·Clinical Research·

Effect of torsional mode phacoemulsification on cornea in eyes with/without pseudoexfoliation

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Abstract

• AIM: To evaluate the effect of torsional mode phacoemulsification on central corneal thickness, corneal endothelial cell density, and morphology in eyes with/without pseudoexfoliation (PEX) syndrome.

• METHODS: Fourty-two consecutive patients with and 42 patients without PEX as a control group scheduled for cataract surgery was studied. Phacoemulsification, using OZiL IP system, was performed with quick chop technique. Using noncontact specular microscopy, the central endothelial cell density (ECD), coefficient of variation, percentage of hexagonal cells, and the central corneal thickness (CCT) were evaluated preoperatively and postoperatively at 1, 7 and 30d.

• RESULTS: The ECD in PEX syndrome was statistically significantly lower than that in the control group preoperatively and postoperatively ($P \leqslant 0.001$).Percentage change in ECD was statistically significantly higher in PEX than that in control group after surgery follow up ($P \leqslant 0.04$).There was no statistically significant difference between both groups comparing percentage of hexagonal cells and coefficient of variation in the cell size before and after the surgery. At 1 and 7d after surgery, percentage change in CCT was statistically significantly higher in PEX group than that in the control group ($P \leqslant 0.041$).

• CONCLUSION: Although torsional mode phacoemulsification and intraocular lens (IOL) implantation provided a safe and favorable surgical outcome in patients with/without PEX, torsional phacoemulsification led to significantly higher ECD loss in the PEX group than that in the control group during the whole follow up period. In addition, more corneal swelling in the PEX group than that in the control group during the early postoperative period has indicated that the corneal endothelium, in presence of PEX endotheliopathy, seems to be more susceptible to the effects of phacoemulsification surgery in eyes with PEX. The increased risk of anterior chamber manipulations in patients with PEX should be taken into account for an increased risk of bullous keratopathy.

• **KEYWORDS:** pseudoexfoliation syndrome; endothelial cell density; endothelial morphology; torsional mode phacoemulsification; corneal endothelium

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INTRODUCTION

Pseudoexfoliation (PEX) syndrome is a common age-related disorder characterized by the production and progressive deposition of a fibrillar extracellular material in ocular and extraocular tissues [1-3]. The deposition of extracellular material on tissues of the anterior segment may predispose to various ocular complications, including zonular weakness, glaucoma, pigment dispersion, small pupil, blood-aqueous barrier dysfunction, posterior synechiae [1,2]. Although PEX is associated with a significant increase in intraoperative complications during cataract surgery, zonular weakness and small pupil have been identified as the most important risk factors for surgical complications [4-6]. Furthermore, a bilateral, asymmetrical, slowly progressive corneal endotheliopathy, including decreased central endothelial cell density (ECD), abnormal endothelial morphological changes, polymegathism, and guttata have been demonstrated in eyes with PEX [7,8]. The cornea may be more susceptible in presence of endotheliopathy to the effects of phacoemulsification surgery. Increased risk of complications of cataract surgery and presence of endotheliopathy may lead to endothelial decompensation with higher ECD loss and more corneal swelling in eyes with PEX. The corneal endothelium is essential for maintaining a relatively dehydrated state and optical transparency of the cornea through a barrier function and a pump-leak mechanism. After injury, the corneal endothelium has also only limited mitotic capacity[9].

Although PEX can be associated with various challenges to successful cataract surgery, phacoemulsification is the preferred technique for removal of cataract in such patients [10-12].

The aim of the development of new technologies and techniques has been to reduce the incision size, reduce phacoemulsification energy, increase efficiency and reduce endothelial cell loss[13-15]. As a new cataract removal modality, OZiL (Infiniti, Alcon) torsional mode phacoemulsification uses torsional handpiece that produces side to side rotary oscillation of the phaco tip. In torsional, although the phaco tip moves at lower resonant frequency compared to conventional ultrasound (U/S), the side to side oscillation of the tip shears the lens with virtually no repulsion and cuts with both direction of tip movement, thereby dramatically improving the flow of nuclear material into the phacoemulsification tip, and reducing U/S energy required for lens removal without compromising efficiency [13-18]. The aim of this study was to evaluate the effect of torsional mode phacoemulsification on central corneal thickness (CCT), corneal ECD, and morphology in eyes with/without PEX.

SUBJECTS AND METHODS

Subjects In this prospective study, 42 consecutive patients with and 42 patients without PEX as a control group scheduled for cataract surgery were studied at Kayseri Training and Research Hospital between January and June 2012. The study protocol was approved by institutional review board and performed according to the Declaration of Helsinki. Written informed consent forms were obtained from all the patients. The diagnosis of PEX was made by the presence of abnormal fibrillar extracellular material on the anterior lens capsule and/or pupillary margin using slit-lamp biomicroscopy following pupillary dilation. Eleven patients with PEX also had glaucoma. These patients were treated with topical medications for glaucoma. Exclusion criteria were previous ocular trauma or intraocular surgery, intraocular inflammation, preoperative anterior chamber depth less than 2.5 mm centrally, preoperative pupil size less than 4 mm after dilation, any corneal pathology, any condition that impeded corneal evaulation by specular microscopy and pachymetry, or for those with incomplete follow-up.

Methods All patients underwent a complete ophthalmic examination. All patients had a similar degree of nuclear opacification (NO3, NO4 or NO5) and a similar degree of cortical opacification (C2 or C3) according to the LOCS III scale. The intraocular lens (IOL) Master (Carl Zeiss Meditec, Dublin, CA, USA) was used for ocular biometry. Pupil size was measured using pupil size chart at the beginning of surgery after dilation with tropicamide 1% and phenylephrine 2.5% drops. Phacoemulsification was performed with quick chop technique, using Alcon OZiL IP system and 0.9 mm miniflared 45-degrees Kelman Aspiration Bypass System (ABS) phaco tip. For quick-chop technique, torsional mode was adjusted as follows: linear torsional amplitude 85% continous mode, vaccum limit 350 mm Hg, aspiration rate 32 mL/min with dynamic rise at +2 and bottle height at 95 cm. Topical anesthesia (proparacaine hydrochloride 0.5%) was used in all cases. All surgery was performed by the same experienced surgeon (Demircan S). A clear corneal incision was made with 2.2 mm keratome. Viscoat (sodium hyaluronate 3.0% -chondroitin sulfate 4.0%) was used to reform and stabilize anterior chamber and protect the corneal endothelium. A 5 to 5.5 mm continuous curvilinear capsulorhexis was made using an ultrata capsulorhexis forceps (Katena, USA). All IOLs (Acrysof SA60AT, Alcon) were inserted into capsular bag with the same injector system (MonarchIII D-Catridge). Sodium hyaluronate 1.0% (Provisc, Alcon) was used for intraocular insertion. The ocular viscoelastic device (OVD) was removed from the anterior chamber and the capsular bag, using the I/A system with balanced salt solution (BSS-plus, Alcon). For endophthalmitis prophylaxis, 0.1 mL moxifloxacin ophthalmic solution 0.5% (Vigamox) was injected into the anterior chamber after closure of the port incisions by stromal hydration, using a balanced salt solution. After surgery, all patients used topical prednisolone acetate 1.0% and moxifloxacin 0.5% 6 times daily for 4wk. Intraocular pressure (IOP) was measured, using noncontact applanation tonometer (NT-510, Nidek). ECD, polymegathism (coefficient of variation, CV), pleomorphism (percentage of hexagonal cells), and the CCT were evaluated preoperatively and postoperatively at 1, 7 and 30d after surgery, using noncontact specular microscopy (SP 3000P, Topcon) [19]. More than 75 endothelial cells per eye were used to calculate the ECD, CV, percentage of hexagonalty with the IMAGEnet i-base imaging system (version 3.5.6, Topcon). During each visit, 3 photographs of each cornea were taken and analyzed indepedently by another ophthalmologist. The mean of the 3 readings was calculated and used as the final reading for each visit. The percentage changes in ECD and CCT at each visit were calculated as follows:

[(preoperative value—postoperative value)/preoperative value]×100

Intraoperative parameters of U/S total time, U/S total equivalant power position-3 (U/S TEPP3), cumulative dissipated energy (CDE), torsional time, average torsional amplitude in position-3 (ATAP3), aspiration time and estimated fluid use (BSS-plus) were automatically calculated and displayed on the monitor of the Infiniti Ozil IP phacoemulsification system.

Statistical Analysis Shapiro-Wilk's test was used, histogram, and q-q plots were examined to assess the data normality. To compare the differences between pseudoexfoliation and age-matched control group, Chi-square analysis was used for categorical variables and independent samples *t*- test was used for continuous variables. For comparison of continuous variables in each group over time,

Table 1 Comparison of patient characteristics and intraoperative parameters n (%), $\bar{x} \pm s$

Variables	Groups		P
	Control (n=42)	PEX (n=42)	
Age (a)	74.74±5.19	76.02±5.03	0.252
Gender (F/M)	17(40.5)/25(59.5)	18(42.9)/24(57.1)	0.825
Eye (R/L)	23(54.8)/19(45.2)	21(50.0)/21(50.0)	0.662
NO3/NO4/NO5	25/12/5	21/15/6	0.409
ACD	3.23±0.36	3.08±0.34	0.055
Pupil size	7.74±0.73	5.75±1.32	<0.001
U/S total time	65.53±19.23	69.95±21.41	0.323
U/S total equivalant power position 3	24.86±3.53	23.71±5.54	0.261
CDE	16.52±5.71	18.39±6.35	0.159
Torsional time	65.03±19.11	69.59±21.26	0.304
Average torsional amplitude in position 3	61.88±8.66	65.76±11.80	0.090
Aspiration time	171.02±36.55	203.00±44.21	0.001
Estimated fluid use	55.95±12.15	71.62±17.42	<0.001

CDE: Cumulative dissipated energy; NO: Nuclear opacification; ACD: Anterior chamber depth.

one way repeated measure analysis of variance was used followed by a Bonferroni correction. Values are expressed as n (%) or mean ±standard deviation (SD). Analysis was conducted, using SPSS for Windows software (Version 16.0, SPSS, Inc.). A P <0.05 was considered as statistically significant. Sample size was based on a power calculation (power: 0.80; P=0.05) using SDs obtained in the previous studies from our clinic. For power calculation, a clinically important change in ECD was defined as a loss of 200 cell/mm^2. Minimum sample size to detect postoperative ECD loss between 2 groups was calculated as 37 eyes in each group.

RESULTS

Table 1 shows patient characteristics and intraoperative parameters. There were no statistically significant differences in age, sex, nuclear opalesence, anterior chamber depth (ACD), U/S total time, U/S total equivalant power position-3, CDE, torsional time, average torsional amplitude in position-3 between the groups. However, pupil size, aspiration time and estimated fluid use (BSS plus) were stastistically significantly different between the groups. Pupil size was smaller, aspiration time and estimated fluid use (BSS-plus) in the PEX group were more increased than those in the control group. A clear ECD and endothelial morphological measurement, due to dense corneal edema at 1d postoperatively, could not be obtained in 2 patients in each group. The ECD in PEX syndrome was significantly lower than that in the control group preoperatively and postoperatively (P≤0.001). Percentage change in ECD was significantly higher in the PEX group than that in the control group throughout the follow up periods (P≤0.04). There was no statistically significant difference between these two groups, comparing the percentage of hexagonal cells and CV in the cell size before and after the surgery. At 1 and 7d after surgery, percentage change in CCT was statistically significantly higher in the PEX group than that in the control group (P ≤0.041). At 30d, there were no statistically significant differences in CCT between both groups (P>0.05, Tables 2, 3). There was no stastically significant difference in IOP between PEX and control group, before and after surgery

Table 2 Comparison of IOP, ECD, CCT and percentage differences in IOP, ECD and CCT between groups over time $\bar{x} \pm s$

Variables	Groups		P
	Control (n=42)	PEX (n=42)	
IOP			
Preop.	14.1±3.3	15.6±4.4	0.069
Postop. 1d	15.5±5.6	19.4±8.6	0.015
Postop. 7d	13.6±4.3	13.9±4.3	0.827
Postop. 30d	12.7±3.3	13.1±4.0	0.645
ECD			
Preop.	2533±320	2304±303	0.001
Postop. 1d	2330±356	2050±316	0.0001
Postop. 7d	2325±365	2043±326	0.0001
Postop. 30d	2331±340	2043±312	0.0001
Δ0_1	-8.19±6.49	-11.08±6.54	0.040
Δ0_7	-8.48±6.12	-11.46±5.78	0.021
Δ0_30	-8.11±5.31	-11.42±5.18	0.004
CV			
Preop.	37.7±5.6	38.3±5.8	0.578
Postop. 1d	39.6±6.6	40.4±5.5	0.561
Postop. 7d	39.3±5.0	40.2±7.7	0.568
Postop. 30d	38.6±4.3	38.3±4.6	0.805
HEX			
Preop.	49.6±8.1	48.0±9.8	0.416
Postop. 1d	48.9±8.9	45.4±10.6	0.112
Postop. 7d	49.9±8.3	45.2±11.0	0.055
Postop. 30d	49.1±7.1	47.3±6.9	0.313
CCT			
Preop.	508±31	499±31	0.176
Postop. 1d	532±44	536±39	0.656
Postop. 7d	521±43	520±36	0.871
Postop. 30d	510±36	501±32	0.238
Δ0_1	4.55±4.24	7.47±4.18	0.002
Δ0_7	2.51±4.38	4.19±3.70	0.041
Δ0_30	0.28±2.22	0.20±1.37	0.851

IOP: Intraocular pressure; ECD: Endothelial cell density; CV: Coefficient of variation; HEX: Percentage of hexagonalty; CCT: Central corneal thickness; Δ: Percentage of change.

Table 3 Comparison of IOP, ECD and CCT each groups over time $\bar{x} \pm s$

Variables	0	1	7	30	*P*
Control group					
IOP	14.1±3.26[a]	15.5±5.6[a]	13.6±4.3[ab]	12.7±3.3[b]	<0.001
ECD	2533±320[a]	2330±356[b]	2325±365[b]	2331±340[b]	<0.001
CCT	508±31[a]	532±44[b]	521±43[b]	510±36[a]	<0.001
PEX group					
IOP	15.6±4.4[a]	19.4±8.6[b]	13.9±4.3[ac]	13.1±4.0[c]	<0.001
ECD	2304±303[a]	2050±316[b]	2043±326[b]	2043±312[b]	<0.001
CCT	499±31[a]	536±39[b]	520±36[c]	501±32[a]	<0.001

IOP: Intraocular pressure; ECD: Endothelial cell density; CV: Coefficient of variation; HEX: Percentage of hexagonalty; CCT: Central corneal thickness. [a,b,c]Statistical significant difference.

excluding the 1d post-operative IOP. There was a significant difference in IOP between the 2 groups, with patients in PEX group having higher IOP than patients in the control group at 1d after surgery (P=0.015).

Five patients (11.9%) in the PEX group and one patient (2.38%) in the control group had IOP spikes of 30 mm Hg or higher in this period. Both groups had a statistically significant decrease in IOP at 7 and 30d postoperatively (P<0.001).

Capsular tension ring was inserted in 12 patients with PEX following continuous circular capsulorhexis (CCC) and hydrodissection due to zonular weakness. In all the other patients, there were no complications intraoperatively.

DISCUSSION

The corneal endothelium may, to some extend, be affected in eyes with PEX. Several studies have suggested that hypoxic changes in the anterior chamber, deposition of extracellular matrix, fibroblastic changes of the endothelium, and increased concentration of transforming growth factor-β may cause a specific corneal endotheliopathy in eyes with PEX[1-3]. It was clinically observed that in patients with PEX keratopathy, only moderate rises of intraocular pressure or minor intraoperative trauma might lead to a relatively early occurring diffuse corneal decompensation [20]. These studies also have suggested that the presence of PEX could have an effect on the viability of the endothelium [20,21]. It has been proposed that an increased endothelial trauma leads to the risk of endothelial decompensation after surgery [21]. In this study, the ECD loss and CCT were used as outcome parameters representing the corneal injury due to the cataract surgery. Recent studies evaluating eyes with a normal ECD reported ECD loss ranging from 4% to 15% after phacoemulsification[22-26]. We found that ECD loss was 8.11% in the control group and 11.42% in the PEX group 1mo after surgery. These findings are consistent with the findings of the previous studies on ECD after cataract surgery[22-26].

In this study, in contrast to previous studies [7,27], the percentage change in ECD was significantly higher in the PEX (11.42%) than that in the control group (8.11%) (P= 0.004) 1mo after surgery. However, there was a relative decrease in ECD at 1 and 7d postoperatively. It can be related to the accuracy in measuring ECD using noncontact specular microscopy due to more corneal edema following phacoemulsification in the PEX group. Wirbelauer *et al*[7] reported that preoperative ECD was 9.9% (P<0.05) lower in patients with PEX (2387±266 cells/mm^2) than in controls (2648±349 cells/mm^2). The mean ECD loss was 11.1% in the PEX group and 10.3% (P<0.001 for both) in the control group, with no intergroup differences after 6mo. The mean endothelial cell area increased in both groups. Also, qualitative analysis revealed no significant differences in the endothelial repair mechanisms. ECD is reduced preoperatively in patients with PEX compared with age-matched controls. In patients with PEX, they found that cataract surgery induced similar endothelial cell changes without increased endothelial cell loss postoperatively [7]. As far as we are concerned, they may not have revealed differences in percentage change in ECD due to the differences in the used surgical technique, such as incision size (7 mm scleral tunnel incision in their study *vs* 2.2 clear corneal incision in our study) and use of torsional mode during removal of cataract in our study. Liu *et al* [13] also demonstrated that the CDE and ECD loss in torsional mode phacoemulsification were lower than those in conventional mode in cataracts of all grades.

Kaljurand and Teesalu [27] reported that there were no significant preoperative differences in endothelium morphology between the groups. The mean endothelial cell loss 1mo after surgery was 18.1% in the PEX group and 11.6% in the control group (P=0.06). Phaco time and used BSS values were significantly higher in patients with PEX but had no significant influence on endothelial cell loss. In regression analysis, phaco power (P=0.02) and age (P=0.004)

had a significant influence on endothelial cell loss. PEX in interaction with overall phaco impact had a negative influence on endothelial cell loss (P=0.05). PEX, as a main effect, was not found to have a negative influence on endothelial cell loss. However, PEX, in cases of high phaco impact, significantly increases the risk of endothelial cell loss. In this study, we did not find significantly difference in U/S time, U/S total equivalant power position-3 U/S TEPP3, torsional time, average torsional amplitude in position 3, and CDE between both groups (P>0.05). The findings of the current study do not support that impact of high U/S power increases the risk of ECD loss. In contrast to their study[27], we found that the preoperative ECD reduction is significantly higher in the PEX group than that in the control group. They found that the mean ECD loss was higher in the PEX group than in the control group; however, the difference between both groups was not statistically significant (P=0.06)[27]. It may be related to having a relatively healthy corneal endothelium in eyes with PEX that was similar to control group in their study. The findings of current study are consistent with those of Hayashi *et al*[28] who found that the mean percentage of ECD loss and transient increase in CCT were significantly greater after cataract surgery in PEX group than in control group. They also suggested that the corneal endothelium in PEX be vulnerable to cataract surgery.

After surgery, the remaining endothelial cells are able to migrate, re-cover the posterior corneal surface by spreading out over a larger surface area, and re-establish the intercellular cell junctions. Thus, the barrier function of the corneal endothelium is efficiently restored.

Despite the fact that the main weakness of this study was the short follow up period, Lundberg and Drolsum[29] reported no further postoperative ECD loss after 4wk, assuming that wound healing is complete or entered a slower phase by this period. The present observation seems to be consistent with another study [30]. So, the 30d follow up was used as a sufficient endpoint in this study. In our study, in the early healing process, between both groups, there was no significant difference in endothelial morphology and CCT thickness after 4wk. In addition, Ostern and Drolsum [31] reported no statistically significant differences in the ECD, endothelial morphology, and corneal thicknesses in eyes with and without PEX at 6-7y after cataract surgery. The corneal injury during phacoemulsification may be attributed to several factors[22-26]. These can be divided into 4 main groups: a) direct mechanical trauma to the endothelium from incision and inadvertent touch of endothelium such as with surgical instruments, lens fragments and IOLs; b) U/S trauma by energy delivered close to the endothelium; c) formation of free radicals; d) the composition and mechanical effects of the irrigating solution (nature, volume and turbulence in the anterior chamber). In this study, we, to determine the effect of PEX on the corneal endothelium as in previous studies, excluded other factors with possible reduction of the endothelial cell function. All surgeries were performed by the same experienced surgeon, using the same techniques and settings, *i.e.* vertical choping technique, the same 0.9 mm ABS Kelman 45 degrees bent tip, the same FMS, similar nuclear gradings, and the same catridge system for IOL implantation, the same OVD and BSS-plus for irrigating solution. As a result, the surgical variations were minimized in the present study.

The ECD in PEX group was significantly lower than that in control group; however, the CV in the cell area and percentage of hexagonal cells were similar in both groups (P>0.05). Compared with control group, PEX group had a reduction in mean ECD around 9.04% preoperatively. Recent studies reported a reduction in ECD ranging from 5.6% to 13.4% [7,8,21,32,33]. We observed that PEX had no impact on hexagonality and coefficient of variation in cell size before and after surgery. However, some researchers found a decrease of hexagonality and an increased CV in eyes with PEX[20,32].

In this study, at 1 and 7d after surgery, percentage change in CCT was statistically significantly higher in the PEX group than that in the control group (P≤0.041). At 30d, there were no statistically significant differences in CCT between both groups (P>0.05, Table 2). While CCT in the control group increased by about 4.55% at 1d after surgery, in the PEX group, it increased by about 7.47% within the same time. Respectively, these values were 2.51% and 4.19% at 7d after surgery. These findings are consistent with the findings of Hayashi *et al*[28]. Salvi *et al*[34] found the CCT in healty, uncompromised eyes increased by approximately 6.44% at 1d after surgery and gradually reduced to preoperative levels by 7d after surgery. Ventura *et al*[35] reported that a healthy cornea is able to restore rapidly for transient increases in CCT. Restoration in corneal thickness may be much slower when the corneal endothelium is diseased. We are of the opinion that swelling rate of cornea in patients with PEX is significantly lower than that in the control group at early postoperative period.

Early postoperative IOP spike was more common and greater in the PEX group than in the control group after surgery. Our findings were consistent with previous studies [11,36]. As previous studies reported, postoperative inflammation and fibrinous reactions occur more frequently in patients with PEX after cataract extraction[10]. Currently, with the advent of

phacoemulsification, these issues after surgery are dramatically reduced to less than 3%[10]. It is unlikely to need for increased antiinflammatory treatment in eyes with PEX after cataract surgery. We didn't observe any sign of increased inflammatory response and fibrinoid reaction in eyes with PEX compared with the control group at slit-lamp examination. It is also known that an asymptomatic low-grade chronic inflammation of the anterior eye segment due to dysfunction of the blood-aqueous barrier may decrease endothelial function in the long term. This could lead to a progressive decline in ECD after intraocular surgery.

Capsular tension ring was inserted with a view to avoiding probable complications due to zonular weakness in 12 patients with PEX following CCC and hydrodissection. Bayraktar *et al* [37] reported that CTR reduced intraoperative complications in eyes with PEX. One of the best techniques is to place the CTR in the bag as soon as the capsulorhexis has been completed. Much of cortex was trapped beneath CTR, requiring additional aspiration force and time to remove the cortex with I/A handpiece. This issue may have led to use higher volume BSS in the patients with PEX than control group. Kaljurand and Teesalu [27] found that the used BSS volume was significantly higher in patients with PEX but had no significant influence on endothelial cell loss.

Although torsional mode phacoemulsification and IOL implantation provided a safe and favorable surgical outcome in patients with/without PEX, Torsional phacoemulsification led to significantly higher ECD loss in the PEX than that in the control group during the whole follow up period. In addition, more corneal swelling in the PEX group than that in the control group during the early postoperative period has indicated that the corneal endothelium, in presence of PEX endotheliopathy, seems to be more susceptible to the effects of phacoemulsification surgery in eyes with PEX. In PEX, due to a lower functional reserve of ECD preoperatively together with factors such as shallow anterior chamber, small pupil, and zonular weakness that increase the level of difficulty of cataract surgery, anterior chamber manipulations intraoperatively should be performed with care at a safe distance away from the corneal endothelium to prevent complications and ECD loss postoperatively.

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