In Vivo Confocal Microscopic Evaluation of Corneal Endothelium and Keratocytes in Patients with Pigment Dispersion Syndrome

Pigment Dispersiyon Sendromunda Kornea Endoteli ve Keratositlerin İn Vivo Konfokal Mikroskobik Değerlendirilmesi

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ABSTRACT

Purpose: To evaluate the presence of endothelial cell and keratocyte loss in pigment dispersion syndrome (PDS).

Materials and Methods: The corneas of 20 subjects with pigment dispersion syndrome were evaluated with in vivo confocal microscopy (Confoscan 3.0). Twenty corneas of healthy subjects without a history of ocular disease served as controls. For each subject, the keratocyte density in the anterior, middle and posterior stroma together with the endothelial cell density (ECD), endothelial cell polymegethism and polymorphism was determined in best-focused two images.

Results: The mean age of 20 patients (10 males, 10 females) with PDS (46.0±14.1 years [range=22-68 years]) was not significantly different than that of 20 healthy control subjects (10 males, 10 females) (45.9±14.2 years [range=21-72 years]) (p=0.98). Endothelial cell density was determined as 2765±362 cell/mm2 in the study group, 2888±320 cell/mm2 in the control group (p=0.263). There were also no significant differences in endothelial cell polymorphism (49.8±12.2, 49.2±13.1; p=0.883) and polymegethism (38.5±6.5, 40.5±8.7; p=0.432). Keratocyte density measured in all sections was similar in two groups (p>0.05). None of the keratocyte and endothelial cell parameters were significantly different between female and male subjects with PDS (p>0.05). Pigment deposition was limited to the corneal endothelium in all cases.

Conclusion: Endothelial cell or keratocyte loss or damage secondary to pigment deposition is not present in the corneas of patients with pigment dispersion syndrome as evaluated with in vivo confocal microscopy.

Key Words: Pigment dispersion syndrome, endothelium, confocal microscopy.

ÖZ

Amaç: Pigment dispersiyon sendromunda (PDS) endotel hücre ve keratosit kaybı varlığını değerlendirmek.

Gereç ve Yöntem: Pigment dispersiyon sendromlu 20 olgunun korneası in vivo konfokal mikroskopi (Confoscan 3.0) ile değerlendirildi. Oküler hastalık öyküsü olmayan sağlıklı kişilere ait 20 kornea kontrol grubu olarak kullanıldı. Her olgu için, ön, orta ve arka stroma keratosit yoğunluğu ile birlikte endotel hücre yoğunluğu, endotel hücre polimegetizmi ve polimorfizmi, en iyi odaklanmış iki görüntüde değerlendirildi. Bulgular: Pigment dispersiyon sendromu olan 20 olgunun (10 erkek, 10 kadın) yaş ortalaması [46.0±14.1 yıl (aralık=22-68 yıl)], 20 sağlıklı kontrol grubuna (10 erkek, 10 kadın), [45.9±14.2 yıl (aralık=21-72 yıl)] göre anlamlı olarak farklı değildi (p=0.98). Endotel hücre yoğunluğu çalışma grubunda 2765±362 hücre/mm2, kontrol grubunda 2888±320 hücre/mm2 olarak belirlendi (p=0.263). Endotel morfolojisini gösteren polimorfizm (49.8±12.2, 49.2±13.1; p=0.883) ve polimegetizm (38.5±6.5, 40.5±8.7; p=0.432) parametrelerinde de anlamlı fark saptanmadı. İki grubun tüm kornea kesitlerinde ölçülen keratosit yoğunlukları benzerlik göstermekteydi (p>0.05). Pigment dispersiyon sendromlu kadın ve erkek olgular arasında keratosit ve endotel hücre parametreleri açısından anlamlı fark yoktu (p>0.05). Pigment birikimi tüm olgularda kornea endoteli ile sınırlıydı.

Sonuç: İn vivo konfokal mikroskopi ile değerlendirildiğinde, pigment dispersiyon sendromlu olguların kornealarında pigment birikimine sekonder endotel hücre ve keratosit kaybı veya hasarı mevcut değildir.

Anahtar Kelimeler: Pigment dispersiyon sendromu, endotel, konfokal mikroskopi.

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Geliş Tarihi - Received: 13.10.2014
Kabul Tarihi - Accepted: 04.12.2014
Glo-Kat 2015;10:196-198

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INTRODUCTION

Pigment dispersion syndrome (PDS) is a relatively common disorder affecting predominantly myopic young individuals and is characterized by pigment liberation from the iris pigment epithelium and its deposition throughout the anterior segment structures such as trabeculum, lens capsule and corneal endothelium.[1] Pigment accumulation on the endothelium manifests as diffuse pigment deposition or in the form of a vertical spindle referred to as Krukenberg spindle.[1] Corneal pigment deposition is a highly characteristic, almost pathognomonic feature of PDS. To date, few studies have studied the effect of pigment deposition on corneal endothelium employing specular microscopy.[2,3] The purpose of the current study was to investigate whether pigment dispersion is associated with quantitative, or qualitative alterations of the endothelial cell layer and keratocytes as evaluated by in vivo confocal microscopy (IVCM).

MATERIAL AND METHODS

The corneal endothelium of 20 consecutive subjects with PDS was comprehensively evaluated with slit-lamp biomicroscopy and IVCM. Twenty corneas of 20 patients with IOP levels <21 mm Hg on repeated testing, normal optic disk appearance and normal visual fields were included as controls. The diagnosis of PDS was made when typical iris transillumination defects were accompanied by pigment aggregation upon the corneal endothelium, dense trabecular pigmentation and an intraocular pressure level of <21 mm Hg on at least two visits in the morning hours (10:00 am). Patients who had an IOP level of >21 mm Hg, glaucomatous optic neuropathy, visual field loss as well as those who received ocular hypotensive medical therapy were excluded from the study. In vivo confocal microscopy was performed using Confoscan 3.0 (Vigonza, Italy) attached to an immersion lens (Achroplan 40x/0.75W, Zeiss, Germany) as previously described in detail elsewhere.[4] The images were evaluated by a single observer who was masked to the patients' identities and disease status. For each subject, the keratocyte density in the anterior, middle and posterior stroma together with the endothelial cell density (ECD), endothelial cell polymegethism and polymorphism was determined in best-focused two images. Parametric test assumptions were controlled before the comparisons. Independent samples t test was used for statistical comparisons [SPSS ver. 12.5 (Chicago, IL)]. Informed consent was obtained from all patients enrolled in this study and approval was obtained from our University Institutional Review Board.

RESULTS

The mean age of the 20 PDS study patients (10 males, 10 females) was 46.0±14.1 years (22-68 years) which was not statistically different from the mean age [45.9±14.2 years (21-72 years)] of the 20 healthy controls (10 males, 10 females); (p=0.98). No difference could be detected between the keratocyte and endothelial cell parameters of the two study groups (Table 1). Furthermore, none of the keratocyte and endothelial cell parameters was significantly different between female and male subjects with PDS (Table 2). Pigment deposition was limited to the corneal endothelium in all cases.

Table 1: *Comparison of endothelial cell parameters between cases with pigment dispersion syndrome and healthy controls.*

Parameter	PDS	Normal	p
Anterior stromal keratocyte density (cells/mm²)	1093±227	1073±207	0.881
Midstromal keratocyte density (cells/mm²)	809±89	822±81	0.641
Posterior stromal keratocyte density (cells/mm²)	781±112	755±110	0.453
EC density (cells/mm²)	2765±362	2888±320	0.263
EC polymegethism (%)	38.5±6.5	40.5±8.7	0.432
EC polymorphism (%)	49.8±12.2	49.2±13.1	0.883

EC; Endothelial Cell, PDS; Pigment Dispersion Syndrome.

Table 2: *Comparison of endothelial cell parameters between cases with pigment dispersion syndrome and healthy controls.*

Parameter	Male subjects with PDS (n=10)	Female subjects with PDS (n=10)	p
Age (years)	45.8±15.4	46.1±13.5	0.248
Anterior stromal keratocyte density (cells/mm²)	1050±195	1136±259	0.409
Midstromal keratocyte density (cells/mm²)	809±99	809±83	1.000
Posterior stromal keratocyte density (cells/mm²)	791±112	771±116	0.697
EC density (cells/mm²)	2834±378	2695±351	0.404
EC polymegethism (%)	39.8±5.9	37.3±7.1	0.403
EC polymorphism (%)	53.8±11.9	45.7±11.7	0.145

EC; Endothelial Cell, PDS; Pigment Dispersion Syndrome.

Pigment deposition on the corneal endothelium appeared as multiple, highly reflective tiny dots with IVCM (Figure). Pigments were either visualized as scattered individual dots or as pigment clumps. Pigments were observed both in the center and the peripheral endothelium.

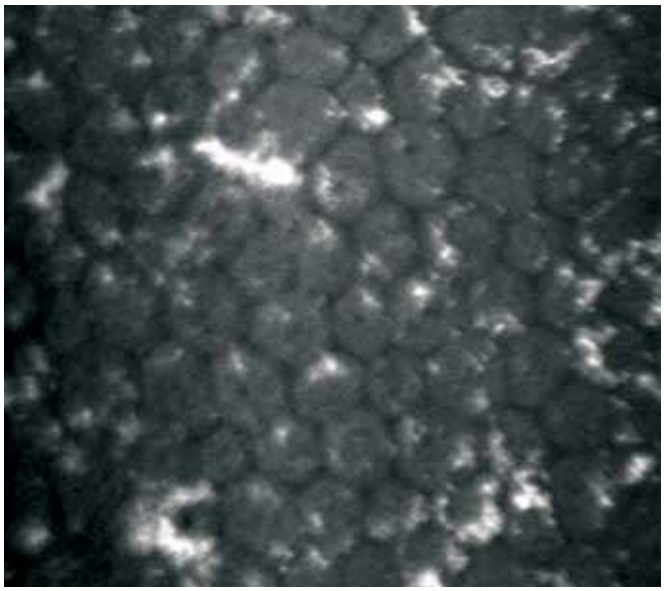

Figure: *Pigment deposition on the corneal endothelial layer of a patient with pigment dispersion syndrome.*

DISCUSSION

Pigment liberation into the anterior chamber induced by posterior bowing of the peripheral iris and consequently irido-zonular friction in PDS is associated with pigmentary glaucoma (PG), a common and progressive form of secondary glaucoma.[1-5] Gradual pigment accumulation is associated with sustained and irreversible endothelial trabecular damage in these cases, as demonstrated in ultrastructural studies.[6] In addition, several anterior segment structures including the corneal endothelium are the sites for pigment aggregation in PDS. In two previously published studies, where specular microscopy was utilized, the endothelial cell densities of patients with PDS were found to be similar to those of control subjects.[2,3] Lehto et al.,[3] reported increased endothelial cell pleomorphism and polymegethism specifically in patients with PDS and PG. However, to the best of our knowledge, alterations of keratocyte cell densities have not been investigated in eyes with PDS in previously published studies. The results of our study which employed IVCM confirm that the corneal endothelial cell layer is not adversely affected in eyes with pigment dispersion as pointed out in prior studies[2,3] Moreover, this investigation revealed that keratocyte densities are not decreased in normotensive PDS patients. Keratocyte densities were evaluated in this study to detect any adverse effect of pigment deposition on the posterior corneal layers; a previous study by Zheng et al.,[7] reported reduction of keratocyte densities in association with accumulation of exfoliation material in the corneal stromas of patients with exfoliation syndrome. There was no gender related differences for the keratocyte or the endothelial cell parameters in our group of subjects with PDS. In the past male gender has been associated with more extensive pigment liberation due to the presence of deeper anterior chambers and a more pronounced reverse pupillary block.[8]

Elevated intraocular pressure and glaucoma medication is known to adversely influence corneal cell counts and thus patients with pigmentary glaucoma were not included in this study.[9]

Assessing endothelial function is important from both a clinical and surgical standpoint. Endothelial cell density and morphology are the two key indicators of endothelial function, which in turn determines the level of corneal deturgescence.[10,11] Endothelium is known to be adversely affected by sources of stress which include metabolic (hypoxia, hyperglycemia), toxic (topical medication including preservatives) and mechanical (surgical or traumatic) factors.[11] Our findings suggest that pigment deposition is not associated with endothelial cell or keratocyte loss or damage in the corneas of patients with PDS. Although we compared the endothelial and keratocyte cell densities of patients with PDS and healthy control eyes in a cross-sectional study, our study did not investigate the temporal relationship of pigment deposition on the change of corneal cell densities in patients with PDS. In the future, a prospective study with a long follow-up will clarify the long-term effect of pigment deposition on the corneal endothelium.

REFERENCES/KAYNAKLAR

1. Ritch R. A unification hypothesis of pigment dispersion syndrome. Trans Am Ophthalmol Soc 1996;94:381-405.
2. Murrell WJ, Shihab Z, Lamberts DW, et al. The corneal endothelium and central corneal thickness in pigmentary dispersion syndrome. Arch Ophthalmol 1986;104:845-6.
3. Lehto I, Ruusuvaara P, Setälä K. Corneal endothelium in pigmentary glaucoma and pigment dispersion syndrome. Acta Ophthalmol (Copenh) 1990;68:703-9.
4. Mocan MC, Durukan I, Irkec M, et al. Morphologic alterations of both the stromal and subbasal nerves in the corneas of patients with diabetes. Cornea 2006;25:769-73.
5. Niyadurupola N, Broadway DC. Pigment dispersion syndrome and pigmentary glaucoma--a major review. Clin Experiment Ophthalmol 2008;36:868-82.
6. Richardson TM, Hutchinson BT, Grant WM. The outflow tract in pigmentary glaucoma: a light and electron microscopic study. Arch Ophthalmol 1977;95:1015-25.
7. Zheng X1, Shiraishi A, Okuma S, et al. In vivo confocal microscopic evidence of keratopathy in patients with pseudoexfoliation syndrome. Invest Ophthalmol Vis Sci 2011;52:1755-61.
8. Orgul S, Hendrickson P, Flammer J. Anterior chamber depth and pigment dispersion syndrome. Am J Ophthalmol 1994;117:575-7.
9. Gagnon MM1, Boisjoly HM, Brunette I, et al. Corneal endothelial cell density in glaucoma. Cornea 1997;16:314-8.
10. Joyce NC. Proliferative capacity of the corneal endothelium. Prog Retin Eye Res 2003;22:359-89.
11. Farjo AA, McDermott ML, Soong HZ. Corneal anatomy and wound healing. In: Yanoff M, Duker JS, eds. Ophthalmology. 3rd ed. China: Mosby. 2009. pp:203-8.