ORIGINAL ARTICLE

Short-term Effects of Phacoemulsification Surgery on Corneal Endothelium in Cataract Cases with Pseudoexfoliation Syndrome

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ABSTRACT

Purpose: Our aim was to evaluate the effect of phacoemulsification surgery on corneal endothelial cell density (ECD), central corneal thickness (CCT) and endothelial cell morphology in patients with pseudoexfoliation syndrome (PEX).

Material and Methods: Thirty-four eyes of 34 cases with PEX and 30 eyes of 30 control cases without PEX scheduled for cataract surgery were included. ECD, CCT, coefficient of variation (CV) and percentage of hexagonal cells were evaluated by using noncontact specular microscopy. The effects of phacoemulsification surgery on corneal endothelium in patients with PEX were compared with the control group.

Results: The mean age was 72.5±8.0 years and there were 21 male (61.8%) and 13 female patients (38.2%) in the PEX group. The mean age was 69.1±8.2 years and there were 19 male (63.3%) and 11 female patients (36.7%) in the control group. The postoperative ECD was significantly lower in PEX group in all visits ($p<0.05$). At postoperative period, the percentage of the decrease in ECD was statistically significantly higher in PEX group ($p<0.05$). On postoperative month 3, there was no significant difference in the percentage of hexagonal cells and CV in the cell sizes between the two groups. The postoperative increase in CCT was significantly higher in PEX group than controls in all visits ($P<0.05$).

Conclusion: Short-term ECD loss was significantly higher in eyes with PEX than the control group. The protective measures for corneal endothelial cells should be taken more strictly in PEX cases during the surgery.

Keywords: Pseudoexfoliation syndrome, Phacoemulsification, Corneal endothelium, Central corneal thickness.

INTRODUCTION

Pseudoexfoliation syndrome (PEX) is an age-related disease, which is characterized by the accumulation of gray-white fibrogranular substance called pseudoexfoliation material (PEM) on the conjunctiva, corneal endothelium, lens surface, pupillary border, iridocorneal angle, ciliary body, trabecular meshwork, lens zonules, anterior hyaloid and nonocular tissues.[1-3] The prevalence of PEX differs in different populations and generally affects the individuals over the 50 years of age.[1] There is a significant relationship between PEX and cataract and some complications may occur during or after the surgery.[3] PEX may convert to pseudoexfoliation glaucoma (PXG), which is more aggressive than primary open angle glaucoma (POAG).[1-3]

In vivo confocal microscopy studies have demonstrated that the eyes with PEX are associated with reduced numbers of corneal epithelium, keratocytes, and endothelium as well as reduction in subbasal nerve density. The viscosity and elasticity of the cornea were lower in PEX. [4]

Corneal endothelial cell changes have been reported in patients with PEX.[5] In their study, Bozkurt et al.[5] found a decrease in the number of corneal endothelial cells in PXG patients.

The aim of this study was to investigate the effects of phacoemulsification and posterior chamber intraocular lens (IOL) implantation surgery on central corneal thickness (CCT), corneal endothelial cell density (ECD), coefficient of variation (CV), and hexagonality in cataract patients with or without PEX.

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MATERIALS AND METHODS

This prospective study included 34 eyes of 34 patients with PEX and 30 eyes of 30 age- and sex-matched control subjects without PEX. All eyes underwent phacoemulsification and posterior chamber IOL implantation surgery at the University of Health Sciences Ulucanlar Eye Training and Research Hospital. All study procedures were conducted in accordance with the Declaration of Helsinki. The study was approved by the Ankara Numune Training and Research Hospital Ethics Committee and written informed consent was taken in all cases.

All cases underwent detailed ophthalmological examinations preoperatively including the best corrected visual acuity (BCVA) with Snellen charts, the slit lamp and dilated fundus examination by +90 D lens, measurement of intraocular pressure (IOP) by Goldmann applanation tonometry, gonioscopic examination with Goldmann three mirror lens, visual field examination with Humphrey perimetry in cooperated cases and optic disc and retinal nerve fiber analysis by Spectral-domain optical coherence tomography (SD-OCT) (Cirrus HD OCT, Carl Zeiss Meditec, Dublin, CA, USA). Morphological classification and staging of cataract were performed according to Oxford clinical cataract classification and grading system.

The inclusion criteria for PEX and control group were: Patients older than 50 years old, eyes with senile cataract, intraocular pressure (IOP) <21 mmHg, iridocorneal open angle (stage 3-4 according to Shaffer staging system), anterior chamber depth of more than 2.5 mm, normal optic disc and fundus appearance with normal visual field and optic disc and retinal nerve fiber layer findings. The additional inclusion criteria for PEX group were: The presence of PXM on lens surface and/or pupillary border without any glaucomatous findings.

Exclusion criteria of our study for PEX and control group were: age under 50 years, history of ocular trauma, surgery, uveitis and contact lenses, presence of diabetes mellitus and collagen tissue disease, eyes with iridocorneal narrow angle (stage ≤2 according to Shaffer staging system), complicated phacoemulsification surgery such as posterior capsule rupture and vitreous loss, the insertion of capsular tension ring and IOP ≥21 mmHg after surgery.

The CCT, ECD, CV and hexagonality were evaluated by specular microscope (Tomey EM 4000 VSY Biotechnology) before the surgery. These measurements were repeated on week 1 and month 1 and 3 after surgery.

Surgical procedure

All surgical procedures were performed by the same surgeon under subtenon lidocaine anesthesia (UE, ES). The eyes underwent lens extraction by conventional phacoemulsification method (Alcon Infiniti, Texas, USA) and intracameral cefuroxime (Aprokam, Thea Pharma) was injected at the end of the surgery. The total ultrasound time (TUT) and total phacoemulsification energy (CDE) were recorded just after the surgery.

Statistical analysis

Study data were analyzed with the Statistical Package for Social Sciences (SPSS) for Windows, version 22.0 (SPSS, Chicago, IL, USA). Descriptive statistics are presented as means±standard deviation (minimum-maximum), frequency distributions, and percentages. The Pearson chi-square test was used for analysis of categorical variables. Normal distribution of variables was tested by visual (histogram and probability graphs) and analytical (Shapiro-Wilk Test) methods. For variables determined to have skewed distribution; Mann-Whitney U test was used between two independent groups and Wilcoxon signed rank test was used as a statistical method among two dependent groups. For the variables with normal distribution, paired sample t-test was used between two dependent groups. The level of statistical significance was accepted as $p<0.05$.

RESULTS

The mean age was 72.5±8.0 years (range: 54-85) and there were 21 male (61.8%) and 13 female patients (38.2%) in the PEX group (n=34). The mean age was 69.1 ± 8.2 years (range: 53-82) and there were 19 male (63.3%) and 11 female patients (36.7%) in the control group (n=30). There were no significant differences in age, gender and the stage of cataract between the PEX and control groups (p=0.09, p=0.89, p=0.61, respectively) (Table 1).

Table 1: *Age, gender and distribution of cataract severity among study groups.*

		PEX (n=34)	Control (n=30)	p
Age (years),		Mean±SD (min-max) 72,5±8,5 (54-85)	Mean±SD (min-max) 69,1±8,2 (53-82)	0,09*
Gender, n (%)				
	Male	21 (61,8)	19 (63,3)	0,89**
	Female	13 (38,2)	11 (36,7)	
Cataract severity (%)				
	Soft	3 (8,8)	3 (10,0)	0,61**
	Moderate	11 (32,4)	13 (43,3)	
	Hard	20 (58,8)	14 (46,6)	

SD: Standard deviation; **n:** number of patients; **%:** percentage in the group; *Mann-Whitney U Test; ** Chi-square test
PEX: Pseudoexfoliation syndrome

The cases in the PEX group had significantly lower ECD values on week 1 and month 1 and 3 after surgery compared to the preoperative values (p<0.001) (Table 2). Similarly, on week 1 and month 1 and 3 after surgery in the control group were significantly lower than the preoperative values (p<0.001, p<0.001, p<0.001, respectively) (Table 2, figure 1).

The amount of decrease in ECD values in the PEX group was significantly higher than control group on week 1 and months 1 and 3 after surgery (p=0.03, p=0.01, p=0.03, p= 0.02, respectively) (Table 3).

The cases in the PEX group had significantly higher CV values on week 1 and month 1 and 3 after surgery compared to the preoperative values (p=0.005, p=0.03. respectively), but there was no significant difference between the CV value on month 3 and the preoperative value (p=0.58). In

Table 2: *Change in values in the 1st week, 1st month and 3rd month after surgery.*

		Pre-op	1st week	*p*	1st month	*p*	3rd month	*p*
ECD Mean±SD (min-max)	PEX (n=34)	2282,0±435,4 (1257-3060)	1865,0±496,4 (1098-2794)	***<0,001****	1894.0±486,3 (1180-2812)	***<0,001****	1914,3±469,7 (1190-2805)	***<0,001****
	Control (n=30)	2366,6±304,4 (1587-2954)	2098,6±354,5 (1038-2632)	***<0,001****	2116.2±368,8 (1116-2645)	***<0,001****	2113,6±392,3 (1038-2647)	***<0,001****
CV Mean±SD (min-max)	PEX (n=34)	42,2±7,3 (31-62)	46,6±7,1 (34-64)	***0,005****	45,1±5,8 (31-58)	***0,03****	42,8±5,0 (31-54)	*0,58**
	Control (n=30)	42,2±7,5 (30-65)	44,6±6,9 (30-58)	*0,22**	43,9±5,7 (32-60)	*0,28#*	42,5±5,7 (35-58)	*0,85#*
Hexagonality Mean±SD (min-max)	PEX (n=34)	44,0±8,8 (29-62)	37,8±8,5 (20-54)	***0,001****	42,0±6,4 (30-60)	*0,14**	45,0±5,0 (35-58)	*0,57**
	Control (n=30)	43,3±8,7 (30-63)	40,7±7,3 (24-55)	*0,26**	42,5±6,9 (27-55)	*0.80**	44,0±7,1 (24-55)	*0,57**
CCT Mean±SD (min-max)	PEX (n=34)	513,0±36,8 (453-584)	548,9±36,8 (464-620)	***<0,001****	534,1±34,5 (440-595)	***<0,001****	524,8±34,0 (431-588)	***<0,001****
	Control (n=30)	512,5±27,5 (451-561)	535,3±31,0 (467-600)	***<0,001****	520,9±27,5 (460-570)	***0,001****	514,5±28,1 (455-565)	*0,55**

Pre-op: Preoperative, **PEX:** Pseudoexfoliation syndrome, **ECD:** Endothelial cell density, **CV:** Coefficient of variation; **CCT:** Central corneal thickness; * Paired Sample T-Test (To compare with pre-op ECD, CV, hexagonality, CCT); # Wilcoxon Signed Ranks Test (To compare with pre-op CV)

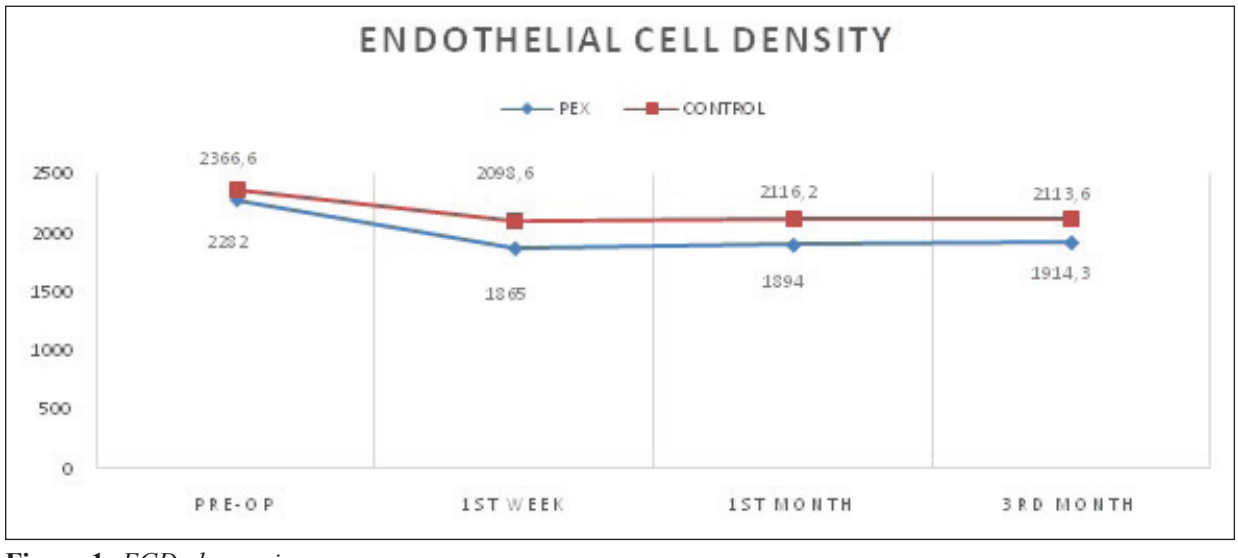

Figure 1: *ECD change in groups.*

ECD: Endothelial cell density Pre-op: Preoperative PEX: Pseudoexfoliation syndrome

Table 3: *Distribution of postoperative differences between groups according to time.*

		Pre-op-1st week	*P**	Pre-op-1st month	*P**	Pre-op-3rd month	*P**
ECD Mean±SD (%)	PEX	417,0±282,9 (%18)	***0,02***	388,2±260,4 (%17)	***0,01***	367,7±238,2 (%16)	***0,02***
	Control	268,0±177,5 (%11)		252,8±218,1 (%10)		254,7±236,5 (%10)	
CV Mean±SD (min-max)	PEX	4,4±8,5 (-11;33)	*0,39*	2,9±7,5 (-14;25)	*0,30*	0,6±6,2 (-14;19)	*0,51*
	Control	2,3±10,2 (-26;24)		2,9±7,5 (-14;25)		0,2±6,3 (-10;19)	
Hexagonality Mean±SD (min-max)	PEX	6,2±9,9 (-22;30)	*0,10*	2,0±7,9 (-13;17)	*0,41*	-1,0±7,9 (-18;15)	*0,90*
	Control	2,6±9,9 (-13;24)		0,8±9,2 (-14;21)		-0,7±8,5 (-15;15)	
CCT Mean±SD (min-max)	PEX	35,9±27,1 (-9;138)	***0,01***	21,1±23,3 (-13;121)	***0,01***	11,8±12,0 (-22;41)	***0,01***
	Control	22,9±12,2 (0;44)		8,4±12,4 (-21;37)		2,0±18,7 (-88;22)	

Pre-op: Preoperative, **PEX:** Pseudoexfoliation syndrome, **ECD:** Endothelial cell density, **CV:** Coefficient of variation, **CCT:** Central corneal thickness, *Mann-Whitney U Test

the control group, there were no significant differences between the preoperative CV values and the values on week 1 and months 1 and 3 after surgery (p>0.05) (Table 2).

The amount of increase in the value of CV of patients in the PEX group compared with the preoperative period was similar to the patients in the control group on week 1 and months 1 and 3 after surgery (p>0.05) (Table 3).

Patients in the PEX group had significantly lower hexagonality on week 1 after surgery compared to the preoperative period (p=0.001) but there were no significant differences between the preoperative and months 1 and 3 after surgery (p=0.14, p=0.57, respectively) (Table 2, figure 3). In the control group, there were no significant differences between the preoperative and the postoperative hexagonality values (p>0.05) (Table 2). Patients in the

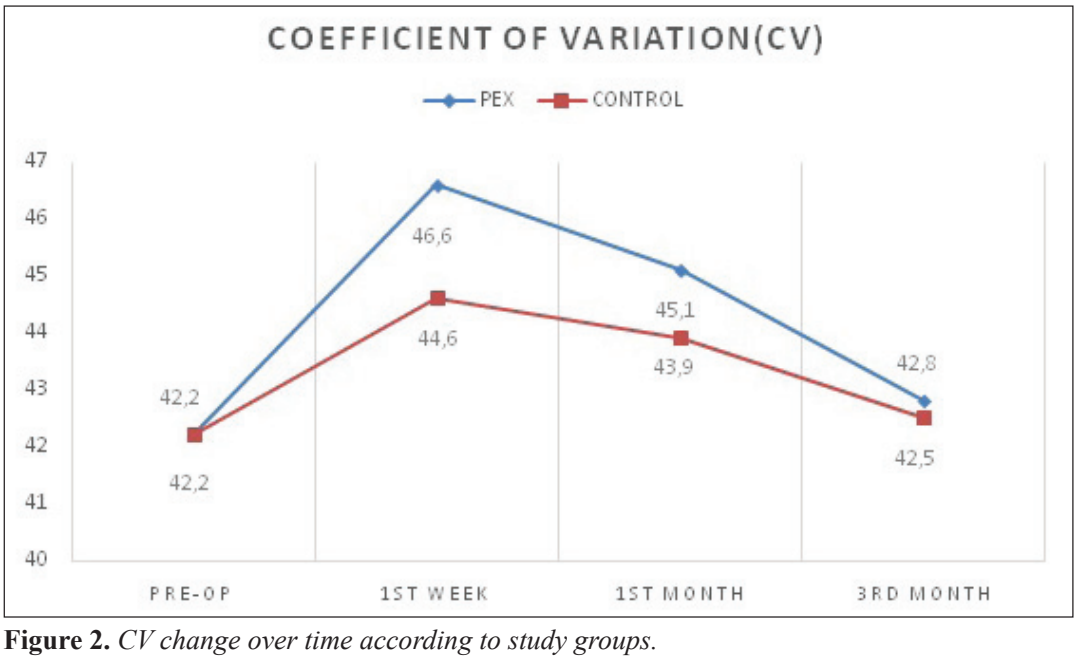

Figure 2. *CV change over time according to study groups.*

CV: Coefficient of variation PEX: Pseudoexfoliation syndrome

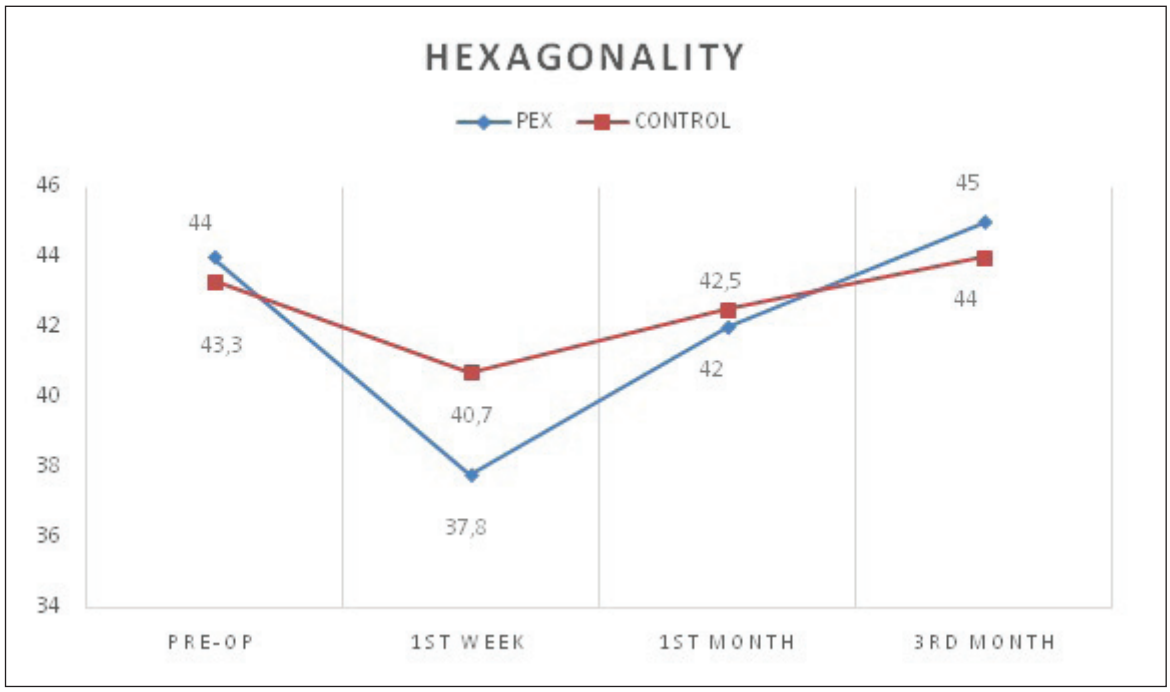

Figure 3: *Hexagonality change over time according to study groups.*
PEX: Pseudoexfoliation syndrome

PEX group had similar decreases in hexagonality values on week 1 and months 1 and 3 after surgery compared to the control group. (p>0.05) (Table 3).

The cases in the PEX group had significantly higher CCT values on week 1 and months 1 and 3 after surgery than the preoperative values (p<0.001, p<0.001, p<0.001, respectively). In the control group, the CCT values on week and month 1 after surgery were significantly higher than the preoperative values (p<0.001, p=0.001, respectively), but the CCT on month 3 after surgery was similar to the preoperative CCT values (p=0.55) (Table 2). The increases in the CCT values of the patients in the PEX group on week 1 and months 1 and 3 after surgery after surgery were significantly higher than the control group (p=0.01, p=0.01, p=0.01, respectively) (Table 3).

The mean TUT of the surgeries was 65.36±33.6 sec in the PEX group and 69.42±38.84 sec in the control group (p=0.37). Similarly the mean CDE value was 18.16±4.64 in the PEX group and 16.79±4.48 in the control group (p=0.11).

DISCUSSION

Surgical trauma may cause endothelial decompensation in eyes with PEX as some corneal endothelial cell pathologies are often related with PEX.[3-5] In our study, we aimed to determine ECD, CV, hexagonality and CCT changes at short-term period in PEX patients after uncomplicated phacoemulsification surgery and compare them with normal subjects.

Tomaszewski et al.[6] investigated ECD values in PEX and PXG cases and found significantly lower values in both PEX and PXG cases compared to normal individuals. Similarly, Wang et al.[7] found significantly lower ECD values in eyes with PEX than normal subjects but no significant differences were found in terms of CV and hexagonality. Terracciano et al.[8] investigated the eyes with PEX by confocal microscopy and found decreased number of epithelial cells and ECD and increased number of activated keratocytes and inflammatory cells in the anterior stroma, suggesting a relationship between PEX and inflammation. Also some corneal nerve plexus changes and decreased corneal sensitivity were observed in eyes with PEX in the same study.[8]

Although cataract surgery is performed with the most advanced techniques without any surgical complications, corneal endothelial cells may be adversely affected in healthy individuals.[9] Some factors may increase this negative effect on corneal endothelial cells.[10] In their study, He et al.[11] found decreased number of corneal endothelial cells after cataract surgery in diabetic cases with significantly higher extent than normal subjects. In our study, we excluded diabetic patients because of the effect of disease on corneal endothelial cells. For the same reason, we also excluded glaucoma cases. Ianchulev et al.[12] observed early postoperative corneal endothelial cell loss

in cases with POAG and advanced age was found to be the most important risk factor.

In our study, we found that decrease in ECD was higher than in eyes with PEX than the control group on month 1 after surgery. Unlike our results, Wirbelauer et al.[13] found no significant difference between PEX and control group in terms of in decreased ECD on postoperative month 6. Hayashi et al.[14] found that corneal endothelial damage was more common in PEX patients after surgery. Hasegawa et al.[15] investigated the risk factors for ECD loss in cataract surgery in eyes with PEX and stated that the shallow anterior chamber was the most important risk factor with advanced cataract stage. Because of the possible effects, the eyes with narrow iridocorneal angle (<stage 3) were not included to our study.

Another important factor that may cause ECD loss after cataract surgery is the parameters used in phaco device during the surgery. In their study, Kaljurand et al.[16] found that the percentage of ECD loss at the first postoperative month was higher in the PEX group in spite of statistically insignificance. However, the percentage of ECD loss was found to be correlated with UST and age after the regression analysis and PEX was stated to have no direct effect on corneal endothelium.[16] However, in our study, nor correlations between the percentage of postoperative ECD loss with CDE, UST and age were shown. Age- and sex-matched patients were included to PEX and control groups and all surgeries were performed by two experienced surgeons by using the same device and similar surgical techniques. Additionally, there was no significant difference between the groups in terms of cataract stiffness preoperatively. Furthermore, the inclusion and exclusion criteria of our study were carefully determined and the possible effects of all other variables were minimized in order to evaluate the effect of PEX.

The relationship between corneal endothelial cell loss and CCT changes after cataract surgery is known. In their study, Perone et al.[17] concluded that the change in CCT after cataract surgery was an indicator of endothelial cell loss. Çankaya et al. [18] showed that CCT increased in all cases in the early postoperative period. However, they showed that CCT returned to normal values in the first postoperative month in the control group and in the third postoperative month in patients with PXS. In our study, the CCT values in the PEX group were significantly higher than the preoperative values on week 1 and on months 1 and 3 after surgery. The CCT values in control group on week 1 and on months 1 and 3 after surgery were significantly higher than the preoperative values, whereas there was no significant change in CCT between the preoperative and on month 3.

It is known that postoperative endothelial cell loss and CCT increase are associated with bullous keratopathy as a surgical complication. Demircan et al.[19] found that the increase in CCT was significantly higher in the PEX than the control group at the postoperative day 1 and week 1 but no significant difference was found between the preoperative values and those obtained on month 1. In the same study, they concluded that increased anterior chamber manipulations increased the risk of bullous keratopathy in cases with PEX.

The elevation of IOP and inflammation are frequently observed after cataract surgery in PEX patients.[20-21] The adverse effects of inflammation in the anterior chamber and high IOP or glaucoma on corneal endothelial cells are also known.[22-23] In the light of these results, patients with high IOP and inflammation after the surgery were not included in our study to prevent potential effects. Also, the cases in which capsular tension ring had been used in the surgery were not included in our study. Bayraktar et al.[24] concluded that the use of capsule tension rings in patients with PEX reduced the frequency of intraoperative complications, but complicated the cortex aspiration.

In our study, short-term effects of phacoemulsification surgery on corneal endothelium and CCT in PEX eyes were examined and the results were compared with the control group without PEX. Although the percentage of ECD loss in the PES group was higher than the control group within 3 months after surgery, it did not lead to clinically significant endothelial insufficiency and bullous keratopathy.

While endothelial cell morphology returned to normal levels in both groups at the first postoperative month, the number of endothelial cell was found to be significantly lower and CCT was found to be significantly higher in PEX group. Based on these results, it was concluded that PEM might cause pathological changes at the microscopic level in the corneal endothelium and might delay corneal healing after the surgery. Therefore, in PEX patients, it is very important to be more sensitive about performing the surgery by experienced surgeons and taking endothelial cell protective measures.

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