To Evaluate Qualitative and Quantitative Changes of Corneal Endothelial Cells in Pseudoexfoliation Syndrome

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Abstract
Background: PEX syndrome significantly influences cell density of corneal endothelium of people with this disease. The clinical uses of cell analysis include the assessment of donor corneal endothelium, effects of intraocular surgery and is essential in evaluating the safety of corneal surgical procedure. The aim of present study to evaluated the qualitative and quantitative changes of corneal endothelial cells in pseudoexfoliation syndrome.

Material & Methods: The present study was conducted in Department of Ophthalmology, Government B.D. hospital, Churu, Rajasthan. This was randomized and single site study to evaluate qualitative and quantitative changes of corneal endothelial cells in pseudoexfoliation syndrome with or without glaucoma by specular microscopy in Indian study population. We included 40 patients and randomized them in to 2 groups of 20 patients each as follows: Group A having Young healthy person serving as control group and Group B having psuedoexfolation syndrome group.

Results: Our study showed that the maximum subjects (n=15) in 55-65 years in age in control group and 8 patients in 66-75 years in age in psuedoexfoliation syndrome group. Male to female ratio was 3:2 in control group and 1.22:1 in PSX group. The mean value of endothelial cell density (cells/mm²) in normal subjects were 2511±171.3 and compare to mean value (2124±116.0) of psuedoexfolation syndrome group was statistically significant (p<0.0001***), cell size variation coefficient in psuedoexfolation syndrome group was statistically significant (p<0.0001***), The hexagonality (%) statistically significant (p<0.0001***), but Central corneal thickness (µm) in normal subjects were 530.8±26.20 and compare to mean value (524.8±16.19) of psuedoexfolation syndrome group was statistically insignificant (p=0.3892 NS).

Conclusion: This study confirms the existence of qualitative and quantitative modifications in endothelial cells of eyes with PEX, particularly when IOP is high. It could also indicate a possible independent biological role of CCT as a risk factor for the development of glaucoma in subjects with PXS.

Keywords: Psuedoexfoliation syndrome, Center corneal thickness, Intraocular pressure, Hexagonality.
Introduction

Pseudoexfoliation syndrome (PES) is an age-related systemic microfibrillopathy, caused by progressive accumulation and gradual deposition of extracellular grey and white material over various tissues\(^1\).

Pseudoexfoliation syndrome is first described by Lindberg in 1917\(^1\). Pseudoexfoliation is considered to be a systemic disorder; pseudoexfoliative material has been reported in lungs, skin, liver, heart, kidney, gallbladder, blood vessels, extraocular muscles and meninges\(^2\). Pseudoexfoliation is a known risk factor for developing cataracts.\(^3\) Complicating factors such as poor mydriasis, zonular weakness, corneal endothelial dysfunction, higher rate of vitreous loss, capsular phimosis, and opacification have all been reported after cataract surgery.\(^4,5\) The prevalence of PXF based on hospital reports from India varies between 1.87% and 13.5%\(^6\).

Pseudoexfoliation syndrome is more common in females than in males. It has been demonstrated that in eyes with PEX, the corneal endothelium actively participates in the production of said pathological material. The sedimentation on cells can lead to their degeneration and, with time, produce alterations in their number and morphology. In addition, hypoxic changes have been described in the anterior chamber as well as variations in the composition and dynamics of the aqueous humor caused by the rupture of the blood barrier in eyes with PEX, which could affect the function of the endothelium\(^7\). So endothelial cell analysis is important for corneal function and viability assessment. The clinical uses of cell analysis include the assessment of donor corneal endothelium, effects of intraocular surgery and is essential in evaluating the safety of corneal surgical procedure. The aim of present study to evaluated the qualitative and quantitative changes of corneal endothelial cells in pseudoexfoliation syndrome.

Material & Methods

The present study was conducted in Department of Ophthalmology, Government D.B. hospital, Churu, Rajasthan. This was randomized and single site study to evaluate qualitative and quantitative changes of corneal endothelial cells in pseudoexfoliation syndrome with or without glaucoma by specular microscopy in Indian study population.

We included 40 patients and randomized them into 2 groups of 20 patients each as follows: Group A having Young healthy person serving as control group and Group B having psuedoexfolation syndrome group.

In all patients who were enrolled on the basis of inclusion criteria, a detailed history and through clinical examination was done including visual acuity, slit lamp examination and IOP measurement. Routine investigation was done. These patients were examined for corneal endothelium, Central Corneal Thickness, Avg. Cell size and Percentage of hexagonality with a non contact type TOMEY EM 3000 Specular microscope with automated analysis.

Results

Our study showed that the maximum subjects (n=15) in 55-65 years in age in control group and 8 patients in 66-75 years in age in psuedoexfoliation syndrome group (table 1). Male to female ratio was 3:2 in control group and 1.22:1 in PSX group (table 2).

The mean value of endothelial cell density (cells/mm\(^2\)) in normal subjects were 2511±171.3 and compare to mean value (2124±116.0) of pseudoexfoliation syndrome group was statistically significant (p<0.0001***), cell size variation coefficient in pseudoexfoliation syndrome group was statistically significant (p<0.0001***), The hexagonality (%) statistically significant (p<0.0001***), but Central corneal thickness (µm) in normal subjects were 530.8±26.20 and compare to mean value (524.8±16.19) of
psuedoexfoliation syndrome group was statistically insignificant (p=0.3892 NS).

**Table 1:** show the Age wise distribution of Normal patients in the study

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Age in years</th>
<th>Control</th>
<th>PSX</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55-65 yrs</td>
<td>15 (75%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>2</td>
<td>66-75 yrs</td>
<td>4 (20%)</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>3</td>
<td>&gt;75 yrs</td>
<td>1 (5%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mean ± S.D</td>
<td></td>
<td>64.80±5.435</td>
<td>71.95±11.31</td>
</tr>
</tbody>
</table>

**Table 2:** show the Gender wise distribution of patients

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Gender</th>
<th>control</th>
<th>PSX</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>12 (60%)</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>8 (40%)</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

**Table 3:** show the Comparison of corneal endothelial Characteristics, Corneal thickness and Intraocular pressure between control & PSX group

<table>
<thead>
<tr>
<th></th>
<th>Normal Mean±S.D</th>
<th>PSX Mean±S.D</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endothelial cell density (cells/mm²)</td>
<td>2511±171.3</td>
<td>2124±116.0</td>
<td>&lt;0.0001 ***</td>
</tr>
<tr>
<td>Cell size variation coefficient</td>
<td>32.23±2.686</td>
<td>39.05±3.0</td>
<td>&lt;0.0001 ***</td>
</tr>
<tr>
<td>Hexagonality (%)</td>
<td>59.30±2.227</td>
<td>46.70±6.45</td>
<td>&lt;0.0001 ***</td>
</tr>
<tr>
<td>Central Corneal Thickness (µm)</td>
<td>530.8±26.20</td>
<td>524.8±16.19</td>
<td>0.3892NS</td>
</tr>
</tbody>
</table>

**Discussion**

In our results showed the maximum no. of patients were 55-75 yrs in between groups and more were male but no significant difference in patients. Aravind H et al. found 3.8% subjects had pseudoexfoliation syndrome, prevalence raised with age but no sex predilection. According to Tarek A Shazly et al. found that incidence of pseudoexfoliation among 4.14% individuals aged 40 years or older in upper Egyptian.

PEX syndrome significantly effect in cell density of corneal endothelium of people with this disease. The cause of decrease endothelial cell density of patients with PEX syndrome is the pseudoexfoliation material, appearing at the earliest stages of PEX, which settles on the endothelium penetrating it in the direction of the Descemet's membrane and breaking the connections between individual six-sided cells, which results in local accelerated apoptosis of these cells. Other factors recognized by researchers, include hypoxia of the anterior chamber, changes in the fibroblasts of the endothelium, and elevated concentration of TGF-α1. 

In order to predetermine which patients possess an increased risk of corneal sublimation a simple index based on endothelial cell density has been performed during routine intraocular procedures. The value of 2000 cells/mm² has been orthodox as a reference line and patients whose endothelial cell density is lower than 2000 cells/mm² are considered to be high risk patients. Quiroga et al. also found that patients with PEX syndrome 21.3% corneas had endothelial cell density below 2000 cells/mm². 

A study done by Zimmermann N et al (2014) to showed a weak correlation between mean intraocular pressure and mean ECD. The analysis of the cell size variation of main study group was a significant part of the conducted study. The mean value of PSX group was (39.05±3.0) compared to normal group (32.23±2.686) were statistically significant (p<0.0001***). Supported
study with L. de Juan-Marcos et al.\textsuperscript{15} were found in CCT, cell size CV or hexagonality percentage between the group of patients with PXS and control group was statistically significant.

Another study done by Acar et al.\textsuperscript{16} presented a lower corneal thickness in patients with PEX syndrome (540.8 \pm 30.2 \mu m) in comparison with the control group (551.5 \pm 28.3 \mu m), but statistical in significance ($P= 0.315$) which were similar with our results.

The our results shows the intraocular pressure in psuedoexfoliation syndrome group (14.69\pm2.028) was statistically insignificant ($p=0.3517$NS) when compare to normal group. Naumann and Schlötzer-Schrehardt\textsuperscript{11} who found that the endothelial alterations observed in eyes with PEX, with moderate IOP increases or after cataract surgery.

**Conclusion**

This study confirms the existence of qualitative and quantitative modifications in endothelial cells of eyes with PEX, particularly when IOP is high. It could also indicate a possible independent biological role of CCT as a risk factor for the development of glaucoma in subjects with PXS.

**References**

1. Lindberg JG: Kliniska undersökningar over depigmenteringen av pupillarranden och genomlyssbarheten av iris vid fall av aldersstarr samt i normala ogon hos gamla personer. In *Clinical studies of depigmentation of the pupillary margin and transillumination of the iris in cases of senile cataract and also in normal eyes in the aged* [Thesis]. Helsinki, Finland: Helsinki University; 1917.


13. Quiroga L, Lansingh VC, Samudio M, Pena FY, Carter MJ. Characteristics of the corneal endothelium and

