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Original Article / Оригинални рад

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The impact of pseudoexfoliation and arteficial tears application on tear film stability in pseudophakic eye

Утицај псеудоексфолијација и коришћења вештачких суза на стабилност сузног филма у псеудофакном оку

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SUMMARY

Introduction/Objective Dry eye development after phacoemulusification is a very common complication of the cataract surgery. Combined with other risk factors, such as pseudoexfoliation (PEX), it makes this complication more frequent.

The aim of this study was to expose the influence of phacoemulsification associated with PEX, on the dry eye development, in the patients who underwent cataract surgery.

Methods The study included 160 eyes (160 patients) who underwent phacoemulsification. The patients were divided in four groups (n=40 patients). Groups I and II involved patients without PEX. The patients from group II were prescribed arteficial tears postoperatively. Patients from groups III and IV had PEX presentation. Patients from group IV got arteficial tears postoperatively. OSDI, TBUT test, fluorescein staining and Schirmer test served as "dry eye" tests in this study. Chi-square test and paried t test.

Results The measurement was taken for every patient preoperatively, on the first and seventh day,the first and third month and the first year. Tests showed postopertively developed dry eye in all groups, with the recovery of the tear film within three months except group III. The highest statistical significance was recorded between groups II and III, three and twelve months after the surgery, $p<0.001$. Values of TBUT (6.09±1.29s) and Schirmer test (8.91±2.14 mm) in III group strongly indicated that dry eye was still present one year after phacoemulsification. The greatest recovery of the tear film was recorded in group II during all measurements.

Conclusion The study showed how strong effect on the tear film have PEX and the usage of arteficial tears during the first posterative year. Based on our experience, we highly recommend the usage of arteficial tears after performing phacoemulsification.

Keywords: phacoemulsification; dry eye; pseudoexfoliation; arteficial tears

САЖЕТАК

Увод/Циљ Развој сувог ока после факоемулзификације је честа компликација операције катаракте. Заједно са другим факторима ризика, као што је псеудоексфолијација (ПЕФ), чини ову компликацију још учесталијом.

Циљ ове студије је био да прикаже утицај факоемулзификације удружене са ПЕФ, на настанак сувог ока, код оперисаних од катаракте.

Методе рада Студија је обухватила 160 очију (160 болесника) код којих је извршена операција катаракте. Они су подељени у четири групе (n=40). Прва и друга група обухватала је болеснике без ПЕФ. Болесници у другој групи добијали су вештачке сузе постоперативно. Трећу и четврту групу чине болесници са ПЕФ. Болесници у четвртој групи добијали су вештачке сузе постоперативно. Индекс обољења предње површине ока, тест бојења флуоресцеином, тест прекида сузног филма и Ширмеров тест коришћени су као тестови индикације сувог ока. За анализу података коришћени су $\chi 2$-тест и упарни т-тест.

Резултати Мерење је вршено код сваког болесника преоперативно, првог и седмог дана, првог и трећег месеца и годину дана после операције. Тестови су показали постоперативни настанак сувог ока у свим групама, са опоравком сузног филма у оквиру три месеца, изузев у трећој групи. Највећа статистичка значајност забележена је између друге и треће групе, три и дванаест месеци након операције ($p<0.001$). Вредности ТБУТ (6.09±1.29s) и Ширмеровог теста (8.91±2.14 mm) у трећој групи снажно указују на присуство сувог ока и након годину дана од факоемулзификације. Најбољи опоравак сузног филма забележен је у другој групи током свих мерења.

Закључак Студија је показала да изражен ефекат на сузни филм имају ПЕФ и употреба вештачких суза током прве постоперативне године. Према нашем искуству, неопходна је примена вештачких суза после операције катаракте.

Кључне речи: факоемулзификација; суво око; псеудоексфолијације; вештачке сузе

INTRODUCTION

Cataract surgery is one of the most commonly performed in ocular surgery as well as in the surgery in general in the world [1].The technique of the cataract surgery can have impact on the dry eye development [2]. The section of the corneal nerves is the basic step of the dry eye occurrence

during the cataract surgery. Additionally, exposure to the microscope light deteriorates the dryness of the eye. Ocular surgeons must bear in their minds that the usage of topical anestehsia and irriagtion fliud during the surgery exacerbates already disturbed ocular surface [3].

Pseudoexfoliation is the age related disorder of the visceral organs, blood vessels, skin and eye [4]. Hystopathologycal verification of the pseudoexfoliations in conjucntival tissue explains their impact on the goblet cells and the function of acessory lacrimal glands [5]. This finding has the influence on the consecution of the dry eye, confirmed by different studies [5,6].

Symptoms associated with dry eye are: pain, irritation, and poor vision [7]. Dry eye symptoms have influence on the life quality[8].

This study was conducted with the aim to examine the impact of the cataract surgery-phacoemulsification, combined with PEX, on the dry eye development in one year follow up period.

METHODS

The study included 160 eyes scheduled for the cataract surgery in the Clinic of Ophthalmology, Clinical Center Kragujevac, Kragujevac, Serbia. It was conducted from the 1st January 2015, until the 1st January 2016. The most important inclusion criterion was no dry eye diagnosis before the cataract surgery. Patients who used medications which provoke dry eye, such as antihistamines, antidepressants, contraceptive pills, antiholinergic drugs, were excluded from the study. The patients with cataract surgery complications were also excluded from the study. The patients with previous history of intraocular surgery, laser treatment or intraocular inflammation, glaucoma, ocular surface diseases, with lid abnormality or pterygium and contact lens users were not allowed to participate in the study.

With the approval of institutional Ethics Committee and according to the tenets of the Declaration of Helsinki, all patients gave their written consent at the beginning of the study.

Patients, who underwent cataract surgery, were divided into four groups according to preoperative clinical feature (PEX and without PEX) and the artificial tear status: the first group (n=40 patients) involved cataract patients without PEX and with no AT (arteficial tears) therapy, in the second group were patients with prescribed arteficial tears in therapy and no PEX presentation. The third and the fourth group, respectively, included cataract patients with PEX, without AT therapy (III group) and with prescribed arteficial tears (IV group).

In PEX groups, one of the most important including criterion was the presence of characteristic pseudoexfoliative material, but without diagnosed pseudoexfoliation glaucoma. According to that, complete ophthalmological examination for excluding glaucoma was performed: intraocular pressure measurement, ophthalmoscopy, gonioscopy, corneal thickness measurement and standard automated perimetry.

Before the surgery, according to the institutional protocol, patients used the topical ciprofloxacin eye drops for five days, five times per day (sol Floxal®, Dr.Gerhard Mann, Chem.-Pharm. Fabric GmbH, Berlin, Germany).

All patients underwent cataract surgery-phacoemuslification, by one surgeon. Patients were prepared for the surgery by applying the mydriatic eye drops (sol Fenilefrin 2,5%®, sol Homatropin 1%®Zajecar pharmacy, Serbia; sol Unitropic® 1%, Unimed pharma S.R.O. Bratislava, Slovakia). After the topical anesthesia was induced with 0.5% tetracaine hydrochloride, phacoemulsification was performed with 2.75mm clear corneal incision and with two side ports wide 1.5mm 90-degree away from the main incision. "Stop and chop" surgery technique was used for the nucleus removing (Stellaris- Bausch & Lomb phaco machine). Phacoemuslification time was no more than 10 minutes. After the capsular bag was cleared, it was filled with cohesive viscoelastic, and foldable monofocal artificial intraocular lens was implanted through the injector system. Viscoelastic was removed by aspiration, and stromal hydration was performed for the ports, with intracameral application of diluted cefuroxim (sol Nilacef® Hemofarm A.D., Vrsac, Serbia; 1mg/0,1 ml balanced salt solution). Postoperatively, locally Tobradex(Alcon- Couvreur NV, Puurs , Belgium) was applied five times per day for one month.

Patients from two groups (groups II and IV) used artificial tears 3 times per day (Sol.Vismed light, TRB, Chemedica AG, Germany) according to our professional opinion.

DRY eye tests

OSDI (Ocular surface Disease Index) – 12 item questionnaire was used to evaluate symptoms associated with dry eye [9]. We had to modify questions 4 and 5, since it was difficult to differentiate variants of the visual acuity due to lens opacity. OSDI score was calcultaed using the formula, ranged from 0-100. Score above 25 was considered as a dry eye.

Tear break up time, indicator of the lipid lay of the tear film, was determined by using fluorescein strips (Fluorets®, Laboratoryof Chauvin - Z.I.Ripotier - 07200 Aubenas, France) before the other planned intervention (measuring of the IOP, Schirmer test) and before the usage of some of the ophthalmic drugs. Under the cobalt blue light, we noticed time until the appearance of the dry spots on the corneal surface. Values less than 10 seconds indicated a dry eye syndrome. Flurescein staining was done for every patient using fluorescein strips (Fluorets®, Laboratory of Chauvin - Z.I.Ripotier - 07200 Aubenas, France), and it was classified by using Oxford Schema (grade 0-V) [10]. Score from 0 to I indicates normal, and from II to V a dry eye.

Local anesthetic (generic tetracain 0.5%) was applied before the test. Tear secretion test was done by using Schirmer strips (Schirmer Tear Test Strips®, Optitech, India), applied in the lateral 1/3 of inferior fornix. Wet part of the paper was observed for every eye separately. Values shorter than 5mm indicated a dry eye syndrome.

Complete ophthalmological examination (visual acuity, intraocular pressure measuring, indirect fundus ophthalmoscopy, and detailed slit lamp examination in mydriasys), including mentioned tests, was performed for every patient one week before the surgery, on the 1st day, 1st week, 1st month, 3rd month, and 1st year after the surgery.

Statistical analysis was done by using SPSS ver.22. For comparison of the data, Chi-square test and Paired t test were used ($p<0.05$, and $p<0.001$ value was accepted as statistically significant).

RESULTS

Patients' characteristics

Examined patients had the mean age of 70.24±7.5 years. Age of our patients ranged from 45 to 81 years. In all groups female to male ratio was equal.

OSDI questionnaire results

Preoperatively, by including criteria, all patients had OSDI score under the limit (<25 points) (Figure 1). Results indicated that all patients had OSDI results above the limit on the 7th postoperative day (I group-32.48±3.75; II group-24.13±3.95; III group-39.46±2.84; IV group-29.18±3.01), with statistically significant differences between all examined groups, $p<0.05$; $p<0.001$.

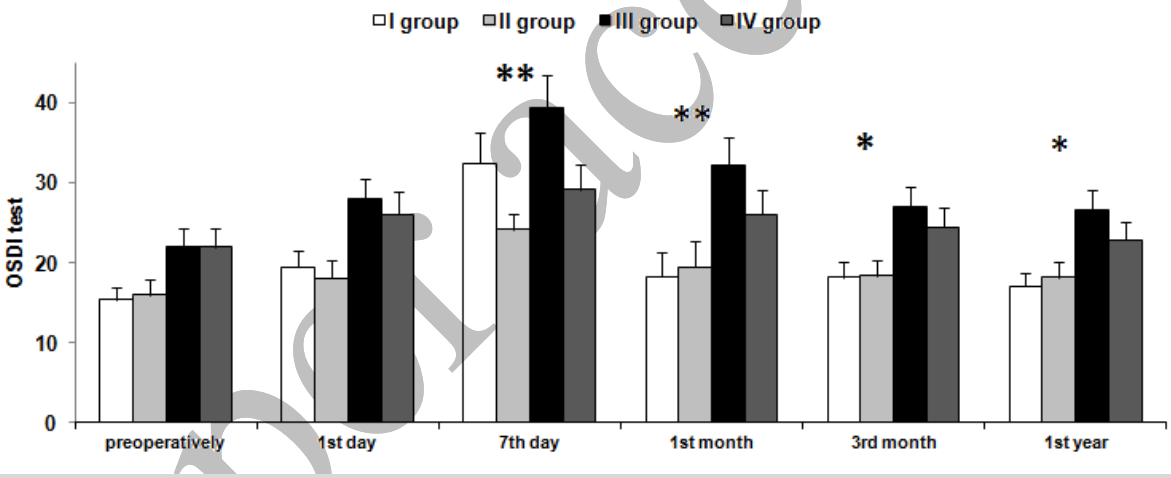

Figure 1.OSDI questionnaire results.

One month after the surgery, patients from groups I (18.29±3.03) and II (19.43±3.19) showed statistically significant lower scores compared to patients from groups III (32.14±3.61) and IV (26.07±3.02), $p<0.05$; $p<0.001$.

OSDI questionnaire scores indicated that patients from all examined groups, except III (group III-27.04±2.53), had normal values three months after the surgery (I-18.18±2.04; II-19.43±2.04; IV-24.46±2.48). Results of the third group were statistically significantly higher than the results of the OSDI test of groups I and II, $p<0.05$.

Those values maintained until the one year after the surgery (group I-17.08±1.65; group II-18.18±1.94; group IV-22.82±2.19). Only group III patients had OSDI score 26.64±2.39 one year after

the surgery, which was statistically significantly higher compared to patients from groups I and II, $p<0.05$).

This comparison indicated that tear film stability was worse in patients with PEX after cataract surgery compared to patients without PEX, no matter of the application of artificial tears.

TBUT test results

Preoperatively, patients with PEX (III-9.08±1.03 s; IV-9.46±1.29 s) had statistically lower results than patients without PEX (I-14.02±1.02 s; II-13.92±1.92 s), $p<0.001$ (Figure 2).

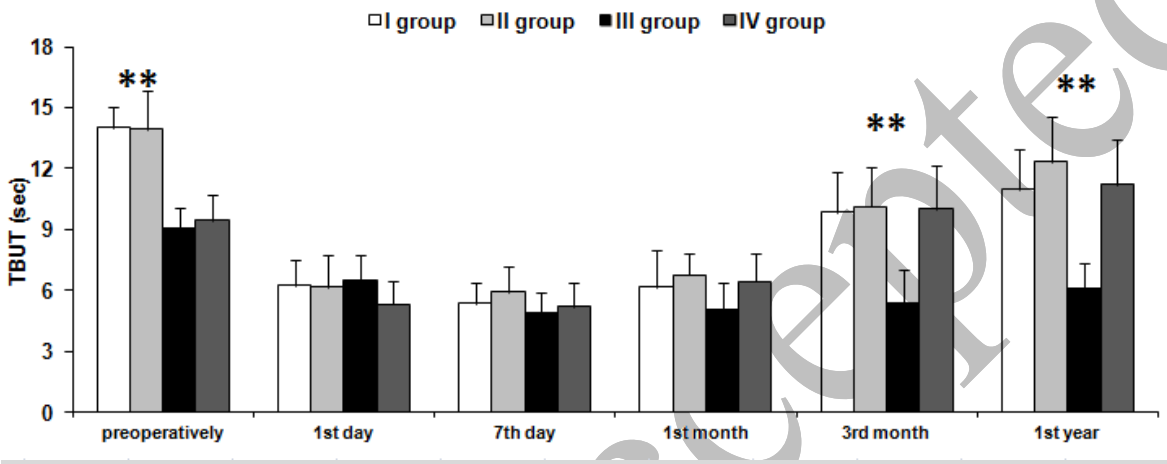

Figure 2.Tear break up time test results.

On the first postoperative day, all examined (I-6.26±1.27s; II-6.16±1.56s; III-6.48±1.28s; IV-5.31±1.19s) patients had TBUT values under the limit (<10seconds), without statistical differences among the groups, $p>0.05$.

The lowest values of the TBUT test were detected in all groups (I-5.38±1.02s; II-5.92±1.27s; III-4.88±1.04s; IV-5.19±1.23 s) on the 7th day after the surgery with no statistically significant differences among the groups, $p>0.05$.

The similar trend of values was maintained during the first postoperative month (I-6.18±1.78s; II-6.78±1.02s; III-5.05±1.36s; IV-6.46±1.37s), without statistical significances among the examinees, $p>0.05$.

The recovery of the tear film and its value above 10 seconds was recorded three months after the surgery in the patients from I (9.87±1.94s), II (10.14±1.92s) and IV (10.02±2.1s) group. Those results were highly statistically significantly different compared to patients from III (5.42±1.63s) group, $p<0.001$.

Until the end of the first postoperative year, all examined patients (I-10.98±2.01s; II-12.35±2.17s; IV-11.22±2.19s) except the patients from the III group (6.09±1.29s) had normal TBUT test results (>10seconds). The III group TBUT test result was highly statistically significantly different than the other examined groups, $p<0.001$.

Oxford ocular surface staining tests results

Oxford ocular staining tests results (Figure 3) obtained on the 7th day after the surgery, revealed highly statistically significant staining in all patients except the patients from the II group, p<0.001. One month after the surgery the II group patients showed no staining, in contrast to all other

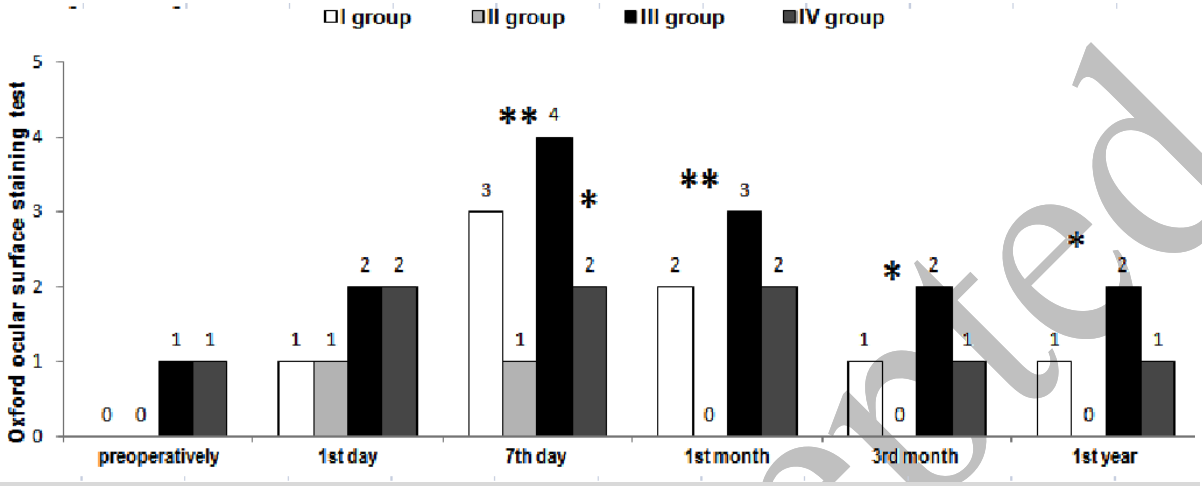

Figure 3. Oxford ocular surface staining tests results.

participants with high statistical significance, p<0.001. After the 3rd month only patients from the group III showed intensive staining (score 3), which was statistically significantly different from all other groups, p<0.05. The same results of the Oxford ocular staining tests were gained one year postoperatively, p<0.05.

Schirmer tests results

The Schirmer test results (Figure 4) indicated that on the surgery day, PEX patients (groups III-10.52±1.34 mm and IV-10.32±1.42 mm) had statistically significant lower values compared to patients from groups I (12.27±1.48 mm) and II (12.78±2.17mm), p<0.05.

The lowest values of the Schirmer test, with high statistical significance (p<0.001), were detected in the 7th postoperative day between the III (5.06±1.32mm) and IV (6.34±1.31 mm) groups of participants compared to the I (10.78±1.28 mm) and II (11.08±2.19 mm) groups.

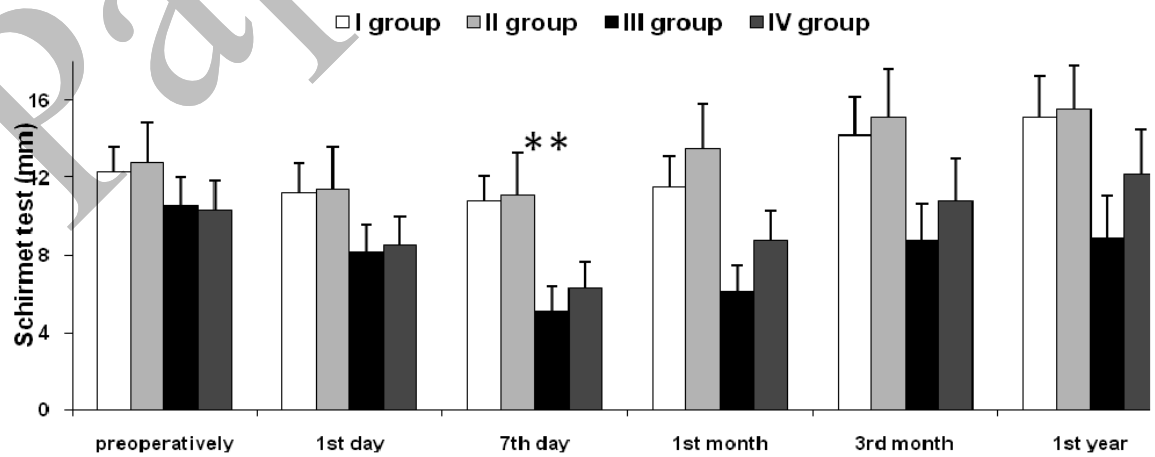

Figure 4.Schirmer tests results.

After one month, patients without PEX (I-11.56±1.52 mm; II-13.52±2.28 mm), had Schirmer test results above the limit (>10mm), with statistically significantly higher values than PEX patients (III-6.14±1.29 mm and IV-8.76±1.53mm groups), $p<0.001$.

All participants, after three months, except III-6.14±1.84 mm group patients, had normal values of the Schirmer test, which was statistically significantly lower compared to others (I-14.15±2.01 mm; II-15.12±2.48 mm; IV-10.82±2.18 mm), $p<0.05$; $p<0.001$.

After one postoperative year, only the III group (8.91±2.14 mm) of patients had abnormal Schirmer test results, with statistically significant lower values than other included participants (I-15.02±2.11 mm; II-15.51±2.24 mm; IV-12.12±2.31 mm), $p<0.05$, $p<0.001$.

DISCUSSION

Dry eye is a very common consequence of the cataract surgery, and it is multifactorial disease of tears film stability and ocular surface. Many different reasons provoke dry eye during ocular surgery.

The section of the corneal nerves, by making the main port and corneal paracentesis, for the surgery, contributes to the defective tears secreting reflex, so the tear production is out of order [11]. Cornea is innervated by long ciliary nerves, an ophthalmic branch of the fifth cranial nerve. Normal blinking and functional tear reflex, controlled by those nerves, are necessary for the health ocular surface [12].

Decreased blinking and reduced tear production can change permeability and metabolic activity of the corneal epithelial cells, by slowing the healing process [13]. Corneal incision provokes releasing of some proinflammatory mediators, which diminishes the tear film stability [14].

Corneal epithelium can be damaged by microscopic light exposure [13] and by intensive irrigation of the ocular surface during the surgery [3]. Goblet cells can be disrupted by intensive irrigation, thus the basis for the tear film instability is originated [15].

Also, tear film can be disturbed by applied topical anesthesia, containing preservatives (benzalkonium chloride) during the surgery [16]. Postoperatively, corticosteroids and antibiotics eye drops were administered, in controlling the inflammation and healing process. They also contain preservatives, disturb tear film stability, by decreasing the mucin producing cells [17].

During the healing process, growth factors are released, with role to regenerate subepithelial corneal axon. The process of regeneration is completed approximately within 1 month. Those facts make the explanation for the aggravation of the dry eye symptoms during the first month after the cataract surgery [18].

Pseudoexfoliation is an age related disorder of the whole body, characterized by abnormal production and accumulation of the abnormal extracellular material in different tissues (skin, visceral organs, eye) [4]. In the eye, PEX material can be detected during detailed ophthalmological examination on the slit lamp: on corneal endothelium, pupilar margin, iridocorneal angle, iris, ciliary

body and lens anterior capsule [19]. Hystological examination of the conjunctivae and periorbital tissues confirm PEX material [20]. The accumulations of PEX material in conjucntical tissue influence the accessory lacrimal glands and goblet cells function [5]. Some earlier studies indicated instability of the tear film in patients with PEX [21].

This study was conducted to demonstrate the importance of the tear film stability after the cataract surgery. Our results from dry eye tests indicated that dry eye symptoms and clinical signs were developed in patients 7 days after the cataract surgery, especially in PEX patients without prescribed artificial tears postoperatively. This fact is similar to earlier studies [3,21, 22]. One month after the phacoemulsification patients without PEX showed better results in all test except in TBUT. This test shows the condition of the lipid component of the tear film [23]. Its stability was achieved three months after the surgery in this study. This date coincided the date of earlier studies [3,22,24]. We noticed that patients without PEX and with prescribed artificial tears postoperatively achieved normal tear film characteristics earlier than patients without postoperatively applied artificial tears. That was also recommended from Yao et al., by their multicenter, randomized, open-label, control study [24]. We recorded the importance of the dry eye development in patients with PEX after the cataract surgery. PEX is worldwide ophthalmological problem, because of its unknown nature and the problems which it provokes in the eye. Earlier studies indicated that dysfunction of the goblet cells and accessory lacrimal glands, provoked by inflammation accumulated PEX material, deteriorated the tear film stability [5,20,25]. Our results indicated that patients with PEX had worse results of all dry eye tests than patients without PEX, especially without the postoperative usage of artificial tears. Until the end of the study, PEX patients with the postoperative application of artificial tears had statistically significantly better results in all applied tests compared to patients with PEX and without the artificial tears. These results were maintained until the end of the study. Comparing these two groups of patients (PEX and without PEX), we can conclude that patients with PEX had worse dry eye test results, which became more obvious after the cataract surgery. Specially, worsening was recorded in patients with PEX who did not use the artificial tears after the surgery. Earlier studies did not compare these two groups of patients, so these results are remarkable [2,3,15,16,21].

CONCLUSION

According to our results, we concluded that dry eye development is very frequent after the cataract surgery, especially in the first three months. PEX and the absence of usage of artificial tears further deteriorate tear film postoperatively, and represent the main reasons for the dry eye even one year after phacoemulsification.

Clinical symptoms of the dry eye can be causes of inappropriate visual acuity and patient's dissatisfaction after correct cataract surgery. So, in conclusion, the usage of artificial tears after the cataract surgery is recommended for all patients who undergo phacoemulsification, particularly if PEX is presented in the operated eye. We must suggest our patients to be patient and to use artificial

tears after the cataract surgery, and they can expect improvement of the clinical signs and symptoms, approximately three months after the surgery.

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