DOI: 10.17816/OV10329-34

THE INFLUENCE OF PHACOEMULSIFICATION ON VARIOUS CORNEAL LAYERS IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME ASSESSED WITH CONFOCAL IN VIVO MICROSCOPY

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For citation: Potemkin VV, Varganova TS, Terekhova IV, Ageeva EV. The influence of phacoemulsification on various corneal layers in patients with pseudoexfoliation syndrome assessed with confocal *in vivo* microscopy. *Ophthalmology Journal*. 2017;10(3):29-34. doi: 10.17816/OV10329-34

Received: 05.07.2017 Accepted: 24.08.2017

✧ Phacoemulsification (PHACO) is the basic procedure of cataract extraction. ***Purpose.*** To assess the impact of PHACO on corneal epithelium layers in patients with pseudoexfoliation syndrome (PEX) by confocal *in vivo* microscopy. ***Methods.*** 24 patients with PEX syndrome and 18 patients without it were enrolled in the prospective study. *In vivo* confocal microscopy was performed with assessment of cellular density in corneal epithelial layers, degree of its desquamation, degree of Bowman membrane stiffening and dendritic cells density. ***Results.*** The epithelial cells density didn't change significantly in groups. Confocal microscopy showed high density of dendritic cells and marked desquamation of the epithelium in patients with PEX ($p < 0,05$) after PHACO.

✧ ***Keywords:*** phacoemulsification; confocal microscopy; pseudoexfoliation syndrome.

ВЛИЯНИЕ ФАКОЭМУЛЬСИФИКАЦИИ НА СОСТОЯНИЕ РАЗЛИЧНЫХ СЛОЁВ ЭПИТЕЛИЯ РОГОВОЙ ОБОЛОЧКИ У ПАЦИЕНТОВ С ПСЕВДОЭКСФОЛИАТИВНЫМ СИНДРОМОМ ПО ДАННЫМ КОНФОКАЛЬНОЙ МИКРОСКОПИИ IN VIVO

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Для цитирования: Потёмкин В.В., Варганова Т.С., Терехова И.В., Агеева Е.В. Влияние факоэмульсификации на состояние различных слоёв эпителия роговой оболочки у пациентов с псевдоэксфолиативным синдромом по данным конфокальной микроскопии *in vivo* // Офтальмологические ведомости. – 2017. – Т. 10. – № 3. – С. 29–34. doi: 10.17816/OV10329-34

Поступила в редакцию: 05.07.2017 Принята к печати: 24.08.2017

✧ Факоэмульсификация (ФЭ) является основным способом хирургического лечения катаракты. ***Цель.*** Оценить влияние ФЭ на состояние различных слоёв эпителия роговицы у пациентов с псевдоэксфолиативным синдромом (ПЭС) по данным конфокальной микроскопии. ***Материалы и методы.*** Было обследовано 42 пациента. Основную группу составили 24 пациента с ПЭС, группу контроля — 18 пациентов без ПЭС. Всем пациентам до и после ФЭ выполнялась конфокальная *in vivo* микроскопия, в ходе которой оценивалась плотность клеток в различных слоях переднего эпителия, степень его

десквамации, выраженность уплотнения боуменовой мембраны и плотность дендритических клеток.
Результаты. У пациентов с ПЭС после ФЭ наблюдалось увеличение плотности дендритических клеток и усиление десквамации эпителия ($p < 0,05$). Плотность клеток эпителия достоверно не изменилась после ФЭ ($p > 0,05$).

✧ ***Ключевые слова:*** факоэмульсификация; конфокальная микроскопия; псевдоэксфолиативный синдром.

INTRODUCTION

Pseudoexfoliation syndrome (PEX) is a relatively widespread systemic disease associated with the production and accumulation of extracellular matrix similar to amyloid [14–16]. The prevalence of PEX steadily increases with age. Although PEX affects multiple tissues and organs, its diagnosis is usually based on the detection of ocular manifestations [12, 17]. The most common diagnostic sign of PEX is the accumulation of pseudoexfoliation material (PEM) in the anterior capsule of the lens, on the pupillary border of the iris, and on the corneal endothelium [12, 14, 17].

Reportedly, PEX significantly affects the corneal endothelium, causing PEX-associated keratopathy and deterioration after phacoemulsification (PE) [9–12, 19]. Patients with PEX have noticeable changes in the ocular surface tissues [2, 3, 11, 16]. In addition, they demonstrate a significant decrease in the tear production and time of the tear film rupture, excess folds of the conjunctiva, and increased conjunctival staining with vital dyes [2]. Since all these signs can worsen after PE [5, 6, 18], it encouraged researchers to conduct a thorough investigation of morphological changes in the corneal endothelium during the postoperative period using *in vivo* confocal microscopy.

MATERIALS AND METHODS

We examined 42 patients (42 eyes) admitted to the 5th Department of Ophthalmology at the City Hospital No. 2. Patients were divided into two groups; the first group included 24 patients (24 eyes) with PEX (the experimental group), whereas the second group included 18 patients (18 eyes) without PEX (the control group). The diagnosis of PEX was based on the detection of PEM in the anterior capsule of the lens, on the pupillary border of the iris, or in the corner of the anterior chamber. Patients in both groups were matched for gender and age (Table 1).

Besides the standard ophthalmological examination, all patients underwent a biomicroscopic evaluation using *in vivo* confocal microscopy before and one month after PE. We used Heidelberg Retina Tomograph 3 (HRT3; Heidelberg Engineering GmbH, Germany) fitted with confocal laser-scanning microscope Rostock Cornea Module. Corneal images were evaluated by one researcher blinded to the clinical characteristics of patients. In addition, *in vivo* confocal microscopy examination was performed under epibulbar anesthesia using disposable sterile caps before and one month after PE. The image area was 400 mm × 400 mm and the acquired images had a resolution of 384 × 384 pixels.

Each patient had approximately 1000 confocal microscopy images taken of the central cornea.

Previously, we developed an algorithm for the evaluation of ocular surface tissues using *in vivo* confocal microscopy to assess qualitative characteristics of the corneal epithelium (Table 2). We used the same algorithm in this study as well [2]. All parameters were evaluated using a point scale. For each group, we calculated the mean score, reflecting the severity of changes.

Table 1

Patients distribution by sex and age (*n* – patients' number)

Таблица 1

Распределение групп по полу и возрасту (*n* — количество пациентов)

Parameter		Experimental group, $n = 24$	Control group, $n = 18$	Significance of the difference, P
Age		74.6 ± 3.8	75.3 ± 4.1	0.51
Gender	Male	6 (25 %)	6 (33.3 %)	0.23
	Female	18 (75 %)	12 (66.6 %)	

Table 2

Assessment algorithm of corneal epithelium with confocal *in vivo* microscopy

Таблица 2

Алгоритм оценки состояния эпителия роговой оболочки при помощи конфокальной микроскопии

Dendritic cells (Lanherhans cells)	0–3 points
Areas of desquamation in the corneal epithelium	0–3 points
Thickening of Bowman's membrane	0–3 points

All patients underwent uncomplicated PE using the phaco-chop technique performed with the Infinity Vision System (Alcon Inc.). Patients were implanted with Akreos AO intraocular lenses (Bausch + Lomb). During the postoperative period, all participants received standard anti-inflammatory treatment with dexamethasone for 4 weeks (with gradual dosage reduction) and levofloxacin for 2 weeks.

We performed the quantitative assessment of the wing cell and basal epithelial cell density using *in vivo* confocal microscopy.

The exclusion criteria of the study were as follows: corneal dystrophy, contact lens use, glaucoma, instillation of antihypertensive drugs and artificial tears, prior surgical intervention on the eye, and the diseases leading to dry eye syndrome.

The statistical analysis was performed using SPSS Statistics v 20.0. The data were verified for normality using the Kolmogorov–Smirnov test, and the *t*-test was used to compare quantitative variables between the two independent groups. We considered $P < 0.05$ as statistically significant.

RESULTS

We estimated the number of dendritic cells, the severity of epithelial desquamation, the thickness of the Bowman's membrane, and the density of wing cells and basal epithelial cells to assess changes in the corneal epithelium. Patients in both groups demonstrated increased density of dendritic cells after PE; however, the differences were statistically significant in the PEX group only ($P = 0.013$; Figure 1). Desquamation of the corneal epithelium was primarily observed after PE. While patients with PEX demonstrated significant changes ($P = 0.018$), changes were non-significant in the control group ($P = 0.07$; Figure 2).

Before PE, patients in both groups were found to have thickening of Bowman's membrane, which remained at the same level after the surgery also ($P = 0.21$; Figure 3).

Patients with PEX had a significantly reduced preoperative density of wing cells compared to controls ($P = 0.03$).

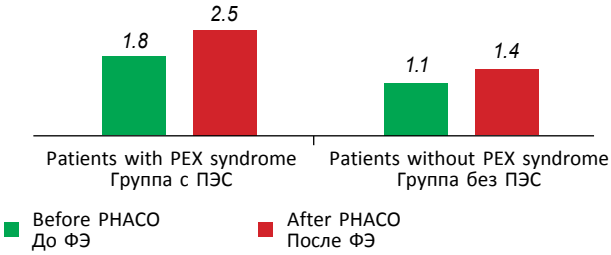

Fig. 1. Evaluation of dendritic cells dencity before and after PHACO (score)

Рис. 1. Оценка плотности дендритических клеток у пациентов до и после ФЭ (в баллах)

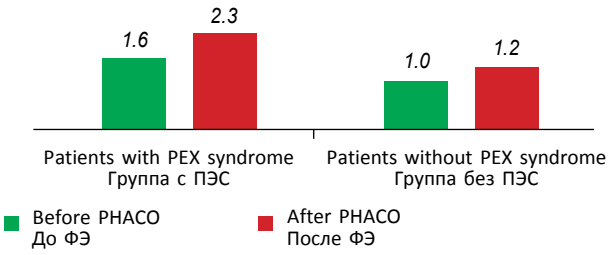

Fig. 2. Assessment of desquamation of epithelium before and after PHACO (score)

Рис. 2. Оценка десквамации поверхностного эпителия у пациентов до и после ФЭ (в баллах)

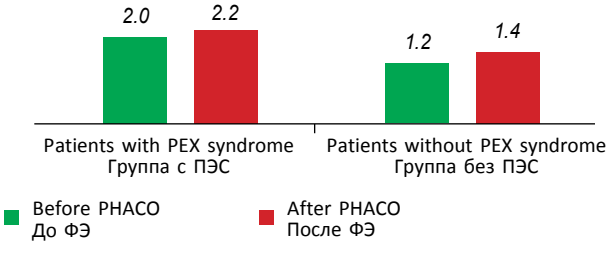

Fig. 3. Assessment of bowman membrane before and after PHACO (score)

Рис. 3. Оценка состояния боуменовой мембраны у пациентов до и после ФЭ (в баллах)

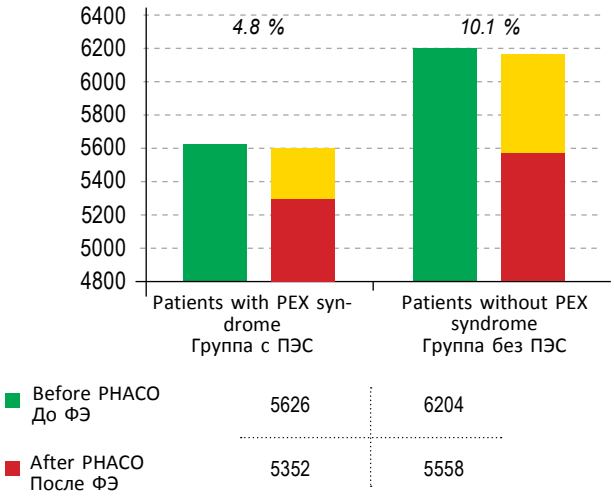

Fig. 4. Evaluation of intermediate epithelial cells dencity before and after PHACO

Рис. 4. Плотность крыловидных клеток эпителия роговицы до и после ФЭ

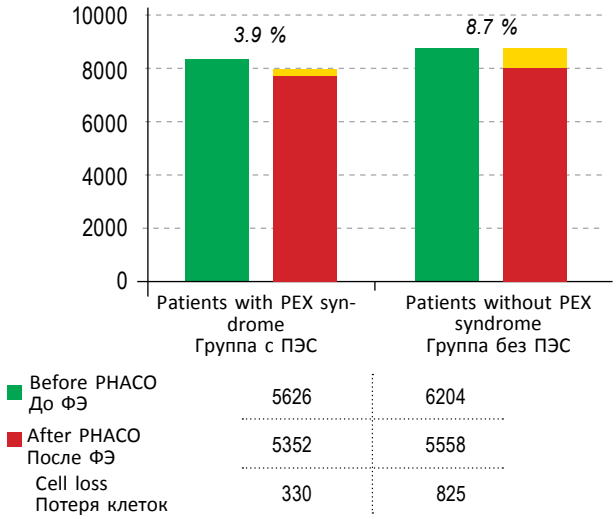

Fig. 5. Evaluation of basal epithelial cells dencity before and after PHACO in groups

Рис. 5. Плотность базальных клеток эпителия роговицы до и после ФЭ в группах исследования

After PE, no significant difference was observed in the wing cell density ($P = 0.84$) and the percentage of the wing cell loss ($P = 0.055$) between the two groups (Figure 4).

The preoperative density of basal epithelial cells was significantly higher in patients with PEX than in patients without PEX ($P = 0.028$). After PE, we observed no significant difference both in the basal epithelial cell density ($P = 0.21$) and the percentage of their loss ($P = 0.066$) between the groups (Figure 5).

DISCUSSION

Several studies have demonstrated tear film instability and ocular surface lesions in patients with PEX [2, 11, 19]. Moreover, these patients often have reduced tear production, decreased tear film stability, excess folds of the conjunctiva, and subjective ocular symptoms [2]. Several researchers have reported a decrease in the number of goblet cells of the conjunctiva and the development of meibomian gland dysfunction in patients with PEX [2, 4, 7, 8]. Although the mechanisms underlying these pathological changes are not entirely clear, we could hypothesize that the atony of the eyelids and conjunctiva significantly contributes to this process because it leads to an impaired meibomian secretion and tear film instability without affecting the basal tear production.

Despite the absence of intensive staining of the corneal epithelium in patients with PEX [2], we could detect histological changes in the corneal epithelium and stroma using *in vivo* confocal microscopy. These changes included increased density of dendritic cells and hyper-reflective intercellular microinclusions, increased desquamation of the epithelium, and thickening of the Bowman's membrane, which indicates the presence of chronic inflammatory and degenerative processes, typical of dry eye syndrome. Moreover, patients with PEX exhibit significant changes in the cellular structure of the cornea, including decreased density of basal epithelial cells, wing cells, and keratocytes of the corneal stroma [1].

Like any other surgical intervention associated with corneal injury and long-term postoperative anti-inflammatory therapy, PE destabilizes the tear film, leading to the emergence or worsening of dry eye syndrome [5, 6, 18].

By analyzing the markers of chronic inflammation and degenerative processes (desquamation of the epithelium and density of dendritic cells after PE), we determined that patients with PEX have more pronounced pathological changes. However, we observed no significant changes in the density of the corneal epithelium during the postoperative period, which is probably associated with its high regenerative potential.

CONCLUSION

The variety of PEX-related changes in the eye and ocular adnexa suggests that such patients require particular attention in terms of their surgical treatment. PEX is a well-known risk factor for intraoperative and postoperative complications, including damages to the ocular surface tissues and tear film, which causes discomfort to a patient and reduces the quality of life. However, the existing microsurgical

techniques allow minimizing these risks. Using *in vivo* confocal microscopy, we managed to demonstrate deterioration of PEX-related changes in the corneal epithelium after PE.

The authors declare no conflict of interest.

Authors' contribution:

Development of research concept and study design: V.V. Potemkin, E.V. Ageeva.

Data collection and processing: V.V. Potemkin, T.S. Varganova, I.V. Terekhova, E.V. Ageeva.

Data analysis and manuscript preparation: V.V. Potemkin, E.V. Ageeva.

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