Research Article (Araştırma Makalesi)

Evaluation of Corneal Changes in Uveitic Patients by Non-Contact Specular Microscopy: A Retrospective Study

Üveitik Hastalarda Korneal Değişikliklerin Non-Kontakt Speküler Mikroskopi ile Değerlendirilmesi: Retrospektif Çalışma

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Özet

Amaç: Üveitik gözler ile sağlıklı gözler arasında speküler mikrokopideki değişimlerin gösterilmesi.

Gereç ve Yöntemler: Retrospektif çalışmaya 2015-2018 yıllarında Selçuk Üniversitesinde takip edilen 66 hasta alındı. Tüm hastaların sağ gözleri değerlendirildi. Kontrol grubu olarak normal göz muayene bulgularına sahip 37 bireyin sağ göz verileri kullanıldı. Hastalar, anterior, intermedyer ve posterior üveit olarak subgruplara ayrıldı. Speküler mikrokopi ölçümleri Confo Scan 4 ile yapıldı. Endotel hücre yoğunluğu (EHY), pleomorfizm (%), polimegatizm (%), santral kornea kalınlığı (SKK) ve intraoküler basınç yönünden (GİB) gruplar karşılaştırıldı. İstatistiksel analizde p değerinin 0.05'den küçük olması anlamlı kabul edildi.

Bulgular: Yaş ortalaması üveitlerde 33.71±15.29, kontrol grubunda ise 37.78±13.17 olarak saptandı (p=0.432). EHY, pleomorfizm ve polimegatizm açısından gruplar arasında anlamlı fark tespit edildi (tüm gruplar; p<0.01). SKK ve GİB açısından ise anlamlı bir fark bulunamadı (sırası ile; p=0.812, p=0.381). Alt grup analizinde EHY açısından ön üveit ile intermediyer ve posterior üveit grubu arasında anlamlı fark tespit edildi (sırası ile; p=0.020, p=0.018). Ancak intermediyer üveiti olan grup ile posterior üveti olan grup arasında anlamlı bir farklılık tespit edilemedi (p=0.999). Monoküler üveiti olan hastaların sağlam gözleri ile karşılaştırmalarında ise tüm değişkenlerde fark vardı (tüm gruplar; p<0.01).

Sonuç: Üveit hastalarında EHY'nun azalmakta, pleomofizm ve polimegatizmin artmaktadır. Bu sonuç, üveit hastalarında erken tedavi ile sekel oluşumunun önüne geçilmesinin önemini gösterdi. İntraoküler cerrahi planlanan üveitik hastalarda speküler veya konfokal mikroskopi taraması önem arz etmektedir.

Anahtar kelimeler: Endotel hücre yoğunluğu, Pleomorfizm, Polimegatizm, Speküler mikroskopi, Üveit

Abstract

Objective: To demonstrate the changes in specular microscopy between uveitic eyes and healthy eyes.

Material and Methods: A retrospective study included 66 patients followed in the Uvea clinic of Selcuk University between 2015-2018. The right eyes of all patients were evaluated. The right eye data of 37 healthy individuals were used as the control group. The patients were divided into subgroups anterior, intermediate, and posterior uveitis. Specular microscopy measurements were made with Confo Scan 4. Comparisons were made between the groups in terms of endothelial cell density (ECD), pleomorphism (%), polymegatism (%), central corneal thickness (CCT), and intraocular pressure (IOP). A p-value less than 0.05 was considered significant.

Results: The mean age was 33.71±15.29 in the uveitis and 37.78±13.17 in the control group (p=0.432). There was a significant difference between the groups in terms of ECD, pleomorphism and polymegatism (all groups; p<0.01). No significant difference was found in terms of CCT and IOP (respectively; p=0.812, p=0.381). In the subgroup analysis, a significant difference was found between anterior, intermediate and posterior uveitis groups in terms of ECD (respectively; p=0.020, p=0.018). However, no significant difference in other groups (p=0.999). In comparison with healthy eyes of patients with monocular uveitis were significant differences in all parameters (all groups; p<0.01).

Conclusion: It is seen that ECD decreases, pleomorphism and polymegatism increase in patients with uveitis. This result showed the importance of preventing sequelae with early treatment in patients with uveitis. Speccular or confocal microscopy scanning is important in uveitic patients scheduled for intraocular surgery.

Keywords: Endothelial cell density, Pleomorphism, Polymegatism, Specular microscopy, Uveitis

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INTRODUCTION

Uveitis is a condition that produces intraocular inflammation and has one or more etiological causes. If not adequately diagnosed and treated, it can cause substantial visual loss and is a major contributor to ocular morbidity and blindness globally (1). The International Uveitis Working Group (IUSG) has defined the current uveitis classification as an anatomical categorization (2,3). The idea that the first zone where inflammation develops is involved forms the basis for this classification. Anterior uveitis is defined as the involvement of the iris and ciliary body; intermediate uveitis is defined as the involvement of the peripheral chorioretinal tissue; posterior uveitis is defined as the involvement of the choroidal and retinal tissues; and panuveitis is defined as the involvement of all affected systems. The type of uveitis is unaffected by complications related to it.

For instance, macular edema complicating anterior uveitis that is HLA-B27 positive is referred to as anterior uveitis (3). Additionally, uveitis can be categorized based on how long the inflammation lasts: acute uveitis is defined as having a duration of fewer than 3 months, recurrent uveitis is defined as having multiple recurrences without treatment within 3 months, and chronic uveitis is defined as having a duration of more than 3 months (4).

An essential metabolic function of the corneal endothelium is to maintain and provide transparency of the cornea (5). Hexagonal cells, which have a restricted capacity for regeneration, make up endothelial cells. In specular microscopy, endothelial cell density (ECD), pleomorphism (cell shape change), and polymegatism (cell size variability) are indicators of a healthy corneal endothelium (6).

Inflammatory mediators that are generated by uveitis in the anterior chamber can interfere with the corneal endothelium's regular operation. The corneal endothelium may develop an accumulation of keratitis precipitates (KP) (7). During the progression of uveitis, structural anomalies might be identified in the corneal endothelium (8). Endothelial integrity may be harmed by these inflammatory alterations. It may be particularly severe to impair the endothelial cells' ability to endure surgical intervention (9).

In this study, we used non-contact specular microscopy to compare the endothelium's responses to inflammatory mediators brought on by uveitis with those of healthy persons in terms of function and shape.

MATERIAL AND METHODS

A retrospective design was used for creating this study. The study comprised patient records who were registered in the Selcuk University Medical Faculty Ophthalmology Uveitis Unit between January 2015 and February 2018.

The information of patients who underwent corneal specular microscopy due to anterior segment involvement and were diagnosed with uveitis during or after admission was assessed. The exclusion criteria for the study included eyes that underwent intraocular surgery, had a history of ocular trauma, any corneal illness, were contact lens wearers, smokers, had diabetes, or whose corneal specular microscopy assessment could not be performed under optimal circumstances. Patients with active panuveitis were not included.

The study comprised 103 people, including 66 uveitis sufferers (56 with unilateral and 10 with bilateral uveitis), as well as 37 control cases. The study included participants in the control group and those with bilateral uveitis in their right eyes. Additionally, individuals' healthy eyes and those with unilateral uveitic involvement were compared. The files scanned as part of the study included information on patients' age, gender, and other demographics as well as measurements of their central corneal thickness (CCT), intraocular pressure (IOP), best corrected visual acuity (BCVA), and endothelial cell characteristics.

The same skilled technician performed the measurements using confocal microscopy (ConfoScan 4.0, Nidek Co Ltd, Osaka, Japan). The patients were requested to fix their attention on the internal fixation light while they were properly positioned for the measurement. Then, without contacting the cornea, the target (20x) was brought closer to the examining eye. After the corneal endothelial cells were found, a scanner automatically captured them. The photographs were shown on the scanner monitor while it was scanning. On the computer, pictures of the various corneal levels were captured. An internal calibration for magnification is included in ConfoScan 4's endothelium analysis tool, which uses patented image processing techniques to recognize polygonal cell representations. These photos were used to automatically calculate ECD, pleomorphism, and polymegatism.

Statistical analysis

All information was encoded before being moved to a digital setting. The Windows package application SPSS, Inc., Chicago, IL, USA) Statistical Package for the Social Sciences version 23.0 was used for statistical analysis. The Kolmogorov-Smirnov test was used to determine whether the data had a normal distribution. Data were discovered that supported the normal distribution. ANOVA and the independent T-test were used to compare the data. Between subgroups, post hoc analysis was done for significant parameters. Statistics were considered significant for P values under 0.05.

The study is approved by the Selçuk University Clinic Research local ethics committee (date: 18.04.2018; decision number: 2018/147). During the study, the Declaration of Helsinki's principles were observed.

RESULTS

A hundred and three individuals, including 66 uveitis patients (Group 1) and 37 control cases (Group 2), were included in the study. In Group 1, 40 (60.6%) of the patients were male and 26 (39.4%) were female. 20 (54.1%) of Group 2 were male and 17 (45.9%) were female. There was no significant difference in gender distribution between the groups (p=0.520). The mean age was 33.71 ± 15.29 years in Group 1 and 37.78 ± 13.17 years in Group 2. There was no statistically significant difference between the groups. (p=0.432). ECD values of Group 1 was 2345±302/mm2, pleomorphism was % 45.52±7.31, polymegatism was % 54.24±8.71, CCT was 526±29 µn, IOP was 14.25±3.07 mmHg. In Group 2, ECD was 2604± 137/mm^2, pleomorphism was % 38.57±7.13, polymegatism was % 48.45±7.75, CCT was 524±30 µn, IOP was 13.70±3.06 mmHg. While a statistically significant difference was found between the groups in terms of cell number, pleomorphism and polymegatism (all groups; p<0.01, p<0.01, p<0.01), no significant difference was found for CCT and IOP. (p=0.812, p=0.381, respectively) (**Table 1**).

Nineteen of the patients in group 1 had anterior uveitis, 16 had intermediate uveitis, and 31 patients had posterior uveitis. In the sub-group post hoc analysis of these patients, a significant difference was found in terms of cell number (p=0.01). This difference was found between the anterior uveitis and the control group, and between the posterior uveitis and the control group. (p<0.01, p=0.002, respectively) There was no statistically significant difference between the intermediate uveitis group and the control group (p=0.139). A statistically significant difference was found between the two groups in the comparison between the anterior uveitis group and the posterior uveitis and intermediate uveitis group (respectively; p=0.020, p=0.018). However, there was no significant difference between the intermediate uveitis and posterior uveitis groups. (p=0.999) (**Table 2**).

There was a significant difference in terms of polymorphism between the control group and all subgroups. (all groups; p<0.01) However, there was no difference between the sub-groups. (respectively; p=0.373, p=0.170, p=1.000)

In terms of polymegatism, there was a significant difference between the control group and all subgroups. (p<0.01, p=0.01, p<0.01, respectively) There was a significant difference between the sub-groups between anterior uveitis and intermediate and posterior uveitis. (p<0.01, p<0.01, respectively) However, there was no difference between intermediary uveitis and posterior uveitis. (p=0.797)

In the analysis of 56 patients with unilateral uveitis, statistically significant differences were found between the uveitic eye and the healthy eye in terms of ECD, pleomorphism, and polymegatism. (all groups; p<0.01) (**Table 3**). This descent in ECD was observed more evidently in the anterior uveitis group.

Table 1. Demographic and clinical characteristics of study patients and control group

Chacteristic	Study group (n_1:66) Mean+SD	Control group (n_2:37) Mean+SD	*p* value*
Age (years)	33.71±15.29	37.78±13.17	0.177*
Gender Male/Female	40/26 60.6% / 39.4%	20/17 54.1% / 45.9%	0.520*
ECD (mm^2)	2345±302	2604± 137	**<0.01***
Pleomorphism	45.52±7.31	38.57±7.13	**<0.01***
Polimegatism	54.24±8.71	48.45±7.75	**<0.01***
CCT	526±29	524±30	0.812*
IOP	14.25±3.07	13.70±3.06	0.381*

n_1: Number of uveitic subject.
n_2: Number of control subject.
ECD; Endothelial cell density, CCT; Central corneal thickness, IOP; Intraocular pressure, SD; Standard deviation.
**Independent T test.*
P value of <0.05 was considered as significant

Table 2. Comparison of endothelial cell parameter values of uveitis subtype with control group

	Anterior Uveitis[a] n_1:19 mean±SD	Intermediate Uveitis[b] n_2:16 mean±SD	Posterior Uveitis[c] n_3:31 mean±SD	Control group[d] n_4:37 mean±SD	*P value*
ECD (mm²)	2184±318[b,c,d]	2436±285[a]	2398±270[a,d]	2604± 137[a,c]	**<0.01**
Pleomorphism (%)	49.86±6.55[d]	46.37±4.73[d]	46.32±5.74[d]	38.57±7.13[a,b,c]	**<0.01**
Polimegatism (%)	51.07±4.49[b,c,d]	41.24±6.80[a,c]	43.70±6.07[a,d]	48.45±7.75[a,b,c]	**<0.01**
CCT (µn)	526±29	526±32	525±28	524±30	0.995
IOP (mmHg)	14.15±3.38	13.75±2.81	14.58±3.06	13.70±3.06	0.670

$n_1/n_2/n_3$: Number of uveitic subject (sub-group)

n_4: Number of control subject.

ECD; Endothelial cell density, CCT; Central corneal thickness, IOP; Intraocular pressure, SD; Standart deviation.

Groups were coded with the letters a, b, c, d. One-way ANOVA test was used to compare the means. Tamhane's T2 post-hoc analysis was performed in paired comparison. Statistical significance was p<0.05. In paired comparisons, the letters shown as superscript indicate the age group in which there is a significant difference between them.

Table 3. Comparison of endothelial cell parameters in unilateral uveitis patients with the healthy eye

	Study group (n_1:66) Mean+SD	Control group (n_2:37) Mean+SD	*P* value
ECD (mm²)	2325±305	2548±268	**<0.01**
Pleomorphysm (%)	54.31±9.33	47.49±7.69	**<0.01**
Polimegatism (%)	46.16±7.42	40.05±7.58	**<0.01**

n_1: Number of uveitic eyes.

n_2: Number of control eyes.

ECD; Endothelial cell density, SD; Standard deviation.

**Independent T test.*

P value of <0.05 was considered as significant.

DISCUSSION

Different techniques can be used to assess the corneal endothelium structure. However, due to their dependability and repeatability, autofocus, digital image capture, and non-contact specular microscopy are more prevalent. It is generally recognized that anterior chamber inflammation affects the corneal endothelium. Specular and confocal imaging have both been used to show changes in endothelial cells (10,11).

On specular microscopy, some anterior uveitis types have been linked to decreased ECD; this is particularly noticeable in patients with Fuchs uveitis syndrome and in eyes with unilateral chronic severe iridocyclitis (12).

According to Alfawaz et al. they noticed a substantial decline in central ECD in eyes with anterior segment inflammation among similar age groups (13). In our study, patients with anterior uveitis had lower ECD than the control group, group with posterior uveitis, and group with intermediate and posterior uveitis. Endothelial abnormalities brought on by both big and small KP as well as alterations in the endothelium brought on by gutta-like lesions unrelated to KP can be used to explain this decline in ECD (7,14). It is known that viral anterior uveitis—particularly cytomegalovirus (CMV) uveitis is linked to a decline in ECD. Both CMV-associated iridocyclitis and corneal endothelitis show a strong association between CMV viral load and loss of ECD (15).

When the patients in our study were assessed for pleomorphism and polymegatism, we found that these values rose. Even if the ECD is normal, the rise in pleomorphism and polymegatism readings may be a key sign that endothelial cell function is beginning to decline. Studies demonstrate that the increased pleomorphism and polymegatism in the corneal endothelium is putting the cornea in a stressed state (16,17). There have been reports of endothelial cells near KP having larger cells and lower cell densities than normal endothelium (18). The photos of the patients in our investigation were taken when the uveitis was dormant. Despite this, we discovered a rise in pleomorphism and polymegatism levels, particularly in patients with anterior uveitis. A considerable drop in ECD was noted when compared to the healthy eyes of the patients with unilateral anterior uveitis. Previous research has demonstrated that anterior segment inflammation results in alterations to the shape and size of the cells as well as a decrease in ECD (13-18). Despite not being statistically significant, the increase in pleomorphism and polymegatism levels in the patient's healthy eyes was surprising. This may be a sign of subclinical uveitis activation, in our opinion. There is evidence from several research that bodily inflammation can have an impact on endothelial cells (9). This explains the ECD change in the intermediate uveitis group without anterior segment inflammation.

Additionally, it has been shown that various hypoxic or inflammatory diseases including smoking, diabetes, or cannabis use are linked to reduced ECD (19). Individuals with the aforementioned illnesses were omitted from our study because it was developed retrospectively to prevent confusion. As a result, we did not examine how the endothelial cell count related to diabetes and smoking.

The ECD of eyes with pseudoexfoliative (PEX) glaucoma was much lower than that of eyes with pseudoexfoliation syndrome, according to Bozkurt et al, but they could not detect a significant difference in pleomorphism and polymegatism (20). ECD was reported to be lower in PEX eyes than in non-PEX eyes in numerous investigations examining corneal endothelial alterations in the PEX condition. According to some research, ECD may be lower in glaucoma patients than in people of the same age (21). In a different study, it was discovered that ECD is lower and endothelial cells had a bigger surface area in people with acute angle-closure glaucoma. According to the same study, open-angle glaucoma and non-acute angle closure did not affect ECD's morphology (22). The patients' IOP levels in our investigation were at a normotonic level. No patients got to care to reduce IOP readings. Additionally, because uveitic episodes were in remission at the time of the shooting, we were unable to identify an increase in IOP. As a result, the potential change in ECD caused by an increase in IOP was avoided.

The patients were in remission, their active times were not compared, and because specular microscopy only looked at a specific area of the endothelium, we were unable to collect data on the entire cornea.

As a result, we discovered that there were fewer ECD produced by intraocular inflammation, which led to a long-lasting alteration in pleomorphism and polymegatism. To minimize the harm caused by uveitic episodes, early identification and treatment are crucial. Additionally, this patient group's endothelial cells had lessened resistance to surgical intervention. The morphology of endothelial cells should unquestionably be assessed with specular microscopy before surgery because these patients may require repeated intraocular procedures.

Ethical approval: The study is approved by Selcuk University Clinical Research Local Ethics Committee (date: 18.04.2018; decision number: 2018/147). All the procedures applied to human participants in this study were compatible with the ethical standards of the national research committee and the 1964 Helsinki Declaration and its later amendments.

Authors' contribution: The authors declare that they have contributed equally to the study.

Conflict of Interest: In this study, there is no conflict of interest among the authors on any subject.

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