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Ocular Surface Changes in Glaucoma Patients Related to Topical Medications

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A B S T R A C T

Topical glaucoma therapy is a long termed, usually lifelong. Antiglaucomatous drugs have toxic effects on ocular surface, due to preservative toxicitiy or the drug itself. Adding a lubricant eyedrops to antiglaucomatous therapy, especially if considering the preservative used, can have protective effect. The purpose of this study was to evaluate the stability of precorneal tear film in glaucoma patient prior and after administration of lubricant eye drops with different tipe of preservatives. The study showed the protective role of ocular surface lubrication especially when using drugs with less harmful preservatives.

Key words: *glaucoma, preservatives, complience, toxicity, tear film*

Introduction

Glaucoma is a cronic disease, life long, and its therapy is long termed aswell. To be effective it has to be used in regular and continuous manner. Topical antiglaucomatous therapy is often associated with simptoms and signs of toxicity, inflamatory changes of the ocular surface and dicrease of tear film break up time (TBUT). TBUT test is test for evaluating precorneal tear film stability. Patients with dry eye and ocular surface disorders can be evaluated by TBUT mesuring. The main causative factor for the toxicity and ocular surface disorders can be the preservative or an active compound of the drug. Preservative is an aditive to the drug with two main purposes – it acts against decay, discoloration and spoilage and it has a role in destroying or inhibiting multiplication of microorganisms. There are two main groups of preservatives, detergent and oxidative. Detergent preservatives can cause cell membrane lysis and acumulate in ocular tisue. They have dose dependent effect. They also interfere with the integrity of superficial lipid layer of the tear film, reduce the TBUT and may contribute to the ocular surface disease.. BAK as the most often used preservative in ophthalmic solutions is the detergent preservative. Second group are oxidative preservatives with Stabilised Oxochloro Complex (SOC) as the main representative. Their key component is sodium chloride and it has mild cytotoxic effect and excelent safety record. In this paper we explored the possible protective role of lubricant eye drops on ocular surface in patients using topical antiglaucomatous therapy. We also explored if there is a difference in protection of lubricants regarding the preservative in the lubricant itself. We compaired the changes on precorneal tear film stability in patients using lubricants with preservaives that are representatives of two main preservative groups.

Methods

This was a prospective study. From Glaucoma cabinet in Department of Ophthalmology of General Hospital Zadar we recruited patients with primary open angle glaucoma. There were total of 60 patients, 28 male (46%) and 32 female (54%) age 45–70 years (median 54.5y) using topical antiglaucomatous therapy with BAK preservative and good regulation of intraocular pressure. They used therapy for 2–5 years and they had no objections or side effects of the therapy. We devided patients into 2 groups of 30 patients. Groups were uniformed in manner that in each group there were 6 patients on latanoprost therapy, 5 patients were using timolol dorsolamide fixed combination, 4 patients were using travoprost and 4 patients used

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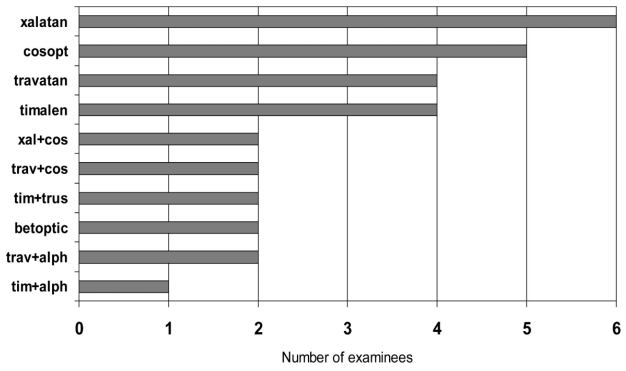

Fig. 1. Examinees according to therapy.

timolol. Two patients in each group used latanoprost and timolol dorsolamid fixed combination, travoprost and timolol dorsolamid, two patients used travoprost and brinzolamid and two patients used betaxolol (Figure 1). In both groups we evaluated tear film quality on slit lamp examination by measuring tear film break up time (TBUT) at baseline. After baseline evaluation we administrated all the patients lubricant eye drops, each group with different preservative. One group used lubricants with BAK preservative and the other with SOC preservative aditional to their topical antiglaucomatous therapy. They used lubricants twice a day in the same regimen in both groups. We reevaluated tear film quality 3 months after the lubricant drops adminstration measuring TBUT. For statistical data analysis we used t-test.

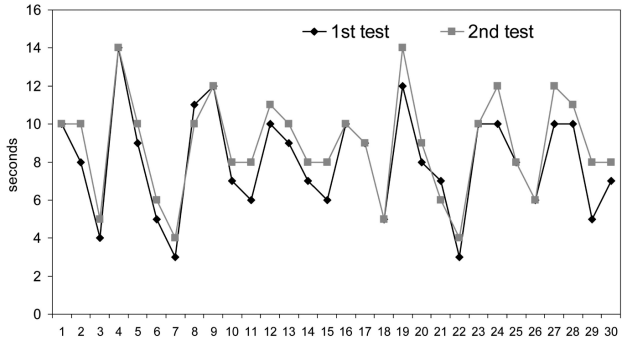

Fig. 2. Tear film break-up time (TBUT) test – BAK group. Test 1 – TBUT measures at baseline. Test 2 – TBUT measures 3 months after lubricant administration.

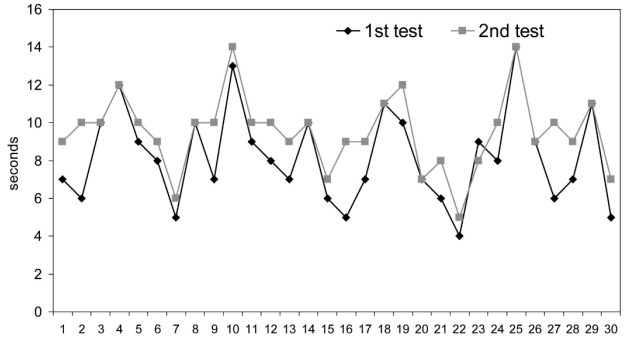

Fig. 3. Tear film break-up time (TBUT) test – SOC group. Test 1 – TBUT measures at baseline. Test 2 – TBUT measures 3 months after lubricant administration.

Results

Baseline TBUT values in first group of patients were 3–14 sec. Three months after using lubricant with BAK preservative we measured the following values changes: in 9 examinees values were unchanged- the same as baseline, in one examenee TBUT was 1 sec less than baseline. In 20 examenees TBUT values three months after lubricant drops adminitration were higher, in 5 examinees for 2 sec, and in the 15 examenees for 1 sec (Figure 2). The change in TBUT between 1st and 2nd test was statistically signifficant ($p<0.05$). In second group of examenees that used SOC lubricant eyedrops, baseline values of TBUT were 4–14 sec. Three month later values remained the same in 9 patients and in one patient TBUT was less than the baseline. In the remaining 20 patients values were higher than the baseline, in 8 examenees for 1 sec, in 8 for 2 sec, in one for 3 sec. In two examenees values were 4 sec higher and in 1 for 5 sec (Figure 3). The change in TBUT between 1st and 2nd test was statistically signifficant ($p<0.05$). Comparing the groups, baseline TBUT (1st test) values were not statistically different ($p>0.05$) and the change in TBUT (2nd test) between the groups was not statistically significant ($p>0.05$).

Discussion and Conclusion

Long term usage of antiglaucomatous therapy can have toxic effect on ocular surface. There are clinical evidence that the number of medications, their prolonged use and total BAK exposure are risc factors to develop ocular surface disease in patients with glaucoma[1].BAK appears to be the main contributor to corneal toxicity in a dose – dependent manner[2].There are reports examinating ocular surface using recently developed confocal cornea microscopy that showed significantly reduced tear production and TBUT reduction, and also changes in corneal epithelial cells and Langerhans cell densities in patients using topical antiglaucoma therapy[3,4]. TBUT test evaluets the stability of the precorneal tear film, and in diferent studies comparing signs, simptoms and predictive tools for dry eye disease and ocular surface disorders it is shown to be the most reliable test combined with vital staining[5]. There are reported studies comparing using of antiglaucoma topical drugs with preservative and preservative free drug, and they mostly report improved quality of life and and less dry eye simptoms when less preservatives used[6,7]. There are aims in modern glaucoma therapy to optimise the concentration of BAK or to use preservative free drugs in order to improve condition of the ocular surface[8]. Ocular surface disease impacts the glaucoma treatment outcome and it can result in noncomplience, lack of adherence and

eventually visual impairment[9]. In some estimations about 20% of patients on topical glaucoma or ocular hypertension treatment may need preservative free medications[10]. Therefore simptoms and signs of ocular surface disease should not be overlooked, and glaucoma treatment should be adapted by avoiding polytherapy- especially considering the number of drops per day, concentration and tipe of preservative used. In that manner we can improve complience and adherence to therapy and final outcome of glaucoma therapy. In this study we premised the protective effect of lubricant eye drops on ocular surface in general and especially if less harmfull preservative used. Our results showed increased tear film stability measured with TBUT test that was statistically signifficant in both groups of patients, using lubricant with BAK and SOC preservative. There was no statistically significant difference between BAK and SOC group in the investigated period of time. There are other studies investigating this protective role and they also concluded that lubricant eye drops restore hyperosmolarity and stimulate tear production[11]. To avoid or at least minimise the chance for ocular surface disease an ophthalmologist should consider avoiding polytherapy, choose preparations with less concentrations of preservatives and less harmful preservatives. Also adding lubricant eye drops in an therapy option. In our study the protective role of lubricats was proved for lubricants in general and with no difference regarding the preservative used in lubricant itself.

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PROMJENE POVRŠINE OKA GLAUKOMSKIH BOLESNIKA POVEZANE SA TOPIČKOM TERAPIJOM

SAŽETAK

Topička terapija glaukoma je dugotrajna, obično i doživotna. Antiglaukomski lijekovi imaju toksični učinak na površinu oka, dijelom radi utjecaja konzervansa dijelom radi same aktivne komponente lijeka. Uvođenje u tearpiju kapi za lubrikaciju može imati protektivni učinak na površinu oka, pogotovo ako se vodi računa o konzervansu u lubrikantu. Cilj ove studije bio je evaluirati stabilnost prekornealnog suznog filma u pacijenata sa glaukomom prije i nakon uvođenja lubricirajućih kapi sa različitim vrstama konzervansa. Studija je pokazala protektivnu ulogu lubrikanata na površinu oka, naročito kod korištenja manje štetnih konzervansa.