

## REVIEWING SOME CLINICAL MANIFESTATION FEATURES OF DRY EYE SYNDROME IN GLAUCOMA PATIENTS UNDERGOING A CONTINUOUS HYPOTENSIVE REGIMEN

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**Abstract.** *This article presents observations of ocular surface clinical condition in patients with primary open-angle glaucoma who had been receiving antihypertensive drugs containing preservatives over an extended period. The study comprises a total of 74 eyes, with patients categorized into three groups. The initial group consists of individuals who had been on a long-term regimen (up to 18 years) of antihypertensive medication containing benzalkonium as a preservative. The second group encompasses 12 patients (24 eyes) who were administered prostaglandin drugs via disposable dropper tubes, devoid of preservatives. The treatment duration for this group ranged from 2 to 2.5 years. Lastly, the third group comprised individuals exhibiting symptoms of conjunctivitis, chosen for the diagnosis of dry eye syndrome based on their subjective complaints. This group includes 10 patients, totaling 20 eyes. Upon analysis, approximately 40% of patients in the main group exhibited symptoms indicative of dry eyes. In the control group that received the preservative-free drug, the occurrence of dry eye symptoms was notably lower at 16.6%, while in the other control group, this frequency stood at approximately 30%. Consequently, the group consistently receiving drugs with a preservative showed a slightly higher percentage in the detection of dry eye.*

**Keywords:** *dry eye syndrome, Schirmer test, Norn test, glaucoma.*

**Relevance.** In recent years, clinical ophthalmology has placed significant emphasis on the issue of dry eye. Our region, characterized by hot and dry summers, elevated dust levels, low annual precipitation, and abrupt temperature changes, provides an advantageous setting for monitoring this patient demographic. The impact of these environmental factors on mucous membranes, particularly those in contact with the external environment, contributes to various pathologies, notably affecting the eyes and upper respiratory tract. Clinicians are particularly intrigued by the influence of regularly used eye drops, specifically antihypertensive ones, the majority of which contain preservatives, on the state of the ocular surface.

In collaboration, L.L. Arutyunyan and co-authors highlight the benefits of preservative-free prostaglandin drugs, emphasizing their non-deteriorating effect on the ocular surface condition. [1]

V.P. Elichev and colleagues have introduced an innovative approach to address artificial dry eye syndrome in glaucoma patients undergoing a continuous hypotensive regimen. It is recognized that the majority of anti-glaucoma drops incorporate a preservative essential for averting bacterial contamination in the bottle. By extending the shelf life of the drops, the preservative prevents biodegradation, ensuring the sustained efficacy of the drug and enabling the utilization of a convenient and secure bottle. Presently, benzalkonium chloride (BC) stands as the most prevalent preservative; however, it is noteworthy that even in minimal concentrations, BC can exert a cytotoxic effect on all structures of the ocular surface. The toxic impact of the

preservative on the ocular surface and the symptoms of dry eye syndrome can be mitigated through tear replacement therapy. The initial tear replacement therapy suggested in the article is preservative-free, and the active ingredients in these medications have demonstrated efficacy in treating and preventing corneal-conjunctival xerosis. [4]

T.V. Gavrilova and L.I. Solovyov expressed a favorable view regarding the use of the ophthalmic lubricant "Okuhil C" in patients who had been consistently instilling antiglaucoma medications for an extended period (some up to 55 years). [3]

**Study Objective:** To assess the impact of preservative containing antihypertensive drops on the condition of the eyeball surface and tear film, considering the climatic and geographical characteristics of Uzbekistan.

**Materials and Research Methods:** Three patient groups were formed for the study. The first group comprised 15 patients (30 eyes) who had been on a long-term regimen of an antihypertensive drug containing benzalkonium as a preservative, with an observation period of up to 18 years. The second group comprised 12 patients (24 eyes) who received prostaglandin drugs via disposable dropper tubes without the preservative, with a treatment duration of 2–2.5 years. Lastly, the third group involved individuals with chronic conjunctivitis symptoms, chosen for dry eye syndrome diagnosis based on subjective complaints. This group included 10 patients, totaling 20 eyes.

All patients underwent a comprehensive ophthalmological examination, encompassing general clinical and laboratory analyses, instrumental and functional examinations. Specialized assessment methods included tear film disruption tests (Norna), Schirmer tests, and tear film meniscometry. Schirmer test was carried out in accordance with the universally accepted procedure. Evaluation of results categorized readings as follows:  $\geq 15$  mm denoted normal; 10 to 15 mm indicated moderate deficiency; 5 to 10 mm signified severe deficiency; and  $\leq 5$  mm represented a severe lack of tear production.

The evaluation of tear film stability, utilizing the Norn test, employed pre-packaged fluorescein test strips – FluoroTouch (Madhu Instruments Pvt. Ltd., India). Prior to inserting the fluorescein test strips into the lower conjunctival fornix, they were moistened with one of the ophthalmic lubricants. The procedure was timed using a stopwatch while the stained surface of the cornea was observed through a slit lamp under focal illumination with a cobalt blue filter. The location and characteristics of such defects as "spots," "cracks," or "holes" were determined in the cornea. A tear film breakup time of 7 seconds or more was considered normal, a moderate decrease was indicated by up to 5 seconds, and a decrease below 5 seconds was regarded as a significant disruption of tear film stability.

The properties of the inferior tear meniscus were evaluated through optical coherence tomography (OCT meniscometry), employing an optical coherence tomographic RTVue\_4.0 by Optovue, USA. Measurements encompassed the determination of the height (h) of the lower tear meniscus, as well as the quantification of its width (b). Additionally, parameters such as the radius and degree of deflection were assessed. It is noteworthy that the standard ratio for the height and width of the tear meniscus is conventionally recognized as 1:1.5.

The symptoms of chronic conjunctivitis were evaluated utilizing the following grading system: (+++) – indicating persistent discomfort behind the eyelids, absence of lacus lacrimalis, and habitual blepharospasm; (++) – denoting the presence of lacus lacrimalis signs in the medial corner, with blepharospasm occurring primarily outdoors in the setting of bright light; (+) –

representing mild chronic conjunctivitis without pronounced blepharospasm, with periodic occurrences of discomfort behind the eyelids.

**Results and discussion.**

Based on our observations, 12 out of 30 eyes in the main group exhibited an accelerated tear film breakup time, measuring 3-4 seconds, while the remaining 18 eyes displayed a tear film breakup time of 6-7 seconds, compared to the normal standard of 10 seconds. The Schirmer test yielded positive results in 17 out of 30 eyes, where hydration of the filter strips was recorded at 6-7 mm. Conversely, in the remaining 13 eyes, the strips demonstrated hydration levels of 10-12 mm, considering the norm of 15 mm.

Within the main group, 12 eyes were classified as (+++), indicating a notable condition, while the remaining 18 eyes were categorized as either (++) or (+).

In the first control group patients, during the Norn test, 20 eyes exhibited a normal result, while in the remaining 4 eyes, the tear film rupture time was reduced to 4 seconds. In the evaluation of total tear production (Schirmer test), normal results were observed in 18 eyes, registering 15 mm within 5 minutes. Conversely, in the remaining 6 eyes of the group, a decrease in tear production was noted.

The ratio of tear meniscus height, width, and deflection degree of the tear film amounted to 0.7/1.0 in 12 out of 24 eyes. In the remaining 12 eyes, it was measured at 1/1.2, indicating a deficiency of tear fluid.

In the second control group (comprising individuals with chronic conjunctivitis), a tear film breakup time of less than 6 seconds was observed in only 6 out of 14 eyes. The average intensity of chronic conjunctivitis symptoms was noted in 10 eyes, and the Schirmer test indicated a decrease in tear production in only 4 out of 20 patients.

**Table 1.**

***Features of clinical manifestations of dry eye syndrome in the main and control groups***

Clinical signs	The main group i.e. hypotensive regimen with preservatives. 30 eyes	1 Control group - preservative-free prostaglandins) 24 eyes	2 control group (dry eye suspects without glaucoma) 20 eyes	Average normal values
Tear film break-up time	12 eyes – 3-4 s (40%) 18 eyes - 6-7 s (60%)	4 eyes – 8 s (16.6%) 20 eyes 10 s (83.3%)	6 eyes – less than 10 sec (30%) 14 chapters - 10 sec (70%)	10 Seconds
Schirmer test result	17 eyes 6-7 mm (56.6%) 13 eyes -10-12 mm (43.4%)	20 eyes – 15 mm or more (83.3%) 4 eyes – 10-12 mm (16.7%)	16 eyes – 12-15 mm (80%) 4 eyes – 10-12 mm (20%)	Hydration of strips in 5 minutes over 15 mm

Conjunctival hyperemia and discomfort (feeling of a foreign body under the upper eyelid)	(+++ ) 12 eyes (40%), (++) 8 eyes (26.7%), ( +) 4 eyes (13.3%)	( +++ ) 12 eyes (50%), (++) 6 eyes (25%), (+) or absent in 6 eyes (25%)	10 eyes (++) (50%) 4 eyes (+) (20%)  practically absent in 6 eyes (30%)	The degree of clinical manifestations was determined by the subject directly during biomicroscopy of the anterior part of the eye
Meniscometry (tear film height, width and deflection radius ratio)	In 18 eyes the ratio was 0.7/1.0 (60%), in the remaining 12 eyes -1/1.2 (40%)	16 eyes - 1/1.4 (66.7) 8 eyes 1 /1.7 (23.3%)	Anterior section OCT was performed only in 8 eyes. On all the 8 ones the norm of 1..1.5 was registered	Norm 1/1.5

**Summary and conclusions.** Thus wise, long-term use of benzalkonium-containing antihypertensive drugs resulted in an accelerated tear film breakup time in nearly all observed patients, with a significant acceleration observed in 40% of cases. General tear production exhibited a noticeable reduction in 56.6% of eyes, underscoring the impact of the preservative on the ocular surface condition. However, not all authors attribute a direct effect of the preservative in antihypertensive drugs to dry eye. Evidently, the more apparent influence in our findings is also associated with the climatic characteristics of our region.

In the control group administered the drug without a preservative, an anticipated negligible impact on the quality of the ocular surface was observed. Consequently, a noticeable acceleration of the Norn test was documented in only 16.6%, accompanied by a comparable reduction in total tear production observed in a similar proportion of patients.

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