TEAR FILM STABILITY IN PATIENTS WITH PSEUDEXFOLIATION

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STABILNOST SUZNOG FILMA KOD PACIJENATA SA PSEUDOEKFOLIACIJAMA

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ABSTRACT

Pseudoexfoliation syndrome is an age related disorder, characterized by abnormal fibrous fiber production and accumulation in different visceral organs as well as in the eye and periocular tissues. Hystological examination recorded the presence of the pseudoexfoliation in the conjunctiva, and they can disturb the accessory lacrimal gland and goblet cell function. This can explain tear film instability in patients with pseudoexfoliations. In our study, we examined the tear film stability in patients with and without pseudoexfoliation, using Schirmer test and tear break up time test. Our results indicated that patients with pseudoexfoliation had lower values of Schirmer and tear break up time tests than patients without it. Pseudoexfoliation is the main reason for the instability of the tear film, because of its negative impact on the conjucntival goblet cells. In conclusion, ophthalmologists must have these data on their mind in the process of the pseudoexfoliation glaucoma treatment and controlling.

Keywords: *pseudoexfoliation, tear film, antigluacomatous drug*

SAŽETAK

Pseudoeksfolijativni sindrom je poremećaj vezan za starost bolesnika, koji se karakteriše abnormalnom proizvodnjom fibroznih vlakana i njihovom akumulacijom u različitim visceralnim organima, kao i u oku i periokularnim tkivima. Histološkim pregledom utvrđeno je prisustvo pseudoeksfolijacija u vežnjači, kao i da mogu dovesti i do poremećaja funkcije pomoćne suzne žlezde i peharastih ćelija. Ovim se može objasniti nestabinost suznog filma kod pacijenata sa pseudoeksfolijacijama. U našoj studiji, ispitivali smo stabilnost suznog filma kod pacijenata sa i bez pseudoekfolijacija, koristeći Schirmer test i test pucanja suznog filma. Naši rezultati su pokazali da su pacijenti sa pseudoeksfolijacijama imali niže vrednosti Schirmer testa i testa pucanja suznog filma, od pacijenata bez pseudoeksfolijacija. Pseudoeksfolijacije su glavni razlog za nestabilnosti suznog filma zbog svog negativnog uticaja na peharaste ćelije vežnjače. U zaključku, oftalmolozi moraju imati na umu ove podatke u procesu lečenja i kontrole pseudoekfolijativnog glaukoma.

Ključne reči: *pseudoeksfolijacije, suzni film, antiglaukomatozni lek*

ABBREVIATIONS

IOP - intraocular pressure
PACG - primary angle closure glaucoma
PEX - Pseudoexfoliation
TBUT test - tear break up time test
XFG - pseudoexfoliative glaucoma
XFS - pseudoexfoliative syndrome

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INTRODUCTION

Pseudoexfoliation syndrome (PEX) is an age-related generalized disorder of the extracellular matrix with increased production and accumaltion of abnormal extracellular material in different tissues of the body (skin, connective tissue portions of visceral organs, eye) (1). Biomicroscop eye examination indicated that pseudoexfoliation material can be found on corneal endothelial, pupilar margin, iridocorneal angle, lens anterior capsule, iris surface and on ciliary body (2). Also, data indicated for PEX material presentation in periorbital tissues as well as on conjunctiva (3). Pathohystological examination of the conjunctiva suggested that pseudoexfoliation can be found on the conjunctiva surfaces with affection on the accessory lacrimal gland and goblet cells functions (4). These findings can indicate on the possibilities of tear film instability. Pseudoexfoliation syndrome is one of the most common cause of elevated intraocular pressure and developing of pseudoexfoliative glaucoma, which is the final step in the process of production and accumulation of PEX material (5).

MATERIAL AND METHODS

The study was performed in Clinic of Ophthalmology, Clinical Centre Kragujevac, from 1st January 2015 until 1st January 2016. The patients included in our study underwent routine ophthalmological examination in the Outpatient Department of the Clinic. All patients (n=150) were divided into three groups according to PEX presentations: PEX syndrome, PEX glaucoma, and age and sex matched control group (without PEX). Detailed slit lamp examination in mydriasis was performed for every patient, as well as Schirmer and TBUT tests. The patients with previous history of intraocular surgery, laser treatment or intraocular inflammation, PACG, contact lens wearer, ocular surface diseases, with lid abnormality or pterygium were excluded from the study. Also, excluding criteria was previous using of artificial tear eyedrops. Glaucoma diagnosis was determined on the earlier clinical examination (elevated IOP, optic head structural changes, visual field defect), without previous antigluacomatous drugs using. The measurement of intraocular pressure was performed by applanation tonometry. Tear break up time, indicator of the lipid lay of the tear film, was determined using fluorescein strips before the other planned intervention (measuring of the IOP, Schirmer test) and using some ophthalmic drug. Under the cobalt blue light, we noticed time until the appearance of the dry spot on the corneal surface. Local anesthetic (generic tetracain 0.5%) was applied before the test. Tear secretion test was done using Schirmer paper, applied in the lateral 1/3 of inferior fornix. Wet part of the paper was recorded for every eye.

Statistical analysis was performed with SPSS 19.0 software (SPSS Inc., Chicago, IL). The distribution of the data was determined by Shapiro–Wilks or Kolmogorov–Smirnov test. The continuous variables were expressed as mean ± standard deviation and the categorical variables as frequency and percent. Pearson chi-square test was used to determine the difference among three groups; and, differences among the groups were analyzed by Kruskal–Wallis test. The dual comparisons among groups with significant values were evaluated with Bonferroni adjusted Mann–Whitney U-test. p value of less than 0.05 was considered statistically significant for all tests.

RESULTS

Our study covered 269 eyes in 150 patients, divided in three groups (n=50). PEX syndrome group included 13 patients with PEX presentation only in one eye, and 37 patients with PEX presented in both eyes (totally 87 eyes). We also examined 82 eyes in XFG group (18 patients with affected only one eye, 18 patients with affected both eyes, and 14 patients with mixed PEX presentation-XFS on eye, and XFG on the other eye).

Patients' characteristics

The mean age of the participants among the group did not show the statistically significant differences, because of its matching. In the XFS group mean age was 69.2±4.3, in XFG group 69.8±3.9, control group 70.0±2.1. Our results indicated that was no statistically significant differences in gender distribution (male:female- XFS-26:24, XFG-24:26; control group-25:25), Table1.

Schirmer tests results

Groups with PEX (XFS and XFG) measurement indicated that patients with XFS and XFG had statistically significant lower values than control group ($p<0.05$), but without statistically significant differences among PEX groups ($p>0.05$). Our results indicated that control group had mean value of Schirmer test 13.5±4.2mm; XFS group had mean value 9.75±2.7mm (range: 5-18mm) and XFG had mean value 8.6±2.5mm. XFS group showed some differences between the participants: participants with one PEX presented eye had lower value of Schirmer test in affected eye (8.4±2.3mm) than in the other eye without PEX (9.2±2.6mm) but without statistically significant differences ($p>0.05$). In XFG group also, we noticed differ-

Table1. Patients` charcteristics

	XFS	XFG	control
ages	69.2±4.3	69.8±3.9	70.0±2.1
female/male	26/24	24/26	25/25

ences between the participants: participants with PEX material in the eye recorded lower Schirmer tests than other without the PEX without statistically significant differences ($p>0.05$), but also it was statistically significant lower than in the patients form control group ($p<0.05$).

TBUT tests results

TBUT tests results showed that PEX groups had statistically significant lower values than the group without PEX ($p<0.001$), with statistically significant differences between the two PEX groups ($p<0.05$). Control group patients had TBUT- 15±2 sec (range 9-15 sec); XFS group showed mean TBUT result10±2 (range 6-15 sec), and XFG- 8±1 (range 5-12 sec). In XFS group, participants with one eye affected with PEX had lower values of TBUT 9±2 sec compare with TBUT results on the other eye (10±2). Participants from the XFG group also had different values of TBUT according to the PEX presentation: eyes without PEX presentation recorded TBUT value- 10±1, with XFS on one eye-10±2 sec, and with both XFG- 8±2 sec.

DISCUSSION

Pseudoexfoliation syndrome is generalized fibrillopathy, characterized by abnormal production and accumulation of the pseudoexfoliative material in the whole body (6). Also, it is well known that PEX material can be detected by histological examination in the conjunctival tissue (3). Presentation of the PEX in conjunctival tissue can have the influence on the tear film stability (4). Tear film stability is predictive factor for the health of the ocular surface (7). If one of the components of the tear film is disturbed, ocular surface disturbances can be observed (8). Kozobolis et al. proved that PEX material in conjunctival tissues provoke the changes of the basic features of the morphology of the goblet cell (4). Though, it was established that density of the goblet cells in the patients with or without the PEX are similar, the alterations in their morphology can cause the changes in the tear film quality, decreasing the basic part of the tear secretion. Hystological examination of the conjunctival tissue discovered the presentation of the PEX (9). Our results indicated that basic tear secretion was decreased in patients with PEX presented in the eye, nevertheless to the stage of its presentation (XFS/XFG) compared with PEX negative patients. The stage of the PEX presentation may be determined by the Schirmer test values: lower values indicated for the advanced stage.

Oncel et al. established that tear film osmolarity was higher in patients with PEX, which can be explained by the dysfunction of the goblet conjunctival cells (10). TBUT test results from our study recorded lower in patients with PEX (XFS/XFG) compared with control group patients with statistically significant difference. XFG and XFS had different values of the TBUT without statistically significant difference. This fact can be useful in clinical practice to determine the stage of the PEX production and accumulation. So, patients with PEX own the dry eye symptoms more often than patients without PEX, as well as inflammation and tissue damage of the ocular surface.

According to the definition of the dry eye The Jones et al., indicated that tear secretion is divided into basic (fundamental tree layers tear film) and reflex (additional secretion peripheral sensory, retinal or psychogenic stimulated) (8). Anesthesia applied before the Schirmer test remains mainly basic secretion, which is the indicator for the tear secretion and goblet cells function (11).

These facts must be accepted and considered in the treatment of the XFG. Earlier studies indicated that XFG is one the most difficult form of glaucoma for controlling, because of its unknown nature (12). So, many antiglaucomatous drugs must be prescribed for its control. Ophthalmologists must have all of these informations when they prescribe the drugs. Particularly, if the two or more antiglaucomatous drugs are needed for the treatment, ophthalmologist must choose the preservative free drugs as well as the artificial tears for protecting the ocular surfaces (13). Patients discomfort when using antiglauocmatous drugs can be the reason for bed compliance in the glaucoma treatment (14). So, the results of the treatment can be also bed and the disease can be in the progression.

The very important thing for caring out the study is that group must be matched. Age matching is important because tear film is more disturbed in older patients (15). So, gender is very significant for the quality of the tear film, because females have lower tear secretion after the age of forty, caused by hormonal disturbances (16).

In conclusion, we can advise the ophthalmologist that they must consider the antigluaocmatous drugs for the treatment of the glaucoma, because of its negative effect on the damaged ocular surface caused by the disturbed tear film. PEX is the main reason for the instability of the tear film, because of its negative impact on the conjucntival goblet cells. Some future studies must establish correlation between the PEX conjunctival deposition and the mechanism of the PEX production. The results of this analysis can be the key for the successful treatment of the XFG.

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