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*Source / Izvornik:* **Collegium Antropologicum, 2015, 39, 43 - 45**

**Journal article, Published version**
**Rad u časopisu, Objavljena verzija rada (izdavačev PDF)**

*Permanent link / Trajna poveznica:* https://urn.nsk.hr/urn:nbn:hr:105:639014

Coll. Antropol. 39 (2015) 1: 43–45
Original scientific paper

# Ocular Surface Disease in Pseudoexfoliation Syndrome

**Ivan Škegro, Smiljka Popović Suić, Rajko Kordić, Sonja Jandroković, Igor Petriček, Tomislav Kuzman, Miro Kalauz, Sanja Perić and Sanja Masnec**

University of Zagreb, School of Medicine, University Hospital Centre Zagreb, Department of Ophthalmology, Zagreb, Croatia

**ABSTRACT**

*Aim of the study is to determine connection between pseudoexfoliation (PEX) syndrome and symptoms and signs of ocular surface disease. Tear film break-up time test, Schirmer II test and assessment of lid parallel conjunctival folds were performed in 40 PEX syndrome patients and 40 controls. All data was statistically analyzed. Results show statistically significant difference in every component between groups, most prominent in tear film break up time test. We have concluded that patients with PEX syndrome have higher predisposition of tear function disorders and that both components of dry eye syndrome are present in PEX syndrome.*

***Key words:*** *pseudoexfoliation syndrome, ocular surface disease, LIPCOF, tear film break-up time test, Schirmer II test*

## Introduction

Pseudoexfoliation syndrome is relatively widespread generalized disease of connective tissue in the elderly population. Approximately 10% of people over 60 years have PEX[1–3]. Deposition of PEX fibrils in the trabecular meshwork makes an important contribution to the occurrence of PEX glaucoma. This special form of elastosis appears to result from interplay between genetic and environmental factors in form of a complex disease[4,5]. Several studies in PEX patents showed association with polymorphisms in the gene lysyl oxidase like 1[6,7].

While the PEX syndrome was for long considered a specific disease of the anterior segment of the eye, today it is known to be a generalized process of the extracellular matrix[8]. Using electron microscopy or specific immunohistochemical markers, deposits of PEX material can be found in numerous organ systems. Also in skin and outer ocular tissues especially in conjunctiva[9]. Increased concentration of fibrogenic growth factors, reduced activities of proteolytic enzymes, subclinical inflammatory processes and increased oxidative stress are all believed to be involved in pathogenesis of this abnormal matrix process[10].

According to definition of Dry Eye Workshop, the term dry eye means multifactorial disease of the tears and surface of the eye which leads to symptoms, visual disturbances and instability of the tear film with possible changes in the ocular surface. They are accompanied by an increase in the osmolarity of the tear film and inflammation of the ocular surface. Damage occurs because of tear deficiency or tear film instability. Dry eye is among the most common diseases in ophthalmology with prevalence according to different studies between 5 and 34%[11]. The dry eye can be divided in two subgroups: hypovolemic and hyperevaporative. Hypovolemic is based on a disorder of the aqueous and mucinous layers of the tear film, while hyperevaporative is based on a disorder of lipid layer. The hypovolemic dry eye is manifested clinically as symptoms of a feeling of dryness, feeling of sand or a foreign body in the eye and stinging. In contrast, in lipid disorder, patient complains of the thickening and redness of the lid margin, the eyes often feel tired and symptoms typically occur during the course of the day and during stress.

## Material and Methods

In this case control study we examined 40 patients with unilateral or bilateral pseudoexfoliation on the eyes and 40 patients without it as control. Reasons for non-inclusion in the study were previous eye surgeries, history of recurrent eye inflammation, diabetes, all of which can

Received for publication May 30, 2014

influence on severity of ocular surface disease, also we didn't include patients who were using any kind of topical eye treatment.

Both groups were as similar as possible. Mean age in the PEX group was 77.55 years (range 72–85) and for the control group 74.72 years (range 69–82). Out of 40 enrolled patients with PEX, 37% were males and 63% were females. In the control group there was the same number of subjects and same gender distribution. The most common illness in both groups were hypertension and hyperlipoproteinemia.

Tear film break-up time test, Schirmer II test and assessment of lid parallel conjunctival folds (LIPCOF) were performed to patients in both groups. For determination of break-up time, fluorescein solution was applied to the inferior fornix, and the participants were asked to close their eyes. Using the blue light of the slit lamp, the time in seconds between eyelid opening and the appearance of initial defects in the tear film was measured. Schirmer II test was performed under local anesthesia with tetracaine hydrochloride 1% using paper strips. Measurements were taken at the fifth minute. LIPCOF was evaluated in the area on the bulbar conjunctiva above the lower lid with a slit-lamp microscope. All tests were performed by same experienced ophthalmologist on Department of Ophthalmology of University Hospital Centre Zagreb.

## Results

The statistical analysis was performed using the Statistical Package for Social Sciences Version 17.0.1 (SPSS Inc., Chicago, Illinois, USA). Data is presented as mean value ± standard deviation. The nonparametric Mann-Whitney U test was used to check the hypotheses if there are differences between control and experimental group. A p-value less than 0.05 was considered statistically significant.

Statistically significant difference was observed in LIPCOF between control and experimental group ($p<0.01$). Subjects in the experimental group had significantly higher results (0.87±0.54) than those in the control group (0.43±0.35). Two other tests/measures, TBUT and Schirmer II test, also showed significant difference between these groups ($p<0.01$). Tear break-up time was almost three times longer for control group (11.17±4.16) compared to experimental (3.97±2.31). Schirmer II test found higher results for the control group as well (12.91±3.42) than in the experimental group (8.32±3.93).

## Discussion

Recent studies have examined the prevalence of dry eye in glaucoma and ocular hypertensive patients. Leung et al conducted a study on 101 glaucoma patients in order to ascertain the prevalence of dry eye. A majority of patients in that study reported symptoms of dry eye. Schirmer tests showed that majority of his patients had a decrease in tear production. Abnormal tear quality (reduced TBUT) was also observed[12].

A large-scale study from Germany, involving 20,506 patients, analyzed the links between glaucoma, dry eye, age, medication, and concomitant disease. Among individuals with glaucoma, more women than men were reported to develop dry eye. The difference in the frequency of dry eye between men and women became more obvious after age 50 years. Hypertension, diabetes mellitus, and dry mouth, nose, and skin were the most frequent concomitant systemic diseases found in the survey. The incidence of dry eye increased with age, the number of IOP-lowering medications, and the duration of glaucoma[13].

Clinical methods of assessing physiologic functions that contribute to evaluate ocular surface disease have been developed over the past decades. Schirmer II consists of placing a filter paper strip on the lower lid margin in the temporal position of an anesthetized patient. Several diagnostic tests evaluate the quantity and quality of the tear film. The measurement of TBUT following the instillation of a fluorescein dye is a widely used technique. More sophisticated clinical tests are currently available, which may have greater sensitivity for detecting OSD in glaucoma patients, but they are not widely available. Some of the techniques for evaluating the health of the ocular surface (such as dry eye) is computerized videokeratoscopy, tear osmolarity and confocal microscopy. Other noninvasive techniques, such as aberrometry, have proven to be useful for assessing ocular surface health[14–17].

In this study, significant differences between two groups have been noted. The fact that eyes of the PEX group displayed statistically significantly different (abnormal) scores in LIPCOF, Schirmer II and TBUT tests compared to patients in the control group, suggests that PEX influence tear secretion and stability possibly related with conjunctival involvement in the condition. Pseudoexfoliation alters basic features of goblet cell morphology, thus affecting tear film stability[18]. This indicates that pseudoexfoliative patients are more likely to develope dry eye manifestations. Similar findings were noted in study conducted by Kozobolis et al.[19].

## Conclusion

Signs and symptoms of ocular surface disease are relatively common in older patients, but signs of dry eye are significantly higher in individuals who have PEX syndrome. There is evidence that topically administered medication affects the structure and the integrity of the ocular surface. This information should be in mind when drugs with benzalkonium chloride or beta blockers are prescribed to those patients. In that case, the use of artificial tears or preservative free topical therapy could be justified.

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*I. Škegro*

*University of Zagreb, School of Medicine, University Hospital Centre Zagreb, Department of Ophthalmology, Kišpatićeva 12, 10 000 Zagreb, Croatia*
*e-mail: ivanskegro@yahoo.com*

## BOLEST OČNE POVRŠINE KOD PSEUDOEKSFOLIJACIJSKOG SINDROMA

## SAŽETAK

Cilj ove studije je utvrditi povezanost između pseudoeksfolijacijskog sindroma (PEX) i simptoma i znakova bolesti očne površine. Test vremena pucanja suznog filma, Schirmer II test i procjena nabora spojnice paralelnih s rubom vjeđe su provedeni kod 40 pacijenata s PEX-om i 40 u kontrolnoj skupini. Svi podaci su statistički analizirani. Rezultati su pokazali statistički značajnu razliku među skupinama u svakoj pojedinoj komponenti, najiraženije kod testa vremena pucanja suznog filma. Zaključili smo da pacijenti s PEX-om imaju veću predispoziciju poremećaja suzne funkcije i da su obje komponente sindroma suhog oka prisutne u PEX-u.