[51]	60 patients were treated with prostaglandin/timolol fixed combinations (PTFCs), 15 with latanoprost+timolol (L+T) unfixed combination, and 15 controls	A case–control, cross-sectional study	Ocular Surface Disease Index questionnaire, tear film breakup time, corneal staining, Schirmer test I, and in vivo confocal microscopy (IVCM).	IVCM documented lower GCD, MMAD, and MMAA ($p<0.001$), and greater InI and InAW ($p<0.05$) in glaucoma patients compared with controls. L+T showed worse values compared with PTFCs and PF-BTFC ($p<0.05$). Preserved PTFCs showed lower MMAD, MMAA, GCD, and greater InI and InAW compared with PF-BTFC ($p<0.05$) and controls ($p<0.001$). Differences were not found among PTFCs. InI and InAW significantly correlated with Ocular Surface Disease Index and breakup time ($p<0.001$), corneal staining ($p<0.05$), and GCD ($p<0.001$); GCD correlated with MMAD ($p<0.05$).

Table 1. Major studies evaluating the role of glaucoma in ocular surface disease development and progression (CONT.)

Study title	Participants and follow-up	Trial design	Materials and methods	Findings
Carnero et al., 2023 comparison of transcriptomic analysis of the conjunctiva in glaucoma-treated eyes with dry eyes and healthy controls[52]	33 patients treated for glaucoma, 9 patients with dry eye, and 14 healthy controls	A cross-sectional study	Bulbar conjunctival specimens were collected with impression cytology	Glaucoma patients showed an intensified conjunctival immune response.
Soriano et al., 2021 meibomian gland changes in open-angle glaucoma users treated with topical medication[53]	A total of 131 eyes from different patients with open-angle glaucoma treated with topical medication and 92 eyes from different patients with untreated ocular hypertension	Prospective	Noncontact meibography (Keratograph 5M; Oculus, Wetzlar, Germany), Tear osmolarity measurement, corneal staining score (Oxford scale), and Ocular Surface Disease Index questionnaire	Glaucoma topical treatments produce meibomian gland dysfunction and this condition can be worsened using topical treatments containing preservative.
Cho, Wan-Hua et al., 2018 meibomian gland performance in glaucomatous patients with long-term ınstillation of IOP-lowering medications[54]	30 healthy participants and 85 patients with glaucoma	Prospective cross-sectional case-control study	The MG and tear assessments, including Standard Patient Evaluation of Eye Dryness questionnaire, lipid layer thickness, MG secretion and dropout, Schirmer test, tear break-up time, and blinking patterns.	Patients with glaucoma had significantly lower Standard Patient Evaluation of Eye Dryness scores, thinner lipid layer thickness, worse mebium quality, and lower MG secretion compared with healthy participants.
Jun Young Ha et al., 2019 effects of preservative on the meibomian gland in glaucoma patients treated with prostaglandin analogues[55]	Eighty OAG patients were randomized into two groups naïve patients with glaucoma (n=80) and healthy controls (n=40)	Retrospective study	Meiboscore, and lid margin abnormality score (LAS). Subjective symptoms OSDI Ocular surface examination, TBUT, Meibomian gland examination assessment of gland morphology (gland dropout), function (meibum expressibility and quality), and the lid margin	All PGA and control groups showed similar ocular surface and MG parameters at the baseline. Both PC- and PF-PGA groups showed increased meibum scores, meiboscores at 12 months compared to the baseline (all $p<0.05$). At the 12-month visit, PC-PGA group showed severe OSDI, shorter TBUT, greater OSS, and worse MG parameters than those of the other two groups (all $p<0.05$).
Lisa M Nijm et al., 2023 glaucoma and dry eye disease: Opportunity to assess and treat[56]	A PubMed database search was conducted to review the literature on DED and glaucoma.	A PubMed database search was conducted to review the literature on DED and glaucoma.	A PubMed database search was conducted to review the literature on DED and glaucoma.	Dry eye disease (DED) has been found to occur at a higher prevalence in participants with glaucoma than in patients without glaucoma. The relationship between glaucoma and DED. The number of antiglaucoma medications used and a greater number of antiglaucoma eyedrops used have been associated with ocular surface disease in glaucoma patients. Antiglaucoma medications have been associated with ocular surface alterations. Management of DED in patients with glaucoma may include modifications to antiglaucoma medications and the use of treatments for DED.

Table 1. Major studies evaluating the role of glaucoma in ocular surface disease development and progression (CONT.)

Study title	Participants and follow-up	Trial design	Materials and methods	Findings
Zaleska-Żmijewska et al., 2019 extracellular Mmp-9-Based assessment of ocular surface inflammation in patients with primary open-angle glaucoma[57]	90 adults (180 eyes) were included: 60 had been diagnosed with POAG and were treated with prostaglandin analogue monotherapy and 30 were suspected of having POAG but did not receive any treatment (control group). Of those treated with prostaglandin eye drops, 30 received a preservative-free formulation (tafluprost) and 30 were treated with a formulation containing the preservative benzalkonium chloride (BAK) (latanoprost).	A prospective, unblinded, and single-center study	Extracellular MMP-9 levels (InflammaDry test), Goldmann applanation tonometry, Schirmer's test with anesthesia, ocular surface staining with unpreserved fluorescein (Oxford scale index), tear breakup time (TBUT), McMonnies questionnaire, and the Ocular Surface Disease index (OSDI).	Clinically significant MMP-9 levels (>40 ng/mL) were detected in tear film from 46.7% of subjects treated with BAK-containing medication. In contrast, only 16.7% of subjects treated with preservative-free medication or untreated individuals demonstrated similar MMP-9 levels. MMP-9 results correlated with other indicators of inflammation and disease severity.
Kim et al., 2021 evaluation of ocular surface disease in elderly patients with glaucoma: Expression of matrix metalloproteinase-9 in tears[58]	Sixty-seven patients were diagnosed with POAG and 47 healthy control subjects	Prospective, case-control study	Schirmer-I test, the Oxford corneal stain scale, tear breakup time (TBUT), and the five-item dry eye questionnaire (DEQ-5). MMP-9 level was performed using the InflammaDry test.	MMP-9 overexpression was observed in 71.6% of the POAG group, 31.9% of the control group showed MMP-9 overexpression.
Sang M Lee et al., 2019 effect of topical glaucoma medication on tear lipid layer thickness in patients with unilateral glaucoma[59]	Thirty patients with unilateral normal tension glaucoma	Cross-sectional comparative study	Tear LLT was measured with the LipiView® ocular surface interferometer (TearScience® Inc, Morrisville, NC, USA) analyzing more than one billion data points of the interferometric image of the tear film. Interferometric color units (ICUs) were used to measure tear film LLT with the interferometer, with 1 ICU equal to 1 nm of LLT.	Lipid layer were significantly thinner than those in normal eyes. Longer duration of glaucoma eye drops and a greater number of glaucoma medications were associated with the lower LLT average and increasing glaucoma medications have a significant correlation with lower LLT minimum in glaucoma eyes (p=0.026)
Mylla Boso et al., 2020 impact of ocular surface disease treatment in patients with glaucoma[37]	Patients with primary open angle or primary angle closure glaucoma under topical treatment for at least 6 months	Prospective interventional study	Patients underwent symptom screening with the ocular surface disease index (OSDI) questionnaire, assessment of objective ocular surface parameters, ocular surface staining and Schirmer test. Tear meniscus height (TMH), bulbar redness, non-invasive tear break-up time (NITBUT), and meibography	The prevalence of OSD signs and symptoms was high in glaucoma patients under medical treatment. Short-term OSD treatment may improve ocular surface disease and IOP control.

Table 1. Major studies evaluating the role of glaucoma in ocular surface disease development and progression (CONT.)

Study title	Participants and follow-up	Trial design	Materials and methods	Findings
Wong et al., 2018 Exploring topical anti-glaucoma medication effects on the ocular surface in the context of the current understanding of dry eye[60]	Thirty-three patients with a diagnosis of open angle glaucoma or ocular hypertension	Cross-sectional, investigator-masked, paired-eye comparison study	Tear film parameters, ocular surface characteristics, and dry eye symptomology of treated and fellow eyes were evaluated and compared.	Treated eyes had poorer non-invasive tear film breakup time (p=0.03), tear film osmolarity (p=0.04), bulbar conjunctival hyperemia (p=0.04), eyelid margin abnormality grade (p=0.01), tear meniscus height (p=0.03), and anesthetized Schirmer value (p=0.04) than fellow eyes. There were no significant differences in dry eye symptomology, meibomian gland assessments, and ocular surface staining between treated and fellow eyes.
Mohammed et al., 2020 Profiling ocular surface responses to preserved and non-preserved topical glaucoma medications: A 2-year randomized evaluation study[61]	36 treatment-naïve patients over 24 months of three differently preserved glaucoma drop preparations: Preservative-free (PF), polyquad (PQ), and benzalkonium chloride (BAK).	Prospective, randomized evaluation	mRNA and protein expression of IL-6, IL-8 and IL-1β Tear samples	BAK-preserved topical drops stimulate a sterile inflammatory response on the OS within 3 months which is maintained thereafter, whereas PF-drops and PQ-preserved drops showed no significant OS inflammation.
Kumar et al., 2019 Ocular Surface Disease with BAK preserved Travoprost and polyquaternium 1(Polyquad) preserved Travoprost[62]	Patients of primary open angle glaucoma (POAG) on medications for more than 6 months. The first group comprised of 40 patients receiving BAK preserved travoprost, the second group included 40 patients receiving polyquad preserved travoprost and 30 of control group not receiving any medical treatment.	rospective, controlled, Pobservational study	Ocular surface disease ındex (OSDI) scores using ocular surface disease ındex (OSDI) questionnaire were assessed and compared in all subjects.	OSDI scores revealed significantly lesser symptoms in polyquad preserved travoprost when compared to BAK preserved travoprost. The OSDI scores in polyquad group were also comparable to the control group. Hence, for long-term glaucoma management poly quad containing travoprost should be preferred over the BAK-preserved travoprost.
Economou et al., 2018 Better tolerance of preservative-free latanoprost compared to preserved glaucoma eye drops: The 12-month real-life FREE study[63]	721 patients	international, prospective, and observational real-life study	Efficacy, local tolerance, and patient satisfaction were the main evaluation criteria.	IOP values were similar between PF latanoprost and preserved eye drops and remained stable at all visits. Ocular signs and symptoms improved after switching to PF latanoprost; the prevalence of conjunctival hyperemia was significantly lower (p=0.0015). At follow-up visit 1, 49.5% of the patients who switched to PF latanoprost decreased or stopped the use of artificial tears. Satisfaction regarding tolerance in patients using PF latanoprost improved significantly after the switch from preserved eye drops to PF latanoprost (p<0.0001).

Table 1. Major studies evaluating the role of glaucoma in ocular surface disease development and progression (CONT.)

Study title	Participants and follow-up	Trial design	Materials and methods	Findings
Lajmi et al., 2021 Relationship between OSDI score and biomicroscopic ocular surface damages in glaucomatous patients treated with preserved antiglaucomatous eye drops[64]	155 glaucoma patients treated with preserved glaucoma eye drops	A cross-sectional study	They all completed the "Ocular Surface Disease Index" (OSDI) questionnaire and underwent complete ophthalmological examination with precise evaluation of the status of the ocular surface. The assessment included Shirmer I testing, tear break up time (TBUT), eyelid, conjunctival and corneal examination with fluorescein and lissamine green staining.	The severity of the OSDI score was statistically associated with patient age ($p<0.001$), treatment duration ($p<0.001$), multiple medications ($p=0.011$), and use of BAK ($p=0.004$). Blepharitis ($p=0.013$), Meibomian gland dysfunction ($p=0.039$), corneal neovascularization ($p=0.025$), and superficial punctate keratitis (SPK) ($p=0.044$) were retained as predictors of a pathological OSDI score. OSDI score is correlated with ethnicity, glaucoma treatment duration, number of medications, BAK use, and clinical ocular surface changes, especially SPK.

function and quality of life. Utilizing laser trabeculoplasty or minimally invasive glaucoma surgeries that spare the conjunctiva and cornea may lessen reliance on topical medications, thereby potentially preventing or alleviating OSD. Recognizing and treating OSD in glaucoma patients can improve their quality of life and medication adherence, ultimately enhancing treatment outcomes. Lopes et al.[41] showed that the cessation of BAK use was found to decrease the signs and symptoms of dry eye in patients with primary open-angle glaucoma. Doğan et al.[42] studied the use of topical antiglaucomatous medications that appears to affect central corneal epithelial thickness in glaucoma patients, with thinner measurements observed compared to controls. Anterior segment optical coherence tomography may be useful for evaluating the impact of antiglaucomatous medications on central corneal epithelial thickness during treatment. Furthermore, oxidation on the ocular surface is important. Sedlak et al.[43] analysed that topical carbonic anhydrase inhibitors preserved with BAK increase oxidative stress in the tear film.

There is evidence that the prostaglandin analogs may also affect to OSD. El Ameen et al.[44] suggested that patients treated with PF latanoprost experience better ocular tolerance compared to those on preserved prostaglandin analogues. Switching to PF latanoprost maintained IOP at levels comparable to preserved prostaglandin analogs while improving ocular surface tolerance. Seong et al.[45] demonstrated that PF latanoprost effect is comparable in reducing IOP to BAK -preserved prostaglandin analogs, but with significantly fewer side effects on the ocular surface. With this effectiveness, PF latanoprost may enhance patient compliance and potentially slow glaucoma progression. Hommer et al.[46] showed that switching to PF tafluprost results in increased tear film thickness, improved breakup time, and a better Dry Eye-Related Quality of Life Score. Therefore, our findings suggest that transitioning to unpreserved tafluprost is advantageous for ocular surface health in patients who have been using preserved prostaglandin eye drops for an extended period. Park et al.[47] studied that PF-tafluprost and PF-dorzolamide/timolol exhibited statistically and clinically significant improvements in life quality, as measured by the OSDI questionnaire, compared to preservative-containing latanoprost, while maintaining comparable IOP reduction in Korean glaucoma patients with OSD. Wong et al.[48] they showed that clinic of OSD and subjective symptoms of DED improved following the switch to low-preservative tafluprost, which also demonstrated comparable IOP-lowering effectiveness.

Conclusion

Glaucoma and OSD are interrelated conditions that significantly impact patient quality of life and visual health. Glaucoma and ocular surface disorders are very common disorders and these diseases affect the eyes. When possible, switching to PF medications should be considered in patients who use multiple drops. Patients who require multiple agents may better options for laser trabeculoplasty or MIGS. Factors including patient age, compliance, stage of glaucoma, and degree of OSD should guide clinician management.

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