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Evaluation of Corneal Endothelium by Specular Microscopy in Pseudoexfoliation Syndrome

Psödoeksfoliasyon Sendromunda Kornea Endotelinin Speküler Mikroskopi ile Değerlendirilmesi

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ÖZ

Amaç: Psödoeksfoliasyon sendromu (PES) olan hastaların kornea endotelini speküler mikroskopi (SM) ile değerlendirmektir.

Araçlar ve Yöntem: Bu prospektif kontrollü çalışmada, PES ve kontrol grubu olmak üzere iki grup oluşturuldu. Göz hastalıkları polikliniğinde yapılan yarık lamba biyomikroskopisiyle psödoeksfoliasyon materyali tespit edilerek tanı konulan 50 hastanın sağ gözü ve herhangi bir sağlık problemi olmayan 50 kontrol grubunun sağ gözü incelenmiştir.

Bulgular: Kontrol ve hasta grubunun cinsiyet ve yaş dağılımı açısından birbirinden farkı yoktu (p>0.005). İstatiksel olarak kornea kalınlığında, gruplar arasında fark bulunamadı (p=0.105). Ancak varyasyon katsayısı, kornea endotel hücre yoğunluğu ve heksagonal hücre oranında PES'li grupla PES olmayan grup arasında istatiksel olarak anlamlı düzeyde fark olduğu tespit edildi.

Sonuç: PES tespit edilen hastalarda kornea endotelinde ciddi morfolojik değişiklikler meydana gelmektedir. Kornea endotelinde meydana gelen bu değişimler nedeniyle, yapılan muayenesinde PES tespit edilen tüm hastaların, katarakt ameliyatı öncesinde speküler mikroskopi ile incelenmesi önerilmektedir.

Anahtar Kelimeler: kornea endoteli; psödoeksfoliasyon sendromu; speküler mikroskopi

ABSTRACT

Purpose: To evaluate the corneal endothelium of patients with pseudoexfoliation syndrome (PES) by specular microscopy (SM).

Materials and Methods: In this prospective controlled study, two groups were formed, namely the PES group and the control group. The right eyes of 50 patients were diagnosed with pseudoexfoliation material by slit lamp biomicroscopy performed in the ophthalmology outpatient clinic, and the right eyes of 50 patients in control group without any health problems were examined.

Results: There was no difference between the control and patient groups in terms of gender and age distribution (p>0.005). Statistically, no difference was found between the groups in corneal thickness (p=0.105). However, coefficient of variation, corneal endothelial cell density and hexagonal cell ratio were found to be statistically significant between the two groups.

Conclusion: Serious morphological changes occur in the corneal endothelium in patients with PES. Because of these changes in the corneal endothelium, it is recommended to perform specular microscopy measurement before cataract surgery of all patients who have PES detected in their examination.

Key Words: corneal endothelium; pseudoexfoliation syndrome; specular microscopy

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INTRODUCTION

Pseudoexfoliation syndrome (PES) is an age-related systemic disease characterized by progressive accumulation of extracellular fibrinous material in the eye and other organs.[1] These deposits are gray-white materials that can be seen with a slit lamp all over the anterior chamber, especially the lens capsule and pupillary rim.

The frequencies of transillumination defect due to iris depigmentation, secondary open-angle glaucoma, phacodonesis due to zonular weakness or lens subluxation are increased in PES.[2] Pseudoexfoliation is often associated with cataracts in advanced age. In cases with concomitant PES and cataracts, the risk of complications during surgery increases due to weak lens zones, insufficient pupillary dilatation, and increased capsule fragility.[3,4]

The transparency of the cornea is achieved by the active work of the endothelium. Corneal endothelium is a layer consisting of a single row of hexagonal cells with very limited regenerative capacity.[5] Quantitative, qualitative, and morphometric analyzes of corneal endothelial cells can be performed with specular microscopy (SM). Parameters such as corneal thickness (CT), coefficient of variation (CV), endothelial cell density (CD) and hexagonal cell ratio (HEX) can be evaluated with SM.[6] CD is 3500-4000 cells / mm^2 between the ages of 3-6 years and decreases annually by approximately 0.5% (6). The average endothelial cell density in healthy adults is 2500 cells/mm^2. When this value falls below 500 cells/mm^2, corneal edema and decompensation may occur.[7]

CV is calculated by dividing the standard deviation of the cell area by the mean cell area. The average CV value in young people is 0.27 (between 0.22 and 0.31).[6] Polymegatism is a measure of variation in individual cell area, and pleomorphism is a measure of variation in cell shape. Understanding endothelial cell loss becomes more meaningful when evaluated together with pleomorphism and polymegatism values. Sixty percent of a healthy corneal endothelium should be hexagonal. The hexagonal cell count of below 50% and the coefficient of variation of over 0.40 indicate an abnormality in the endothelial cell layer. The risk of corneal edema after intraocular surgery is very high in these patients.[8]

In this study, our aim is to compare the corneal endothelial status of PES patients with the control group using a specular microscopy device (Specular Microscope CEM-530, NIDEK).

MATERIALS and METHODS

This study was conducted in the ophthalmology clinic of our hospital between March 2019 and February 2020. Yozgat Bozok University ethics committee approved the study (2017-KAEK-189-2019.02.28-22) and we received informed consent from all participants. The Helsinki Declaration Principles were adhered to throughout the study. Fifty patients with PES and 50 healthy age- and gender-matched individuals were included in the study.

A complete and detailed ophthalmologic evaluation including best-corrected visual acuity, intraocular pressure (IOP) measurement, slit-lamp biomicroscopy and fundoscopy were performed in all participants. The diagnosis of PES was made based on the detection of pseudoexfoliation material with slit lamp biomicroscopy. The right eyes of all participants were scanned with SM (Specular Microscope CEM-530, NIDEK). CT, HEX, CD and CV were determined from the SM images.

Patients with glaucoma, hypertensive or diabetic retinopathy, epiretinal membrane, corneal opacity, high hypermetropia or myopia (>6D), corneal disease, history of ocular surgery and trauma. Also, patients using contact lenses were excluded from the study.

We performed statistical analysis using the SPSS® 22.0 (Statistical Package for Social Sciences, IBM Inc., Chicago, IL, USA) package program. The chi-Square test was used to compare categorical variables. Shapiro-Wilk test was used to evaluate the distribution of normality. Descriptive statistics were made. We used Mann Whitney-U test for the comparison of non-normally distributed data and Student t-test for binary comparison of normally distributed data. Statistically, a p-value of less than 0.05 was considered as significant.

RESULTS

In our study, the right eyes of 50 patients who were diagnosed with PES based on the pseudoexfoliation material detected by slit lamp biomicroscopy performed in the ophthalmology outpatient clinic and right eyes of 50 controls that did not have any health problems were evaluated. The average age in the patient group was 68.32, and 69.22 in the control group. There was no significant difference between these two groups in terms of age, gender, and intraocular pressure (p>0.05). The sociodemographic characteristics of the patients are shown in Table 1.

Table 1. Sociodemographic results of groups.

Variables	PES Group (n=50)	Control Group (n=50)	p value
Age	68.32±8.28	69.22±8.02	0.582
Sex (Female/Male)	24/26	23/27	0.316
IOP (mmhg)	12.22±3.07	11.74±1.80	0.344

PES: Pseudoexfoliation syndrome; IOP: Intraocular pressure.
Continuous data are presented as mean ± standard deviation.

SM scans did not reveal any difference between the two groups in terms of CT (p=0.105). However, there was a statistically significant decrease in corneal endothelial cell density and ratio of hexagonal cells in the PES group compared to the control group (p=0.005, p=0.008, respectively). Moreover, a significant difference was found between the two groups in terms of coefficient of variation (p=0.014). The SM data of the patients are shown in Table 2.

Table 2. Specular microscopy findings of the patients.

Variables	PES Group (n=50)	Control Group (n=50)	p value
CD	2335.46±313.43	2494.24±233.96	0.005
CV	34.04±4.73	31.82±4.10	0.014
HEX	63.42±4.68	65.88±4.33	0.008
CT	529.42±34.31	540.94±36.10	0.105

PES: Pseudoexfoliation syndrome; CT: Corneal thickness (µ); CD:The cell density in the corneal endothelium (cell/mm2); CV:Coefficient of variation (the cell area standard deviation/mean cell area µm2); HEX: percentage of hexagonal cells(%).
Continuous data are presented as mean±standard deviation.

DISCUSSION

In our study, we found a statistically significant decrease in corneal endothelial cell density, and hexagonality, and increase in the coefficient of variation in SM measurements in patients with PES compared to the control group. Also, there was no significant difference in corneal thickness between the two groups.

There is no consensus on the level of corneal thickness in patients with PES. Although Miyake et al. and Özcura et al. reported that there was an increase in CT in patients with PES[9,10], Zheng et al. reported no such difference.[11] Tomaszewski et al. reported that although they found a difference in CT between pseudoexfoliative glaucoma patients and the control group, they could not find a difference between control group and PES patients.[12] Similarly, in our study, no significant difference was found between the two groups in CT.

Theabald et al. found that corneal endothelial cells take up pseudoexfoliative material by phagocytosis.[13] Knorr et al. reported that corneal endothelial cell damage, cell spillage, intraendothelial inclusions and retroendothelial accumulations were more common in patients with PES.[14] In the electron microscopy study of the corneal endothelial cells conducted by Schlötzer-Schrehardt et al., they found an increase in the number of cells spilled into the anterior chamber and the amount of phagocyted melanin granules, hypertrophy in the secretory organelles, and decrease in cytoplasmic density, loss of polarity, loss of cell hexagonality, and adhesion to the Descemet's membrane in the early stages of PES.[15]

Tomaszewski et al. found that there was a significant decrease in the number of CD in the PES group compared to the control group.[12] Similarly, in our study, a significant difference was found between the PES group and the control group in terms of the number of CD in addition to the CV and HEX. The reason for lower CD in patients with PES might be due to the penetration of pseudoexfoliation material, which occurs in the earliest stages, into the endothelium and Descemet's membrane and acceleration of the local apoptosis of hexagonal cells due to breakage of the connection between these cells. In addition, pseudoexfoliation material increases anterior chamber

hypoxia, alters fibroblasts in the endothelium, and increases TGF-α1 concentration, all of which also impact endothelial cell loss.[16,17]

In Bozkurt et al.'s study, a statistically significant decrease was found in CD patients with PES compared to the control group, similar to our results. Unlike our findings, they found no difference in terms of polymegatism and pleomorphism.[18] In the study of Juan-Marcos et al., in parallel with our study, a decrease in CD and HEX and an increase in CV was found in patients with PES, and no difference was found in CT.[19] In Inoue et al.'s study, while a decrease in CD and CT was found in patients with PES, no difference was found in HEX and CV.[20] Also, in Wang et al.'s study, similar to this study, a decrease in CD was observed in patients with PES, but no difference was found in HEX, CV and CT.[21]

Events affecting the corneal endothelium, together with cell density, also affect the morphological pattern of the endothelium. For this reason, pleomorphism and polymegatism in endothelial cells can be used as a more specific indicator. Based on our study as well as previous studies, we believe that because of these changes in the corneal endothelium, it is recommended to perform specular microscopy measurement before cataract surgery in all patients with PES detected during examination.

In some studies, it has been reported that fibrinous reaction and inflammation occur more frequently after cataract operation in patients with PES.[22,23] In patients with PES, this situation may occur as a result of long-term effect of deterioration of the blood-aqueous barrier and creates a higher susceptibility to corneal decompensation in the later period.[24]

Patients with PES have a higher risk of complications during cataract surgery due to zonal weakness[25], weak mydriasis[26], impaired blood-aqueous barrier[27], and pigment dispersion.[28] Due to the negative effects of PES, operations of these patients should be performed by experienced surgeons, and the patients should be followed very carefully before, during, and after the operation.

Since PES makes surgery difficult and increases the risk of complications in cataract surgeries, we recommend specular microscopy to be routinely performed in patients with PES before cataract surgery. We anticipate that patients with endothelial weakness in specular microscopy should be operated by an experienced surgeon, especially.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Author Contribution Rate

Concept/Design: MSS. Data Collection and/or Processing: MSS, SAB, HAB. Data analysis and interpretation: MSS, SAB, HAB. Literature Search: MSS, SAB, HAB. Drafting manuscript: MSS. Critical revision of manuscript HAB. Supervision: SAB.

REFERENCES

1. Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. Surv. Ophthalmol. 2001;45(4):265-315.
2. Conway RM, Schlötzer-Schrehardt U, Küchle M, Naumann GO. Pseudoexfoliation syndrome: pathological manifestations of relevance to intraocular surgery. Clin. Exp. Ophthalmol. 2004;32(2):199-210.
3. Scorolli L, Campos EC, Bassein L, Meduri RA. Pseudoexfoliation syndrome: a cohort study on intraoperative complications in cataract surgery. Ophthalmologica. 1998;212(4):278-280.
4. Streho M, Rohart C, Guigui B, Fajnkuchen F, Chaine G. pseudo-exfoliation syndrome in cataract surgery retrospective study of 37 cases. Investig. Ophthalmol. Vis. Sci. 2008;49(13):386-386.
5. Wirbelauer C, Anders N, Pham DT, Wollensak J. Corneal endothelial cell changes in pseudoexfoliation syndrome after cataract surgery. Arch. Ophthalmol. 1998;116(2):145-149.
6. Yee RW, Matsuda M, Schultz RO, Edelhauser HF. Changes in the normal corneal endothelial cellular pattern as a function of age. Curr. eye res. 1985;4(6):671-678.
7. Bourne RR, Minassian DC, Dart JK, Rosen P, Kaushal S, Wingate N. Effect of cataract surgery on the corneal endothelium: modern phacoemulsification compared with extracapsular cataract surgery. Ophthalmology. 2004;111(4):679-685.
8. Benetz, BA, Yee R, Bidros M, Lass, J. Specular microscopy. Krachmer JH, Mannis MJ, Holland EJ, eds. Cornea: Fundamentals, Diagnosis and Management. 3.ed. China: Mosby, Inc; 2010;3:177-203.
9. Miyake K, Matsuda M, Inaba M. Corneal endothelial changes in pseudoexfoliation syndrome. Am. J. Ophthalmol. 1989;108(1):49-52.
10. Özcura F, Aydin S, Dayanir V. Central corneal thickness and corneal curvature in pseudoexfoliation syndrome with and without glaucoma. J. Glaucoma. 2011;20(7):410-413.
11. Zheng X, Shiraishi A, Okuma S, et al. In vivo confocal microscopic evidence of keratopathy in patients with pseudoexfoliation syndrome. Investig. Ophthalmol. Vis. Sci. 2011;52(3):1755-1761.

12. Tomaszewski BT, Zalewska R, Mariak Z. Evaluation of the endothelial cell density and the central corneal thickness in pseudoexfoliation syndrome and pseudoexfoliation glaucoma. J. Ophthalmol. 2014;2014:123683.
13. Dvorak-Theobald G. Pseudo-exfoliation of the lens capsule: relation to true exfoliation of the lens capsule as reported in the literature and role in the production of glaucoma capsulocuticulare. Am J. Ophthalmol. 1954;37(1):1-12.
14. Knorr HJ, Jünemann A, Händel A, Naumann GH. Morphometrische und qualitative Veränderungen des Hornhautendothels bei Pseudoexfoliationssyndrom. Fortschr Ophthalmol. 1991;88(6):786-789.
15. Schlötzer-Schrehardt UM, Dörfler S, Naumann GO. Corneal endothelial involvement in pseudoexfoliation syndrome. Arch. Ophthalmol. 1993;111(5):666-674.
16. Schlötzer-Schrehardt U, Naumann GO. Ocular and systemic pseudoexfoliation syndrome. Am. j. Ophthalmol. 2006;141(5):921-937.
17. Naumann GO, Schlötzer-Schrehardt U, Küchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist: intraocular and systemic manifestations. Ophthalmology. 1998;105(6):951-968.
18. Bozkurt B, Güzel H, Kamış Ü, Gedik Ş, Okudan S. Psödoeksfoliasyon Sendromlu ve Senil Kataraktlı Gözlerin Ön Segment Biyometri ve Kornea Endotel Özellikleri. Turk J Ophthalmol. 2015;45(5):188-192.
19. De Juan-Marcos L, Cabrillo-Estévez L, Escudero-Domínguez FA, Sánchez-Jara A, Hernández-Galilea E. Morphometric changes of corneal endothelial cells in pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Arch Soc Esp Oftalmol. 2013;88(11):439-444.
20. Inoue K, Okugawa K, Oshika T, Amano S. Morphological study of corneal endothelium and corneal thickness in pseudoexfoliation syndrome. Jpn. J. Ophthalmol. 2003;47(3):235-239.
21. Wang M, Sun W, Ying L, Dong XG. Corneal endothelial cell density and morphology in Chinese patients with pseudoexfoliation syndrome. Int. J. Ophthalmol. 2012;5(2):186-189.
22. Wålinder PEK, Olivius EO, Nordell SI, Thorburn WE. Fibrinoid reaction after extracapsular cataract extraction and relationship to exfoliation syndrome. J Cataract Refract Surg. 1989;15(5):526-530.
23. Zetterström C, Olivestedt G, Lundvall A. Exfoliation syndrome and extracapsular cataract extraction with implantation of posterior chamber lens. Acta Ophthalmol. 1992;70(1):85-90.
24. Bourne WM, Nelson LR, Hodge DO. Continued endothelial cell loss ten years after lens implantation. Ophthalmology. 1994;101(6):1014-1023.
25. Skuta GL, Parrish RK, Hodapp E, Forster RK, Rockwood EJ. Zonular dialysis during extracapsular cataract extraction in pseudoexfoliation syndrome. Arch. Ophthalmol. 1987;105(5):632-634.
26. Carpel EF. Pupillary dilation in eyes with pseudoexfoliation syndrome. Am. J. Ophthalmol. 1988;105(6):692-694.
27. Brooks AMV, Gillies WE. Fluorescein angiography and fluorophotometry of the iris inpseudoexfoliation of the lens capsule. Br. J. Ophthalmol. 1983;67(4):249-254.
28. Guzek JP, Holm M, Cotter JB, et al. Risk factors for intraoperative complications in 1000 extracapsular cataract cases. Ophthalmology. 1987;94(5):461-466.