Corneal Endothelial Cell Changes in Pseudoexfoliation Syndrome After Cataract Surgery

Christopher Wirbelauer, MD; Norbert Anders, MD; Duy T. Pham, MD; Josef Wollensak, MD

Objective: To characterize possible differences in endothelial cell changes after cataract surgery in patients with pseudoexfoliation syndrome (PSX).

Methods: In this prospective, age-matched, controlled clinical study, 25 consecutive patients with PSX and 25 control patients with senile cataracts only were studied. All patients were treated with standardized cataract surgery. Sequential quantitative and qualitative morphometric endothelial cell analyses of the central and paracentral cornea were performed preoperatively and postoperatively at 1 day, 4 weeks, and 6 months using noncontact specular microscopy.

Results: Preoperative endothelial cell counts were 9.9% (P<.05) lower in patients with PSX (2387±266 cells/mm²) than in controls (2648±349 cells/mm²). The mean endothelial cell loss was 11.1% in the PSX group and 10.3% (P<.001 for both) in the control group, with no intergroup differences after 6 months. The mean endothelial cell area increased in both groups. Also, qualitative analysis revealed no significant differences in the endothelial repair mechanisms.

Conclusions: Endothelial cell density is reduced preoperatively in patients with PSX compared with age-matched controls. In patients with PSX, cataract surgery induced similar endothelial cell changes without increased endothelial cell loss postoperatively.


The corneal endothelium is essential for maintenance of normal corneal hydration, thickness, and transparency. This cellular monolayer is highly vulnerable and has only limited regenerative capacity. In patients with pseudoexfoliation syndrome (PSX), quantitative and qualitative morphological changes of the corneal endothelium have been demonstrated in specular and electron microscopic studies.1-4 It has been postulated that these changes represent an abnormal or unstable endothelium, predisposing to an endotheliopathy that may be more susceptible to the effects of intraocular surgery.5-13 The presence of PSX increases the incidence of intraoperative and postoperative complications during cataract surgery. Insufficient mydriasis and possible zonular instabilities can complicate the intraoperative course. Thus, higher corneal endothelial cell loss with impairment of the endothelial barrier and pump function can occur after intraocular manipulations.

This study sought to investigate the reactions of the corneal endothelium associated with cataract surgery in patients with PSX.

Table 1 summarizes important preoperative and intraoperative variables. Eight of the 25 patients with PSX previously underwent surgery on the nonexamined eye. Fourteen of the 17 patients for whom this was the first operation had bilateral involvement, and 3 were affected unilaterally. The semiquantitative analysis of PSX material on the anterior lens capsule revealed mild deposition in 4 (16%) patients, moderate in 18 (72%), and marked in 3 (12%). The pupillary dilatation was reduced in patients with PSX (Table 1).

The quantitative results of the corneal endothelium revealed preoperatively in the PSX group (mean±SD, 2387±266; range, 1886-2891 cells/mm²) a significant reduction of 9.9% (P<.02) total ECD compared with the control group (mean±SD, 2648±349; range, 2071-3190 cells/mm²) (Table 1). Also, regional morphometric data revealed reduced ECDs in central and paracentral areas in the PSX group compared with the control group (Table 2). Preoperative mean paracentral cell counts in the control group were 6.7% (178 cells/mm²) higher than central...
PATIENTS AND methods

PATIENTS AND CLINICAL EXAMINATION

Twenty-five consecutive patients with clinically diagnosed PSX were studied prospectively in a controlled clinical setting. Each patient underwent a complete preoperative ophthalmologic examination, including anterior segment biomicroscopy, Goldmann applanation tonometry, gonioscopy, and binocular ophthalmoscopy. The diagnosis of PSX was made with the patient in mydriasis with the typical biomicroscopic findings of the presence of white grayish exfoliation material on the anterior lens capsule and/or the pupillary margin. The amount of PSX material on the anterior lens capsule was graded semiquantitatively (score: +, mild; ++, moderate; +++ marked). Preoperative maximum mydriasis (2.5% phenylephrine hydrochloride, 1% tropicamide) was measured with standardized calipers. The control group consisted of 25 age-matched patients who had no ocular disease other than senile cataracts and who were referred to our service for routine cataract surgery. Preoperative measurements were repeated 2 to 4 days after surgery because high-quality images could not be taken in some cases. All measurements were performed by the same experienced examiner (C.W.).

Subsequently, each endothelial image was studied with both incorporated computerized image analysis methods. To determine the endothelial cell density (ECD), the endothelial cells were counted in a manually determined rectangular frame with a constant area of 4.0 x 4.5 cm on the monitor (0.045 mm² on the corneal endothelium). All complete cells within the border of the rectangle and all partial cells intersecting 2 adjacent borders were marked.

Because endothelial cell counting alone is not sufficient for detecting subtle qualitative and functional changes in the endothelial monolayer, a cell analysis also was performed using the automatic center method algorithm. The center of adjacent cells were marked with a mouse and digitized. This permitted a determination of the ECD and mean cell area, thus describing the cell size. Using this algorithm, an immediate qualitative analysis of the morphological characteristics of the cell is possible. Polymegathism was assessed using the coefficient of variation of cell area, which is independent of cell area or density, and pleomorphism was assessed by the percentage of hexagonal cells.

To determine the ECD by the fixed frame method, a mean of 125 cells were sampled, and 130 cells were routinely digitized using the center cell analysis method. A second measurement had to be repeated in 64 (16%) of the determinations due to differences between both counting methods of more than 5% or 150 cells. Reevaluations were more frequent in the early postoperative period. The central and paracentral ECDs were calculated from the resulting mean of both counting methods. Total morphometric values were determined from central and paracentral variables.

STATISTICAL ANALYSIS

Any statistical differences noted between the 2 groups regarding age, intraocular pressure, pupil diameter, preoperative and postoperative endothelial cell variables, or ultrasound time and power were analyzed using the Mann-Whitney U test (intragroup differences). To compare sex distribution, the χ² test was used. Statistical differences with P<.05 were considered significant.

Changes in the individual groups were analyzed with the Wilcoxon signed rank test (intragroup differences). An α level of 5% was chosen for comparison. Bonferroni adjustment was made for multiple testing, and P<.008 was accepted as the significance level.
198 cells/mm²). This suggests a diffuse endothelial cell morphology—presented no preoperative differences in our study. Thus, differences in ECDs were smaller compared with controls (Table 1). A posterior capsular break with intraocular lens implantation was more frequent in the PSX group (6/25, 24%) than in the control group (1/25, 4%; \( P = .003 \)).

Within the first postoperative day, the ECD showed a marked total decrease of 11% in the PSX group and 9.5% in the control group (\( P < .001 \) for both). This endothelial cell loss was observed during the remainder of follow-up, with only modest regional differences between both groups (Table 1). The mean endothelial cell loss ranged in the central cornea from 7.7% to 10.8% and in the paracentral regions (Table 2). The central cornea was more affected in the PSX group than in the control group, however, without intergroup differences.

When surgery was performed on the other eye, the endothelial variables revealed a similar pattern, with reduced total ECD compared with controls (Table 1). The mean (+SD) intraoperative ultrasound time (89±50 seconds) and power (38%±16%) did not differ between groups (Table 1). A posterior capsular break with vitreous loss occurred in 1 patient with PSX. The intraocular lens was implanted in the ciliary sulcus only in this patient. In all other patients there were no complications.

Within the first postoperative day, the ECD showed a marked total decrease of 11% in the PSX group and 9.5% in the control group (\( P < .001 \) for both). This endothelial cell loss reflects the immediate surgical effect and was without difference in both groups. In the PSX group, central and paracentral cell loss occurred more homogeneously over the entire cornea, reducing the ECD by 10.6% and 11.3% (\( P < .001 \) for both), respectively (Table 2). In the control group, endothelial cell loss was 6.1% in the center and 12.2% (\( P = .003 \)) in the paracentral regions (Table 2). The central cornea was more affected in the PSX group than in the control group, however, without intergroup differences.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group (n=25)</th>
<th>PSX Group (n=25)</th>
<th>PSX Other Eye (n=17)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>77.1±6.5</td>
<td>78.0±8.8</td>
<td>77.8±9.3</td>
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<td>Sex, F:M</td>
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<td>18:7</td>
<td>13:4</td>
<td>.37†</td>
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<td>Intraocular pressure, mm Hg</td>
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<td>Mydriasis, mm</td>
<td>7.9±0.6</td>
<td>6.6±0.9</td>
<td>6.7±0.9</td>
<td>&lt;.001†</td>
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<td>Total ECD, cells/mm²</td>
<td>2648±349</td>
<td>2387±266</td>
<td>2382±310</td>
<td>.02†</td>
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<tr>
<td>Total mean cell area, µm²</td>
<td>383±50</td>
<td>424±48</td>
<td>425±56</td>
<td>.01†</td>
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<tr>
<td>Total CV, /100</td>
<td>0.36±0.03</td>
<td>0.36±0.05</td>
<td>0.35±0.03</td>
<td>.83†</td>
</tr>
<tr>
<td>Total 6A, %</td>
<td>52.4±8.6</td>
<td>61.1±5.6</td>
<td>61.0±5.6</td>
<td>.06†</td>
</tr>
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</table>

*Data are given as mean±SD. Total values indicate the mean of central and paracentral parameters. PSX indicates pseudoexfoliation syndrome; PSX Other Eye, the eye that was not operated on in patients with PSX; ECD, endothelial cell density; CV, coefficient of variation of cell area; and 6A, percentage of hexagonal cells.

†Control group vs PSX group (Mann-Whitney U test).
‡Control group vs PSX group (\( x^2 \) test).
§P<.05, changes from preoperative values: control group vs PSX group (Mann-Whitney U test).

Table 1. Preoperative and Intraoperative Variables*

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<tr>
<th>Variable</th>
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<th>PSX Other Eye (n=17)</th>
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<td>PSX Other Eye (n=17)</td>
<td>( P )</td>
</tr>
<tr>
<td>ECD, cells/mm²</td>
<td>2648±349</td>
<td>2387±266</td>
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<td>.02†</td>
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<tr>
<td>Area, µm²</td>
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<td>CV, /100</td>
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<td>.83†</td>
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<tr>
<td>6A, %</td>
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<td>61.1±5.6</td>
<td>61.0±5.6</td>
<td>.06†</td>
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</tbody>
</table>

*Data are given as mean±SD. PSX indicates pseudoexfoliation syndrome; ECD, endothelial cell density; CV, coefficient of variation of cell area; and 6A, percentage of hexagonal cells.

†P<.05, control group vs PSX group (Mann-Whitney U test).
‡P<.008, postoperative compared with preoperative values (Wilcoxon signed rank test).
§P<.05, changes from preoperative values: control group vs PSX group (Mann-Whitney U test).
Pseudoexfoliation syndrome is a systemic disorder that probably results from multifocal abnormal metabolic processes of unknown etiology leading to primary cell changes and is characterized by accumulation of fibrillar material containing basement membrane components in the anterior segment of the eye and other organ systems. It is a frequent clinical feature seen in patients with cataracts because the prevalence increases with age. In patients with PSX, insufficient mydriasis was determined to be the most significant risk factor for zonular breaks or rupture of the posterior lens capsule with consequent vitreous loss during extracapsular cataract extraction. In addition, the risk of endothelial decompensation from a more pronounced endothelial trauma was assumed after intraocular procedures. Because these studies also have suggested that the presence of PSX could have an effect on the viability of the endothelium, we undertook serial examinations of the corneal endothelial responses to cataract surgery under controlled clinical conditions.

In the present study, patients with PSX had a significantly reduced preoperative ECD compared with age-matched controls. There was high concordance between both eyes in patients with PSX without previous surgery. Also, other studies reported a reduction of the central ECD ranging from 13% to 21%.©1998 American Medical Association. All rights reserved.
the PSX group, with modest differences after 6 months compared with the control group. Because pleomorphism is indicative of a compromised endothelium with a reduced functional reserve, these subtle changes might reveal an impaired regeneration.

We excluded other factors with possible reduction of the endothelial cell function to determine the effect of PSX on the corneal endothelium. Frequently, pathological conditions such as a cornea guttata or glaucoma can be detected in patients with PSX. The presence of a preoperative cornea guttata is considered to be a particular risk factor for a postoperative endothelial cell loss. The addition of several preoperative factors could result in an increased endothelial instability and a more severe response to the effects of the surgical procedure, with a higher rate of acute and continued chronic cell loss compared with healthy eyes that have not undergone surgery.

As some recent clinical studies have reported, postoperative inflammation and fibrinous reactions occur more frequently in patients with PSX after cataract extraction. It is also known that an asymptomatic low-grade chronic inflammation of the anterior eye segment due to impairment of the integrity of the blood-aqueous barrier may diminish endothelial function in the long term. This could lead to a progressive decline in ECD after intraocular surgery, as it was demonstrated that in humans cell transformation continues for many years after recovery of a wound area damaged during lens extraction. Thus, the corneas of eyes affected with PSX might have a higher incidence of late postoperative decompensation. Future investigations examining alterations of pump function by pachymetry or cell permeability by fluorophotometry will possibly provide more information concerning the corneal endothelial function in patients with PSX.

In conclusion, we demonstrated that in patients with PSX, despite preoperative reduced ECDs compared with controls, no increased endothelial cell loss and no clinically relevant differences in the endothelial repair mechanisms were found after uneventful cataract surgery with scleral tunnel incision, phacoemulsification, and intraocular lens implantation. However, the risk of anterior chamber manipulations in patients with PSX with posterior capsular rupture and anterior vitrectomy should be emphasized. This could cause increased acute mechanical alterations and endothelial trauma, reducing the number of cells and, at the same time, increasing the rate of cell loss to a level at which functional decompensation might ensue. Due to preoperative reduced endothelial cell counts and a decreased functional reserve, these circumstances require caution and precise, careful techniques during surgery in patients with PSX.

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REFERENCES