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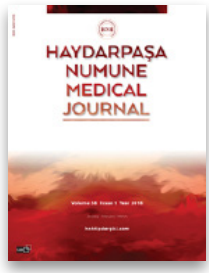

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ORIGINAL ARTICLE

Early Postoperative Effects of Uncomplicated Phacoemulsification on Corneal Parameters in Patients with Pseudoexfoliation Syndrome

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Abstract

Introduction: To compare early postoperative effects of uncomplicated phacoemulsification surgery on corneal endothelial cells and thickness in patients with pseudoexfoliation syndrome (PEX).

Methods: One eye each of 32 patients with PEX and 32 age-matched non-PEX subjects was evaluated preoperatively and on the 1st, 7th, and 30th days after uncomplicated phacoemulsification surgery in this retrospective case-control study. Nuclear firmness, corneal edema (CE), anterior chamber reaction (ACR) intensity were graded by a slit-lamp microscope. Endothelial cell density (ECD), coefficient of variation in cell area (CV), hexagonal cell ratio (HEX), and central corneal thickness (CCT) were measured using a non-contact specular microscope.

Results: There was no significant group-difference in age, sex, corneal edema (CE), anterior chamber reaction (ACR), coefficient of variation in cell area (CV), and hexagonal cell ratio (HEX). Mean effective phaco time (EPT) was significantly lower intraoperatively ($p<0.001$) and logarithm of the minimum angle of resolution (logMAR) values of best-corrected visual acuity (BCVA) were significantly higher on both 1st ($p<0.001$), 7th ($p=0.011$), and 30th ($p=0.025$) days postoperatively in the PEX group than in the non-PEX group. Mean ECD was significantly lower in the PEX group than in the non-PEX group on 7th ($p=0.013$), and 30th ($p=0.037$) days postoperatively. The mean CCT significantly differed only on the 1st ($p<0.001$) day postoperatively.

Discussion and Conclusion: Eyes with PEX presented lower corneal ECD and decreased BCVA after uncomplicated phacoemulsification surgery. Further, there was no association between CCT and PEX existence preoperatively and in the early postoperative period.

Keywords: Central corneal thickness; corneal endothelium; phacoemulsification; pseudoexfoliation syndrome.

Pseudoexfoliation syndrome (PEX) is the widespread intraocular and systemic formation and accumulation of an anomalous flake-like fibrillar extracellular material. This age-related disorder is clinically diagnosed by slit-lamp examination, which allows the observation of pseudoexfoliative material (PEM) on the anterior segments of the globes[1]. It is now regarded as the most common identifiable cause of open-angle glaucoma worldwide. It is also related to the development of cataract. The prevalence of PEX increases with age and varies broadly across racial and ethnic populations[2]. In PEX, PEM fibrils are synthesized multifocally by numerous intraocular cell types, including the preequatorial lens epithelium, nonpigmented ciliary epithelium, trabecular endothelium, corneal endothelium,

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vascular endothelial cells, and virtually all cell types of the iris. The resulting histopathological alterations can lead to many intraocular complications, such as glaucoma, cataract, poor mydriasis, and zonular instability[3]. The risk of complicated cataract surgery increases in patients with PEX due to the atrophy of the iris and pupillary ruff, with insufficient mydriasis, weak zonula, vitreous loss, and increased risk of capsule/zonular rupture[4]. Moreover, the corneal endothelial involvement of PEM may potentiate complications of cataract surgery[5]. In recent years, specular and electron microscopic studies have illuminated new clinical trials allowing both quantitative and qualitative corneal endothelial cell changes in eyes with PEX. Along with lower endothelial cell density (ECD) [6], changes in the percentage of hexagonal cells (an index of pleomorphism) and the coefficient of variation in cell size (a measure of polymegathism)[7] have been shown in eyes with PEX compared to eyes without PEX. Furthermore, some studies have shown decreased[8] or increased[9] central corneal thickness (CCT) in eyes with PEX compared to those without.

This study was designed to evaluate the degree of corneal endothelial changes, ocular inflammation, and central corneal thickness between eyes with and without PEX after uncomplicated phacoemulsification surgery.

Materials and Methods

This retrospective, cross-sectional case-control study was conducted at a tertiary eye care referral center. The study was approved by the regional committee for medical and health research ethics (E-18-2407/2019) and conducted in accordance with the Declaration of Helsinki and legal regulations. Informed written consent was obtained from all patients before receiving the examinations. One eye from each of 32 patients with PEX and 32 control subjects without PEX, who underwent uncomplicated phacoemulsification surgery, was studied. The diagnosis of the syndrome was based on the typical slit-lamp appearance of pseudoexfoliative material at the anterior lens capsule and/or at the pupillary margin. A complete ophthalmological examination, including best-corrected visual acuity (BCVA), non-contact tonometry, and a non-contact specular microscope, was performed preoperatively and on the 1st, 7th, and 30th days after the cataract surgery for all patients. Visual acuity results were converted to the logarithm of the minimal angle of resolution (logMAR) units from the Snellen chart. Measurements with a non-contact specular microscope (EM-4000, TOMEY; Nagoya, Japan) were performed via an automated method by the same technician. All measurements were performed at least three times using the "center" method, and at least 110 cells were included in each measurement. Endothelial cell density (ECD) (cells/mm^2), coefficient of variation in cell area (CV) (%), hexagonal cell ratio (HEX) (%), and central corneal thickness (CCT) (µm) were noted. Polymegathism was assessed using the CV, which is independent of cell area or density, and pleomorphism was assessed by the HEX.

Exclusion Criteria

The exclusion criteria for the study included the presence of active intraocular infection, previous ocular surgery or ocular trauma, a history of uveitis and glaucoma, pathology of the vitreous or macula, and ocular surface disease. The latter encompasses any corneal pathology such as cornea guttata, any type of corneal scar, keratoconus, and contact lens use. According to the Emery-Little classification, nuclear firmness was preoperatively assigned to groups as grade I (very soft nuclear) (transparent and nonnuclear), grade II (soft nuclear) (yellow or yellow-white), grade III (medium-hard nuclear) (dark yellow), grade IV (hard nuclear) (brown or amber), and grade V (extremely hard nuclear) (dark brown or black).

Surgical Procedure

A single surgeon (SKK) performed all cataract surgeries using the standardized phacoemulsification technique. The pupils were dilated with topical cyclopentolate hydrochloride 1% (Siklopleji®, Abdi İbrahim, İstanbul, Türkiye) and tropicamide 1% (Tropamid®, Bilim İlaç, İstanbul, Türkiye) preoperatively. Topical anesthesia was applied (Proparakain HCl 0.5%), and two side ports were opened. Anterior chamber stabilization was achieved with injected viscoelastic material (Healon GV®, AMO). A 2.8 mm clear corneal incision with a double-beveled slit knife was created between the 10 and 12 o'clock meridians. Perioperative adrenaline was injected intracamerally as an adjunct to preoperative topical mydriatics in all patients for the maintenance of mydriasis. Iris retractor hooks were used only in three eyes with PEX ($p>0.05$) in which adequate mydriasis was not achieved intraoperatively. Capsulorhexis with a diameter of about 5.5 mm followed, and the nucleus was emulsified using bimanual phacoemulsification (WhiteStar® Signature, Abbott Medical Optics [AMO], Santa Ana, CA, USA) with the divide-and-conquer technique. Irrigation/aspiration of cortical material was semi-automatic and bimanual. After cortex cleaning, a foldable hydrophobic acrylic intraocular lens (Acrysof SA60AT®, Alcon) was implanted into the

Table 1. Patient characteristics and intraoperative factors by group

Parameter	PEX group (n=32)	Non-PEX group (n=32)	p
Mean age (y)	72.68±5.61	69.84±7.98	0.093
Male/female sex (n)	18/14	19/13	0.800
Mean nuclear firmness	2.93±0.56	2.71±0.77	0.139
Mean EPT (s)	12.67±10.27	35.78±26.86	0.000*
Mean UST (s)	96.59±44.24	108.65±62.16	0.537
Mean AVG (%)	6.98±3.55	7.56±5.57	0.845

Data are presented as mean±standard deviation. *: Statistically significant difference. PEX: Pseudoexfoliation syndrome; EPT: Effective phaco time; UST: Ultrasound time; AVG: Average ultrasound power.

capsular bag. The viscoelastic material was then removed, and the anterior chamber was reformed with balanced salt solution (BSS®). A 0.5%/0.1 mL dose of cefuroxime (1 mg/0.1 mL) was injected into the anterior chamber following corneal wound and side port hydration with BSS. In the postoperative period, patients were treated with topical moxifloxacin hydrochloride (Vigamox® 0.5% ophthalmic solution, Alcon) four times a day for one week and topical prednisolone acetate (Predforte® 1% ophthalmic solution, Allergan) four times a day for one month. Ultrasound time (UST) (seconds), average ultrasound power (AVG) (%), and effective phaco time (EPT) (seconds) were recorded at the end of the surgery. EPT was calculated by multiplying the total phaco time by the percentage power used and represents how long the phaco time would have been if 100% power, continuous mode had been utilized[10].

Postoperative Assessments

Anterior chamber reaction (ACR) intensity was graded according to the Standardization of Uveitis Nomenclature (SUN) criteria postoperatively. The SUN criteria normalized scoring for these measures: Cells are counted in a field size of 1×1 mm slit-beam and scored based on the number of cells observed (0 [<1 cell], 0.5+ [1–5 cells], 1+ [6–15 cells], 2+ [16–25 cells], 3+ [26–50 cells], and 4+ [>50 cells]). The grading for flare is less quantitative, based on 0 (none), 1+ (faint), 2+ (moderate, iris, and lens details clear), 3+ (marked, iris, and lens details hazy), and 4+ (intense, fibrin, or plastic aqueous)[11]. Corneal edema grading according to the Oxford Cataract Treatment and Evaluation Team (OCTET) was noted. Corneal edema defined as an increase in central corneal thickness with or without Descemet folds was graded as transient corneal edema (+) (grade I); transient corneal edema with Descemet membrane folds of <10 (++) (grade II); and transient corneal edema with Descemet membrane folds of >10 (+++) (grade III).

Table 2. Comparison of mean corneal edema and ACR intensity

Parameter	PEX group (n=32)	Non-PEX group (n=32)	p
Corneal edema			
1 day postop	0.67±0.77	0.62±0.75	0.775
7 day postop	0.07±0.27	0.09±0.39	0.859
30 day postop	0.04±0.20	0.03±0.17	0.813
ACR intensity			
1 day postop	0.71±0.46	0.84±0.62	0.458
7 day postop	0.03±0.19	0.15±0.36	0.146
30 day postop	0.04±0.20	0.03±0.17	0.813

Data are presented as mean±standard deviation. *: Statistically significant difference. ACR: Anterior chamber reaction; PEX: Pseudoexfoliation syndrome.

Statistical Analysis

Statistical analyses were performed using the SPSS program version 15.0 (SPSS Inc., Chicago, Illinois, USA). Results were expressed as the mean±standard deviation. The Kolmogorov-Smirnov (K-S) test was used to determine whether the data showed normal distribution. It was determined that there was no normal distribution, as the p-values of the distributions tested for normality using the K-S test were <0.05. Accordingly, non-parametric tests were used in the analysis of the data. Differences between the PEX group and the non-PEX group in endothelial cell density (ECD), coefficient of variation in cell area (CV), hexagonal cell ratio (HEX), central corneal thickness (CCT), anterior chamber reaction (ACR) intensity, corneal edema, best-corrected visual acuity (BCVA), operative factors, and other continuous variables were compared using the Mann-Whitney U test (intergroup differences). The Wilcoxon signed-rank test for paired samples was used to test the significance of the difference between the scores of two associated measurement sets (preop-30-day postop BCVA). Discrete variables between the two groups were compared using the chi-square test. Differences with a p-value <0.05 were considered statistically significant.

Table 3. Comparison of mean BCVA, ECD, CV, HEX, and CCT

Parameter	PEX group (n=32)	Non-PEX group (n=32)	p
BCVA (logMAR)			
Preop	0.83±0.37	0.95±0.65	0.989
1 day postop	0.43±0.27	0.17±0.13	0.000*
7 day postop	0.17±0.16	0.08±0.09	0.011*
30 day postop	0.10±0.13	0.04±0.09	0.034*
p-value (Pre- vs. Postoperative30th day BCVA)		<0.0001†	<0.0001†
ECD (cells/mm^2)			
Preop	2329.93±333.29	2411.75±298.63	0.398
1 day postop	1944.40±535.29	2099.27±395.59	0.323
7 day postop	1730.84±568.84	2072.00±481.57	0.022*
30 day postop	1709.26±591.65	2048.00±471.93	0.029*
CV (%)			
Preop	39.12±5.28	41.96±7.92	0.228
1 day postop	46.03±8.51	49.55±10.31	0.234
7 day postop	47.65±7.82	44.87±7.87	0.183
30 day postop	45.34±6.83	45.18±6.95	0.851
HEX (%)			
Preop	45.06±7.62	43.21±6.13	0.199
1 day postop	39.61±8.33	37.62±8.60	0.269
7 day postop	35.30±7.47	37.87±5.49	0.100
30 day postop	39.13±6.44	37.84±6.75	0.533
CCT (µm)			
Preop	517.90±27.50	532.06±39.81	0.113
1 day postop	535.50±28.85	576.13±35.95	0.000*
7 day postop	540.00±33.96	551.56±37.26	0.267
30 day postop	521.04±23.49	533.96±32.89	0.189

Data are presented as mean±standard deviation. *: Statistically significant difference; †: Wilcoxon signed-rank test for paired samples. BCVA: Best-corrected visual acuity; ECD: Endothelial cell density; CV: Coefficient of variation in cell area; HEX: Hexagonal cell ratio; CCT: Central corneal thickness; PEX: pseudoexfoliation syndrome.

Results

Data for 32 eyes of 32 patients in the PEX group and 32 eyes of 32 patients in the non-PEX group were analyzed. The mean age was 72.68±5.61 years in the PEX group and 69.84±7.98 years in the control group (p=0.093). There were 14 women and 18 men in the PEX group, and 13 women and 19 men in the non-PEX group (p=0.800). There was no statistically significant difference in age and sex between the groups (Table 1). Intraocular pressure readings were within the normal range preoperatively and postoperatively in both the PEX and non-PEX groups. Mean cataract firmness was 2.96±0.54 (grade) in the PEX group and 2.65±0.86 (grade) in the non-PEX group (p=0.087). Differences between the two groups in mean nuclear firmness, BCVA, ECD, CV (polymegathism), HEX (pleomorphism), and CCT preoperatively; UST, AVG (except EPT) intraoperatively; and corneal edema (CE), anterior chamber reaction (ACR) intensity (Table 2), CV, and HEX postoperatively were not statistically significant.

Mean EPT was significantly lower in the PEX group than in the non-PEX group (p<0.001) (Table 1). Both groups showed significant improvement in mean BCVA postoperatively (p<0.001), but BCVA values (logMAR) were significantly worse in the PEX group than in the non-PEX group on both the 1st (p<0.001), 7th (p=0.011), and 30th (p=0.025) days postoperatively. Although there was no statistically significant difference between groups in mean ECD values preoperatively and on the 1st day postoperatively, mean ECD was significantly lower in the PEX group than in the non-PEX group on the 7th (p=0.013) and 30th (p=0.037) days postoperatively. None of the eyes with or without PEM exhibited clinical signs of corneal endothelial decompensation postoperatively. The mean CCT differed significantly only on the 1st (p<0.001) day postoperatively between the two groups throughout the follow-up period (Table 3).

Discussion

PEX is a systemic disorder and a frequent clinical feature seen in patients with cataracts because its prevalence increases with age. It is also presumed that patients with PEX are more prone to intraoperative complications[12] and endothelial decompensation[6,13] after intraocular procedures. Preventing corneal endothelial cell damage during phacoemulsification surgery is crucial. The use of ultrasonic energy during nuclear emulsification is nearly always associated with endothelial cell loss[14]. Despite Wirbelauer and colleagues not finding any significant group-difference in phaco time and power[15]; Kaljurand and colleagues found phaco time significantly higher in the PEX group than in the non-PEX group[16]. However, in our study, although differences between the two groups in mean nuclear firmness, UST, AVG were not significant; mean EPT was significantly lower in the PEX group than in the non-PEX group ($p<0.001$). Significantly lower EPT values in the PEX group might be explained by the surgeon's conservative approach initially and diligence to lower EPT in patients with PEX due to the reality of its preoperatively well-known clinical risks. Additionally, effectively introducing ultrasound (US) energy into the eye while eliminating or limiting its negative influence on tissue other than the lens[17,18], especially in surgical conditions that are difficult or when the cataract is severe, as well as in eyes with disorders other than cataract[19], is particularly important. Therefore, as much as possible, reduced phacoemulsification energy might have been administered by the surgeon.

This study, in common with many former similar studies, assessed endothelial parameters of the central cornea and did not take into consideration regional differences of endothelial cell density, which might be significant[20-22]. The corneal endothelium plays an important role in maintaining normal corneal hydration, thickness, and transparency. This cellular monolayer is highly vulnerable because when some corneal endothelial cells die, the remaining cells cannot divide fast enough to replace the dead cells. Instead, they become larger and stretch to cover dead cells to sustain the intact monolayer mosaic[23]. The integrity of the corneal endothelium is substantial for successful visual results after cataract surgery, as cataract surgery itself is among the factors that can cause endothelial cell damage[24]. It was also reported that ultrastructural evidence suggested focal in situ production of PEM by corneal endothelial cells is associated with focal degeneration, melanin pigment deposition, and abnormal extracellular matrix production in the endothelial cell layer resulting in dysfunction[6,25]. Even though the structural deformity of endothelial cells and difficult surgical techniques necessary for eyes with PEX, there were some previous studies in the literature showing that there is no significant difference in endothelial cell loss after cataract surgery between eyes with PEX and those without PEX[15,16,26]. However, in the current study, despite the similarities in preoperative corneal morphology, nuclear firmness, and intraoperative parameters; mean ECD values were significantly lower in the PEX group than in the non-PEX group on postoperative 7th and 30th days. Hayashi and colleagues observed similar outcomes in mean ECD after cataract surgery that supports ours[13]. This finding shows that corneal endothelial cells are more susceptible and prone to be damaged in the eyes with PEX than in the eyes without PEX after uncomplicated phacoemulsification surgery in the early postoperative period. We did not find any significant difference preoperatively and postoperatively in the measurements of pleomorphism and polymegathism between the PEX and non-PEX group. This finding was in agreement with previous studies[8,26,27].

Although there was no cystoid macular edema on postoperative clinical examination or significant group-difference in corneal edema and anterior chamber reaction (ACR) intensity, best-corrected visual acuity (BCVA) was significantly worse on the 1st, 7th, and 30th days postoperatively in the PEX group than in the non-PEX group. This loss in BCVA at 1 month may be attributed to the weakening of the ciliary zonules in eyes with PEX, which could influence postoperative refractive outcomes following intraocular lens (IOL) implantation[28]. Presumed decreased blood-aqueous barrier seen with PEX or possible iris contacts in the PEX group, which could have resulted in postoperative inflammation, may be other reasons. Fibrillin deposition around the microvasculature in eyes with PEX could have increased the leakage of proteins into the aqueous humor and thus compromised the blood-aqueous barrier[29]. Additionally, this result also implies that the vulnerability of the corneal endothelial cells in eyes with PEX can affect visual acuity in the early postoperative period. We are unable to comment on longer-term visual outcomes in this study, but it is possible that BCVA may improve in eyes with PEX after the first month.

On the first postoperative day, central corneal thickness (CCT) was significantly increased in both groups, indicating edema. CCT had returned to preoperative levels one month after the operation. Our data revealed that CCT returns to preoperative values soon after irrespective of the degree

of corneal endothelial cell density (ECD). No association existed between central corneal thickness and corneal endothelial cell numerical density. This result confirmed the findings of previous studies[16,24,30].

Limitations

There were some limitations to this study. First, the surgeon responsible for all study operations was aware of the presence or absence of PEX preoperatively. However, not knowing the presence of this condition could increase the risk of surgical complications. Should any complications have occurred, the surgeon would have the appropriate tools during surgery for excellent outcomes. Additionally, the postoperative examiner was not blinded to which study group each subject belonged to. Because after surgery, frequent and thorough follow-up visits were vital for early detection and treatment of complications such as an increase in intraocular pressure (IOP), formation of synechiae, or development of fibrin. Secondly, the study groups had small sample sizes. However, the sample sizes of our report are comparable with those of similar studies in the literature. Another limitation was the evaluation of ACR intensity carried out via slit-lamp biomicroscope instead of a flare meter.

Conclusion

In conclusion, despite the similarities in preoperative and intraoperative parameters, corneal endothelial cell density (ECD) and best-corrected visual acuity (BCVA) after uncomplicated phacoemulsification surgery were significantly lower in eyes with pseudoexfoliation syndrome (PEX) than in eyes without PEX in the early postoperative period. This indicates the susceptibility of corneal endothelial cells to phacoemulsification surgery in PEX eyes. There was no association between central corneal thickness (CCT) and the existence of PEX preoperatively and in the early postoperative period. Due to reduced endothelial cell counts and decreased functional reserve, caution, an experienced surgeon, and careful surgical techniques are required during cataract surgery in PEX eyes. Additional studies are needed to evaluate corneal endothelial cell density after surgery in eyes with PEX.

Ethics Committee Approval: The study was approved by the University of Health Sciences Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (no: E-18-2407, date: 07/02/2019).

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