# OCULAR SURFACE EVALUATION IN PATIENTS TREATED WITH PROSTAGLANDIN ANALOGUES CONSIDERING PRESERVATIVE AGENT

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## SUMMARY

**Purpose:** The aim of this study was to evaluate the ocular surface in patients treated with prostaglandin analogues considering contained preservative agent.

**Methods:** 60 patients with glaucoma or ocular hypertension treated with prostaglandin analogue monotherapy were enrolled in this observational study. 20 patients with glaucoma suspect or ocular hypertension without local or systemic glaucoma medication formed the control group. Demographic data and medical history were recorded for each participant. Patients filled in the Ocular surface disease index© (OSDI) questionnaire and underwent an ophthalmological examination including assessment of conjunctival hyperaemia according to Efron, tear film break up time (BUT) and fluorescein staining according to the Oxford grading scheme. Treated participants were divided into 3 groups according to the preservative contained in the currently used prostaglandin analogue: the preservative-free group (18 patients), the polyquaternium group (17 patients) and the benzalkonium chloride (BAK) group (25 patients).

**Results:** The control group had significantly lower fluorescein staining than the preservative-free group (p=0.001), the polyquaternium group (p=0.007) and the BAK group (p=0.002). The conjunctival hyperaemia was significantly lower in the preservative-free group compared to the polyquaternium group (p=0.011). There was no significant difference among the other groups. The difference neither in the OSDI score nor in the BUT was statistically important.

**Conclusion:** This study confirmed that the ocular surface is worse in patients treated with prostaglandin analogue monotherapy than in people without glaucoma medication. A significant difference among treated patients depending on a preservative agent was not proved.

**Key words:** benzalkonium chloride, glaucoma, ocular surface disease, preservatives, prostaglandin analogues

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## INTRODUCTION

Ocular Surface Disease (OSD) is a multifactorial disease of the ocular surface, linked with unpleasant ocular sensations, visual complaints, instability of the lachrymal film and damage to the ocular surface. One of the external causes of dysfunction of the lachrymal film is the long-term use of drops containing preservative agents (2, 31), which is applied above all in the treatment of glaucoma.

Glaucoma is a chronic, irreversible neuropathy of the optic nerve, connected with a progressive loss of retinal ganglion cells, leading to characteristic morphological changes on the disc of the optic nerve and in the nerve fibre layer, as well as to defects in the visual field (11, 24, 35).

At present the sole risk factor in the occurrence and progression of glaucoma that can unequivocally be therapeutically influenced is intraocular pressure. Due to their good efficacy, toleration, safety and simplicity of dosing, prostaglandin analogues have become the pharmaceuticals of first choice (11, 35). They reduce intraocular pressure by increasing the outflow of intraocular fluid via the uveoscleral pathway and to a lesser degree also via the trabecular pathway. The mechanism of effect is based on the regulation of matrix metalloproteinases and remodelling of the extracellular matrix, which results in a change to the permeability of tissues (38). Preparations containing latanoprost, travoprost, bimatoprost and tafluprost are currently available on the Czech market (9). Their most frequent side effects include hyperaemia of the conjuctiva, changes to the eyelashes, increased pigmentation of the iris and periocular pigmentation of the skin. In the case of eyelashes there is an increase in their number, length and thickness, which sometimes may be desirable for cosmetic reasons, but not in the case of unilateral therapy. These changes occur more frequently upon treatment with bimatoprost and travoprost (1). Increased pigmentation of the skin is reversible, unlike pigmentation of the iris, which is permanent. As yet no fundamental differences have been found in its incidence upon treatment with individual prostaglandin analogues (1). The question of hyperaemia of the conjunctiva shall be discussed below. Less frequent local side effects of prostaglandin analogues include cysts of the iris, cystoid macular edema, anterior uveitis or reactivation of herpetic keratitis. Systemic adverse effects are extremely rare (1).

The aim of glaucoma treatment is on one hand to avert its

progression, and on another to prevent a reduction of the patient's quality of life, which can be attained among other factors by minimising ocular discomfort upon chronic local treatment (8, 31, 40). As a result it is essential to approach each patient individually, and to choose therapy according to that patient's requirements (34). Safety of treatment should be the first priority in the case of glaucoma (21). The majority of side effects of local therapy in patients with glaucoma are caused rather by preservative agents than active substances (2, 37).

Preservative agents are added to eye drops for the purpose of preserving the sterility of the solution. In ophthalmology the most widespread preservative agent is benzalkonium chloride (BAK) (2, 26, 27, 29). This concerns a well water-soluble nitrogen cation surface active agent which belongs to the group of quaternary ammonium salts. It dissolves bacterial walls and cytoplasmic membranes. Preservative agents, in particular BAK, have adverse effects on the surface tissues of the eye, and their long-term use causes sub-clinical inflammation of the conjunctiva, a loss of goblet cells and fibrous proliferation in the substantia propria of the conjunctiva and Tenon's membrane (2, 37), which subsequently intensifies postoperative scarring and may lead to a failure of filtration operation (2). BAK influences the lachrymal film both through its detergent effect on the lipid layer and through its toxicity with regard to the goblet cells producing mucin. Both of these mechanisms lead to instability of the lachrymal film and its increased evaporation. BAK also induces apoptosis of trabecular cells, and if it is absorbed by the nasal mucosa, in responsible individuals it may cause bronchoconstriction (2). However, Rossi et al. (31) state that short-term exposure to BAK is not linked with changes to the ocular surface.

Toxicity of BAK depends on the dose (2), upon glaucoma treatment the endeavour is therefore to reduce the number of applied drops with BAK through the use of a fixed combination, a preparation without BAK or entirely without preservative agents (11, 30).

It is difficult to ensure that a preservative agent is not toxic whilst it at the same time has a sufficient antimicrobial effect. An alternative to BAK, available in the Czech Republic, is polyquaternium. This belongs to the group of polycationic polymers. It disturbs the cellular membrane of bacterial cells, but does not act as a detergent, and its large molecule does not penetrate into mammalian cells (29). It was developed in the 1980s as a preservative agent for contact lens solutions, at present it is also a component of anti-glaucomatous drugs and artificial tears. Although it is less toxic than BAK (18, 26), it also leads to cell death and the release of pro-inflammatory cytokines (26).

Preparations without preservative agents are linked with higher costs, they are often produced in single-dose packages, which may cause problems upon handling, especially among less dextrous patients and patients with pronounced damage to sight. Furthermore, in order to preserve the required properties of the active substance it is sometimes necessary to enrich the pharmaceuticals with a special admixture. For example, currently the only latanoprost that does not contain preservative agents (Monopost®) contains a complex of polymers with functions of surfactant, which ensures a stable pH and the required viscosity of the solution, stability of the active substance at room temperature, prevents the absorption of latanoprost into the inner surface of the packaging (1) and facilitates its penetration into the eye (33).

Batra et al. (4) advocate a combined approach to glaucoma treatment, which also incorporates management of OSD, leading to an improvement in the monitoring of intraocular pressure and a reduction of the need for drainage operations. The ocular surface should be regularly observed in patients with glaucoma or ocular hypertension (3, 11, 19, 30, 31). The most widely used diagnostic tests include questionnaires, evaluation of the stability of the lachrymal film (break up time (BUT)), colour eye staining (with fluorescein, lissamine green or rose bengal). However, combinations and interpretations of these tests are not uniform, there is a lack of a universally recognised consensus for the diagnosis of OSD (19, 20). Labbé et al. (19) see prospects in the introduction of measurement of osmolarity of the lachrymal film. Its correlation with the number of used preparations has been demonstrated. This phenomenon is explained on the basis of the chemical properties of the preservative agents, which act especially upon the lipid layer of the lachrymal film, thus reducing its stability, increasing evaporation and thus also osmolarity (19).

The aim of our study was to evaluate the condition of the ocular surface in patients treated with prostaglandin analogues, with consideration of the contained preservative agent.

## METHOD

### Study design

The observation study included patients treated in monotherapy with prostaglandin analogues for glaucoma (primary or secondary), or for ocular hypertension, who were examined at the glaucoma centre of the Department of Ophthalmology of the University Hospital in Olomouc from the beginning of September 2014 to the end of February 2015. A control group comprised patients with suspect glaucoma or ocular hypertension without local or general anti-glaucomatous treatment. In the case of a repeated visit of the patient during the observation period, the data obtained on the patient's first visit was used for the evaluation in this study. The inclusion criteria were as follows: age over 18 years, treatment by prostaglandin analogues in monotherapy, minimum length of current anti-glaucomatous treatment 4 months. The exclusion criteria included: surgery or injury to eye less than one year before the conducted evaluation, active inflammatory ocular pathology, wearer of contact lenses, presence of systemic disorder associated with dry eye syndrome, application of concomitant local eye therapy with content of preservative agents in the last 3 months. The study was conducted in accordance with the Helsinki declaration. All the patients were informed in detail and expressed their consent to their inclusion in the study.

### Procedure

For all patients demographic data, personal and ocular anamnesis were recorded, including the length of treatment with the current medical preparation and the frequency of application of artificial tears. The patients completed a questionnaire composed of a Czech translation of the Ocular surface disease index© (OSDI) (25). At the following clinical

examination the observed eyes were first of all evaluated for the level of hyperaemia of the conjunctiva according to Efron (10), and immediately following the application of 1 drop of 0.2% fluorescein solution the BUT (as the interval between the last blink and formation of the first dark stain) was read on a slit lamp with the use of a blue cobalt filter and 16x enlargement, after which the degree of colouring of the conjunctiva and cornea was stipulated according to the Oxford classification (5).

**Characteristics of group**

In the observed group a total of 80 patients (156 eyes) were included in the study. Of these, 20 patients (40 eyes) within the age range of 20-70 years (median 61.5 years), 7 men and 13 women, formed the control group. 60 patients (116 eyes) treated with a prostaglandin analogue were divided into 3 groups according to the preservative agent used in the preparation: without preservative agents – 18 patients (36 eyes) within the age range of 22-76 years (median 60.5 years), 6 men and 12 women; with the preservative agent polyquaternium – 17 patients (34 eyes) aged 18-79 years (median 64.0 years), 6 men and 11 women with the preservative agent BAK – 25 patients (46 eyes) aged 23-83 years (median 65.0 years), 12 men and 13 women. An overview of the used pharmaceutical preparations in the groups is presented in table 1. If the treatment was applied only to one eye and the second eye was without treatment, the patient was included in the relevant group according to the used preservative agent in the pharmaceutical preparation and only the treated eye was evaluated.

**Data analysis and statistical evaluation**

The data of the included patients was recorded in forms, following the performance of calculation of OSDI it was converted into electronic form, subjected to a descriptive analysis and statistically processed. For the statistical processing the statistical software IBM SPSS Statistics 22 was used. The data was described with the help of indicators of descriptive statistics – mean, standard deviation, minimum and maximum value and median. With regard to the size of the group and the character of the data, a non-parametric Kruskal-Wallis test was used for comparison in quantitative attributes. For a comparison of the groups in qualitative attributes a Fisher's exact test was used. All the statistical tests were performed on the level of significance of 0.05.

## RESULTS

Neither the difference in the age composition nor the representation of the individual sexes was statistically significant in the compared groups (table 2, table 3). In the group without preservative agents the values of length of treatment with the current preparation were statistically significantly lower in comparison with the group with polyquaternium ($p = 0.001$) and the group with BAK ($p = 0.004$) (see table 3). No significant differences were demonstrated between the groups of polyquaternium and BAK ($p = 1.000$). A normal OSDI value was recorded in the group without preservative agents in 56% of patients, in the polyquaternium group in 59%, in the BAK group 72% and in the control group 85%. Values attesting to severe OSD were represented only in the BAK group, in 8% of patients (graph 1). A comparison of the representation of BUT values in individual groups is illustrated in graph 2. The difference between the groups in the resulting OSDI and BUT values was not statistically significant (see tables 3, 4). The lowest degree of staining the conjunctiva and cornea with fluorescein was recorded in 33% of patients in the group without preservative agents, 44% in the polyquaternium group, 41% in the BAK group and 75% of patients in the control group. The highest degree of staining of the conjunctiva and cornea in this study (Oxford III) was attained by 6% of patients in the polyquaternium group and 7% of patients in the BAK group (graph 3). In the control group there was a statistically significantly lower level of staining of the conjunctiva and cornea with fluorescein in comparison with patients in the groups without preservative agents ($p = 0.001$), polyquaternium ($p = 0.007$) and BAK ($p = 0.002$). No significant differences were demonstrated between the other groups (see table 4). In the group without preservative agents there were statistically significantly lower values of hyperaemia of the conjunctiva in comparison with patients in the polyquaternium group ($p = 0.011$). No significant differen-

**Table 1** Overview of used pharmaceutical preparations

| Group | Current treatment | Number | |
|---|---|---|---|
| | | patients | eyes |
| Without preservative agents | Monopost® | 13 | 26 |
| | Taflotan® | 5 | 10 |
| polykvadium-chlorid | Travatan® | 17 | 34 |
| BAK | Arulatan® | 1 | 2 |
| | Latanoprost Actavis® | 2 | 4 |
| | Lumigan® | 2 | 4 |
| | Unilat® | 5 | 10 |
| | Xalatan® | 11 | 18 |
| | Xaloptic® | 4 | 8 |

Note.: BAK – benzalkonium-chlorid

**Table 2** Representation of sex

| | | Group | | | | | | | | p (Fisher's exact test) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | controls | | Without preservative agents | | polyquaternium | | BAK | | |
| | | Number | % | Number | % | Number | % | Number | % | |
| sex | men | 7 | 35 % | 6 | 33 % | 6 | 35 % | 12 | 48 % | 0,741 |
| | women | 13 | 65 % | 12 | 67 % | 11 | 65 % | 13 | 52 % | |

Note.: BAK – benzalkonium-chlorid

**Table 3** Age composition of groups, Ocular surface disease index© and length of current treatment

| Group | | Age (years) | OSDI | Length of treatment (months) |
|---|---|---|---|---|
| **Without preservative agents (n=18)** | Median | 60,5 | 10,8 | 12,5 |
| | Minimum | 22 | 0 | 4 |
| | Maximum | 76 | 27,8 | 57 |
| | Mean | 57,8 | 11,2 | 17,7 |
| | SD | 14,7 | 8,6 | 15,6 |
| **polyquaternium (n=17)** | Median | 64 | 10 | 30 |
| | Minimum | 18 | 0 | 12 |
| | Maximum | 79 | 32,1 | 85 |
| | Mean | 61 | 11,5 | 40,5 |
| | SD | 15 | 8,7 | 23,1 |
| **BAK (n=25)** | Median | 65 | 9,4 | 36 |
| | Minimum | 23 | 0 | 5 |
| | Maximum | 83 | 40 | 133 |
| | Mean | 65 | 10,3 | 49,6 |
| | SD | 12 | 9,3 | 39,3 |
| **Controls (n=20)** | Median | 61,5 | 5,6 | |
| | Minimum | 20 | 0 | |
| | Maximum | 70 | 27,5 | |
| | Mean | 58,3 | 6,6 | |
| | SD | 11,6 | 7,3 | |
| P (Kruskal-Wallis test) | | 0,125 | 0,155 | **0,001** |

Note: OSDI – Ocular surface disease index©; BAK – benzalkonium chloride; SD – standard deviation

ces were demonstrated between the other groups (see table 4, graph 4). Artificial tears were not applied or known by 90% of patients in the control group, 67% in the group without preservative agents, 59% in the polyquaternium group and 76% in the BAK group (graph 5).

## DISCUSSION

In several clinical trials (14, 19, 20, 28, 36) more than one half of patients using anti-glaucomatous therapy stated subjective complaints in connection with OSD.

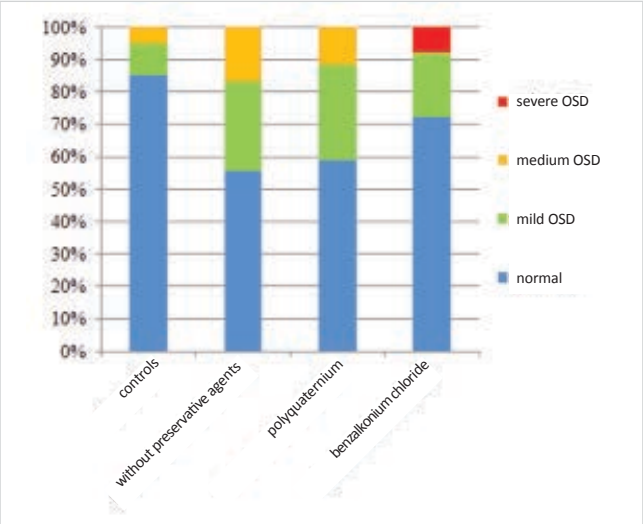
According to Pisella et al. (28) it is necessary to minimise the side effects of treatment, which contributes to an increase of its efficacy, support for compliance and continuation in treatment. Local therapy should not reduce the success of any applicable surgical treatment of glaucoma. Inconspicuous signs of ocular toxicity such as spot keratopathy attest to chronic damage to cells, which may have long-term consequences. The application of preservative agents generates a reduction of cellular proliferation and viability in the cornea, with subsequent impairment of healing and jeopardising of the epithelial barrier (28).

The incidence of symptoms of OSD in treatment with anti-glaucomatous agents depends on the quantity of the preservative agent, increases with the number of applied drops and decreases following conversion into a preparation without preservative agents, which among other factors is evidence

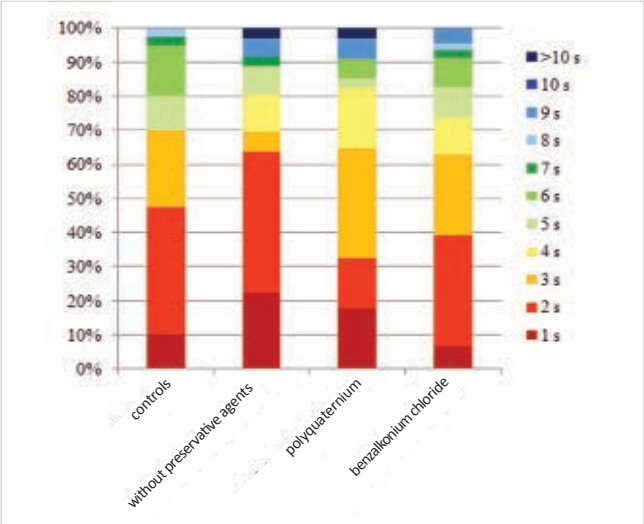
**Table 4** Results of evaluation of ocular surface

| Group | | Hyperaemia of conjunctiva | BUT (s) | Staining of conjunctiva and cornea |
|---|---|---|---|---|
| **Without preservative (n=36)** | Median | 1 | 2 | 1 |
| | Minimum | 0,5 | 1 | 0 |
| | Maximum | 1,6 | 11 | 2 |
| | Mean | 1 | | 0,9 |
| | SD | 0,3 | | 0,7 |
| **polyquaternium (n=34)** | Median | 1,2 | 3 | 1 |
| | Minimum | 0,6 | 1 | 0 |
| | Maximum | 2,2 | 11 | 3 |
| | Mean | 1,4 | | 0,9 |
| | SD | 0,5 | | 1 |
| **BAK (n=46)** | Median | 1,2 | 3 | 1 |
| | Minimum | 0 | 1 | 0 |
| | Maximum | 2,5 | 9 | 3 |
| | Mean | 1,3 | | 0,9 |
| | SD | 0,6 | 2 | 0,9 |
| **Controls (n=40)** | Median | 1 | 3 | 0 |
| | Minimum | 0 | 1 | 0 |
| | Maximum | 2,2 | 8 | 1 |
| | Mean | 1 | | 0,3 |
| | SD | 0,6 | | 0,4 |
| P (Kruskal-Wallis test) | | **0,008** | 0,263 | **0,001** |

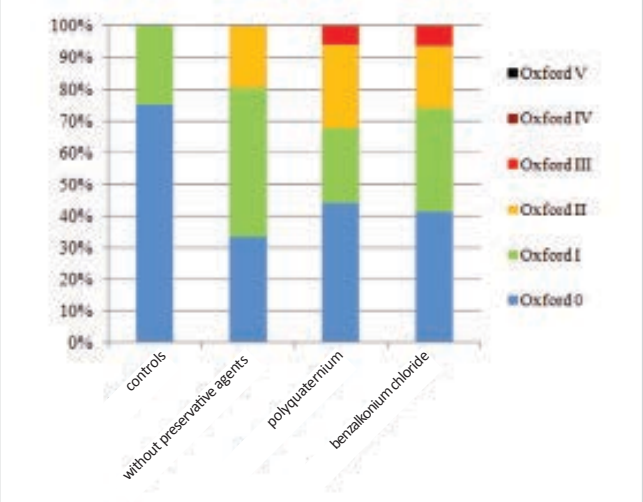
Note: BUT – break up time; BAK – benzalkonium chloride; SD – standard deviation



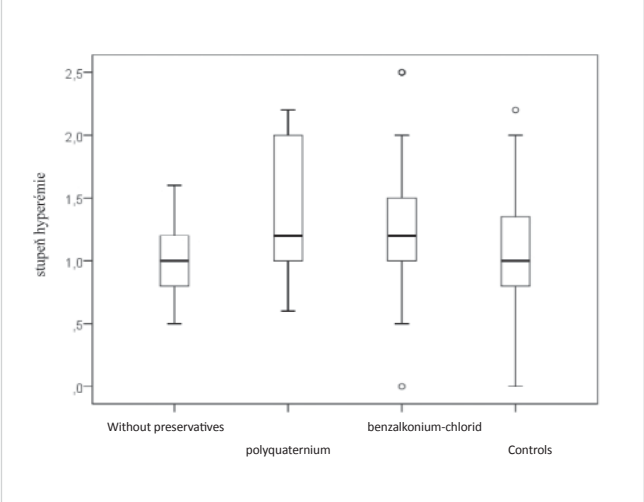

**Graph 1:** Ocular surface disease index©
Note: OSD – ocular surface disease



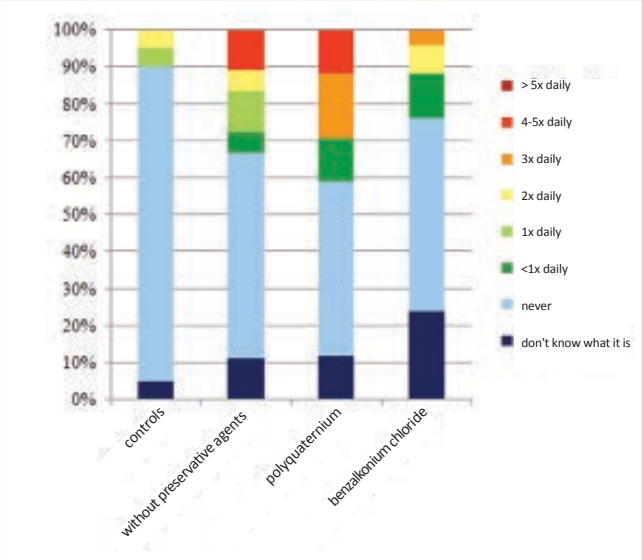

**Graph 2:** Break up time




**Graph 3:** Barvení spojivky a rohovky fluoresceinem




**Graph 4:** Conjunctival hyperaemia




**Graph 5:** Frequency of application of artificial tears

of the reversibility of symptoms of OSD (28).

Uusitalo et al. (39) compared the efficacy and tolerance of tafluprost without preservative agents as against latanoprost with BAK. 3 months after the replacement of latanoprost with tafluprost, the value of intraocular pressure was the same, whilst there was a significant reduction of subjective complaints (by up to 50%), staining of the cornea and conjunctiva, hyperaemia of the conjunctiva, and conversely an increase in the values of the Schirmer test and BUT.

In a study (15) dealing with the efficacy and toleration of tafluprost without preservative agents in patients originally treated with a prostaglandin analogue with BAK, 3 months after the change of therapy intraocular pressure was significantly reduced, subjective complaints improved and objective side effects were reduced. The incidence of medium to severe hyperaemia of the conjunctiva decreased from 43.2% to 1.9%.

Rouland et al. (33) compared the efficacy and safety of latanoprost with BAK. After 84 days from the beginning of treatment (commenced after the elapse of a wash-out interval)

the value of intraocular pressure was comparable, whereas in the group without preservative agents there was a significantly lower incidence of subjective complaints and medium to severe hyperaemia of the conjunctiva (21% versus 29%), no difference in staining of the cornea was recorded.

In a multicentric study (17) conducted in the Czech Republic, the efficacy and safety of tafluprost without preservative agents was evaluated on patients with newly commenced treatment or who had been transferred from another anti-glaucomatous therapy to tafluprost. The most frequent reasons for the change to tafluprost were local intolerance of the existing treatment (irritation of the eye and hyperaemia of the conjunctiva) (67.7%), and its insufficient efficacy (34.6%). Following the change to tafluprost intraocular pressure was significantly reduced, and subjective tolerance improved.

After insufficient efficacy, adverse effects are the second most common reason for change of therapy (43). Clinical trials (15, 17, 28, 33, 39) demonstrate that replacement of a preparation with BAK with a preparation without BAK leads to an improvement of the condition of the patient's ocular surface.

Cvenkel et al. (8) evaluated subjective and objective symptoms of OSD in patients treated with anti-glaucomatous drugs with preservative agents, who in comparison with an untreated control group had significantly shorter BUT and a higher degree of colouring of the conjunctiva and cornea according to the Oxford classification, which was in correlation with the number of drops applied per day.

Rossi et al. (32) monitored the presence of OSD in patients using anti-glaucomatous drugs with conservative substances in relation to the number of drops applied per day. Although the level of hyperaemia of the conjunctiva and the frequency of incidence of spot defects of the cornea increased with the number of applied drops per day, the difference between the groups was not significant, as was the case upon comparison of OSDI. In a further study, Rossi et al. (31) recorded abnormal BUT in 30.5% of eyes and spot keratopathy in 31.7% of eyes in patients being treated for glaucoma or ocular hypertension.

Leung et al. (20), upon monitoring OSD in glaucoma patients, determined that each further drop containing BAK per day is linked to a doubling of the probability of abnormal staining of the conjunctiva and cornea with lissamine green, although the dependency between the number of drops containing BAK per day and BUT, the Schirmer test and OSDI was not significant. The correlation between the results of OSDI and the performed clinical trials to the diagnosis of OSD was also weak.

Saade et al. (36) recorded abnormal OSDI in 68% of patients treated with anti-glaucomatous drugs, but in only 13% of subjects in the untreated control group. Abnormal BUT and staining of the conjunctiva and cornea with lissamine green was observed in 68% of treated patients and 17% in the control groups. They stated an index for quantification of local therapy (calculated as the number of drops applied per week multiplied by the length of treatment in years), which correlates with OSDI.

Matthews et al. (23) confirmed direct proportionality between the number of used anti-glaucomatous drugs and the degree of staining of the cornea. They consider OSDI to be a weak tool for identifying OSD in glaucoma patients due to its inability to differentiate between complaints caused by damage to the visual field.

Fechtner et al. (13) and Garcia-Feijoo et al. (14) in independent studies quantified the incidence of OSD in patients undergoing therapy with anti-glaucomatous drugs with the help of OSDI, which was abnormal in 48% and 59% of probands respectively. In patients treated for less than 6 years, OSDI was significantly lower than in patients treated for more than 6 years (14).

Baudouin et al. (3) identified risk factors for the development of OSD in patients treated with anti-glaucomatous drugs. These include age, length of treatment, number of drops applied per day, change of local therapy due to intolerance, value of intraocular pressure and degree of progress of glaucoma. They demonstrated OSD in 51% of patients, hyperaemia of the conjunctiva in 60.3%, staining of the cornea with fluorescein in 34.7% and BUT below 5 in 20.9% of patients.

Of Czech authors, Výborný et al. (41, 42) focus on preservative agents in anti-glaucomatous drugs, calculating the daily dose of BAK in eye drops with regard to the size of the drop, concentration of BAK and frequency of application.

In our study the statistically significantly lower values of the length of treatment with the current preparation in the group without preservative agents in comparison with the group with polyquaternium and the group with BAK are most probably due to the relatively recent introduction of prostaglandin analogues without preservative agents onto the Czech market. In the groups treated with anti-glaucomatous drugs, in comparison with the controls there was a more frequent incidence of an abnormal OSDI result, similarly as in the study by Saade et al. (36). The difference between the groups in the resulting OSDI and BUT values was not statistically significant, and a similar conclusion was reached also by Rossi et al. (32) and Leung et al. (20).

The absence of a difference in subjective ocular symptoms among patients undergoing therapy with anti-glaucomatous drugs and control patients is explained by Martone et al. (22). They demonstrated that the number of nerve fibres in the cornea is significantly lower in patients undergoing local anti-glaucomatous therapy than in healthy volunteers.

The statistically significant lower degree of staining of the conjunctiva and cornea in our control group in comparison with the treated groups corresponds with the results of the study by Cvenkel et al. (8) and Saade et al. (36). The absence of a difference in staining of the ocular surface between the groups treated with a prostaglandin analogue with a preservative agent and without a preservative agent are also described by Rouland et al. (33).

In the group without preservative agents there were significantly lower values of hyperaemia of the conjunctiva in comparison with patients in the polyquaternium group. Similar results were attained also in independent studies by Uusiatalo et al. (39), Hommer et al. (15) and Rouland et al. (33), who however compared a prostaglandin analogue without preservative agents with prostaglandin analogues containing BAK. Hyperaemia of the conjunctiva depends on the dose of the active substance (15), and is intensified by a higher concentration of BAK, although the precise mechanism has not yet been clarified (39).The results of meta-analyses (6, 12, 16) demonstrate that

the incidence of hyperaemia of the conjunctiva is lower upon treatment with latanoprost than with travoprost. On the basis of this it is possible to assume that the higher incidence of hyperaemia of the conjunctiva in the polyquaternium group may be caused by the active substance of the preparation, because in the Czech Republic travoprost is the only available prostaglandin analogue with the preservative agent polyquaternium. However, Crichton et al. (7) did not demonstrate a significant difference in hyperaemia of the conjunctiva, BUT or staining of the cornea between patients treated with bimatoprost, travoprost or latanoprost with preservative agents.

We explain the absence of a difference in the observed parameters between the individual treated groups by means of the fact that symptomatic patients were in most cases quickly transferred to a more suitable preparation. Moreover, in problematic patients there is frequently a relatively quick replacement of preparations or non-compliance.

Our study is limited by the size of the examined group, which is caused by the monocentric nature of the study and relatively stringent inclusion criteria. With regard to the size of the groups we did not demonstrate a mutual correlation of the demographic data and observed parameters. We also did not take into account the treatment used before the current preparation.

The different partial results of the studies may be explained by the various diagnostic schemas used in the assessment of OSD. However, there are also further factors which may influence the reproducibility of the tests used for demonstrating OSD. These include natural fluctuation during the day, national variability, systemic therapy, natural environment and other factors (8).

## CONCLUSION

Glaucoma is a serious sight-threatening disease. The side effects of anti-glaucomatous therapy should not be overlooked, because they may have an impact on compensation of glaucoma, the result of filtration operation, compliance and above all the patient's quality of life. Their elimination leads not only to greater satisfaction on the part of the patient and doctor, but also to a reduction of the overall costs of treatment. Our study confirmed that the condition of the ocular surface in patients undergoing monotherapy with prostaglandin analogues is worse than in untreated individuals, which corresponds with the results of foreign authors. However, no statistically significant differences were demonstrated between treated patients depending on the contained preservative agent. For this reason further studies on larger groups of patients are required, with the use of a uniform evaluation of OSD.

## LITERATURE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