ORIGINAL ARTICLE

Comparison of iris area, Schlemm's canal, and corneal tomography parameters in unaffected eyes with unilateral fuchs uveitis syndrome patients

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ABSTRACT

Purpose: We aimed to compare iris area, Schlemm's canal, and corneal tomography parameters in patients with unilateral Fuchs uveitis syndrome (FUS) with their unaffected eyes.

Materials and Methods: Anterior segment optical coherence tomography (AS-OCT) were performed for sixteen unilateral FUS patients after an ophtalmological examinaton. The iris area was calculated by marking 3 mm from the pupil edge at 3 and 9 o'clock positions. Schlemm's canal length and area were calculated using the device's calipers. All patients underwent corneal tomography.

Results: The average age of patients was 43.8±11.3 years. In eyes affected by FUS, there was no significant difference in nasal and temporal iris area, measuring 1.086±0.054 mm² and 0.999±0.059 mm² (p=0.11 and p=0.49). The nasal and temporal Schlemm's canal lengths in affected eyes were 245.4±24.2 µm and 241.3±20.5 µm, and nasal and temporal Schlemm's canal areas were 0.006±0.001 mm² and 0.006±0.001 mm², with no significant difference compared to unaffected eyes (p=0.58, p=0.16, p=0.79, and p=0.64, respectively). Subgroup analysis based on the presence of glaucoma and heterochromia also revealed no significant differences. Corneal tomography parameters were also found similar between the eyes (p>0.05 for all).

Conclusion: Our study found similar iris area measurements between affected and unaffected eyes. These results support that iris stromal thickness measured by AS-OCT is not sensitive enough to distinguish affected eye from unaffected eye in unilateral FUS. Remarkably, the histological changes in the Schlemm's canal anatomy, reported in patients with glaucoma in past studies, are not detected in glaucomatous eyes affected by FUS.

Keywords: Fuchs uveitis syndrome, heterochromia, iris area, corneal tomography, Schlemm canal.

INTRODUCTION

Fuchs' uveitis syndrome (FUS) is an inflammatory disorder that typically affects the anterior uvea and vitreous, which presents unilaterally with an insidious onset, low-grade activity, and is often asymptomatic.[1] It is usually characterized by stellate keratic precipitates, iris atrophy with or without heterochromia, mild flare, minimal cells in the anterior chamber, vitreous involvement, and the lack of posterior synechia and cystoid macular edema.[2] FUS is associated with complications such as cataracts, glaucoma, and vitreous opacities.[3, 4] In developing countries, FUS prevalence has been reported as 1-6%.[5]

It is accepted that iris changes are considered to be sensitive and reliable indicators for FUS. Heterochromia resulting from anterior stromal atrophy, depigmentation of the iris stroma, and loss of the iris pigment epithelium is one of the key signs of FUS.[6] Patients with dark or brown irises may exhibit mild heterochromia or no heterochromia, while heterochromia is more commonly observed in Caucasian descent.[7]

It was reported the prevalence of secondary glaucoma ranged from 6.3% to 59% in patients with FUS.[8,9] Several potential causes have been proposed, including neovascularization

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in the iris stroma and anterior chamber angle, trabeculitis, trabecular sclerosis, collapse of the Schlemm's canal, and steroid treatment. In FUS patients underwent chronic secondary glaucoma, electron microscopy suggested that the glaucoma may be due to the collapse of the Schlemm's canal rather than hyaline membrane formation or sclerosis in the trabecular meshwork.[10] There is limited number of studies evaluated Schlemm's canal using anterior segment optical coherence tomography (AS-OCT) in eyes with FUS.[11]

In this study, we aimed to compare iris area and Schlemm's canal parameter with unaffected eyes in patients with FUS.

MATERIALS AND METHODS

The study included 16 patients with FUS who were followed in our uvea clinic. The study was approved by Institutional Ethics Committee. The study was conducted in accordance with tenets of Helsinki Declaration. All participants gave written informed consent. .

The diagnosis of Fuchs' uveitis syndrome (FUS) was made based on the following findings observed under slit-lamp biomicroscopy: chronic anterior uveitis, typical keratic precipitates (white, stellate , translucent, small to medium in size, scattered to entire endothelium), vitritis, iris atrophy and depigmentation, lack of posterior synechia and cystoid macular edema, and abnormal vasculature in the iris and trabecular tissue. Patients with bilateral FUS, those who previously underwent intraocular surgery including cataract surgery, those with a history of laser treatment or trauma, and those with concurrent corneal abnormalities or other anterior segment anomalies such as intumescent cataract were excluded from the study.

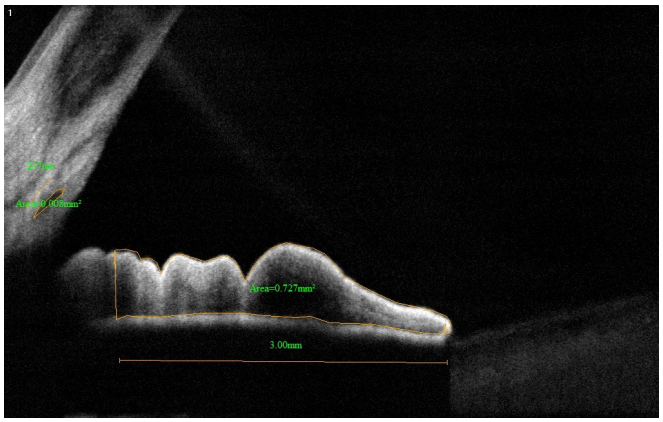

Figure 1: *Estimations of Schlemm's canal length, Schlemm's canal area and iris are on anterior segment optical coherence tomogrraphy in patients with Fuchs uveitis syndrome.*

After a routine ophthalmologic examination, all patients underwent anterior segment optical coherence tomography (AS-OCT) (RTvue OCT; Optivue Inc, Toledo, OH, USA) in a standard illuminated room. During the examination, patients were asked to open their eyes as widely as possible and avoid blinking. Images of the nasal and temporal angles (at the 3 and 9 o'clock positions) were obtained separately by directing the patients to focus on an external fixation target. The Schlemm's canal was identified in the images as a thin, black, transparent space. The diameter of the Schlemm's canal was measured as the meridional axial length of the thin, black, transparent space. The length and area of the Schlemm's canal were calculated using the device's calipers. The average of three measurements was calculated and recorded. A single horizontal line (3 mm in length) was drawn starting from the pupillary margin at the 3 and 9 o'clock positions along the lower edge of the iris . The iris stromal area above the horizontal line was manually marked, and the nasal and temporal iris area was calculated using the device's calipers. Additionally, corneal tomography (Sirius, CSO, Italy) was obtained in all patients.

Statistical analysis

The data were analyzed using the IBM SPSS Statistics Standard Concurrent User V 29 software (IBM Corp., Armonk, New York, USA). Descriptive statistics are presented as count (n), percentage (%), mean, standard deviation, and standard error. In numerical variables, normality of data distribution was assessed using the Shapiro-Wilk test. Mixed-effects linear models were used to compare the numerical values between affected and unaffected eyes. Bonferroni correction was used in all comparisons. Independent samples t test was used to compare the nasal iris area, temporal iris area, nasal Schlemm's canal length, temporal Schlemm's canal length, nasal Schlemm's canal area, and temporal Schlemm's canal area between patients with and without heterochromia and those with and without glaucoma in the affected eyes The Yates-corrected chi-square test was used to compare the presence of glaucoma and heterochromia in the affected and unaffected eyes . A p-value <0.05 was considered statistically significant.

FINDINGS

In the study, 32 eyes of 16 patients were evaluated. Mean age was 43.8±11.3 years (range: 24-61 years). Of the patients, 9 (56.3%) were men and 7 (43.7%) were women.

Table 1: *Comparison of corneal tomography parameters, iris area and Schlemm's canal parameters between affected and unaffected eyes in patients with Fuchs uveitis syndrome.*

	Groups		Test Statistics	
	Unaffected eyes *n*=16	Affected eyes *n*=16	*F* value	*p* value
IOP (mmHg)	12.43±0.57	11.62±0.73	1.273	0.277
HVID (mm)	12.02±0.19	11.93±0.12	0.158	0.698
CCT (µm)	559.9±13.2	576.5±18.0	0.920	0.355
Anterior chamber depth (mm)	3.66±0.11	3.82±0.14	0.873	0.367
Anterior chamber volume (mm^3)	151.4±8.0	156.5±8.5	0.335	0.572
Iridocorneal angle	43.78±2.49	46.57±2.51	0.874	0.367
HACD (mm)	11.969±0.144	11.957±0.150	0.013	0.911
K1 (D)	43.069±0.591	42.584±0.626	1.977	0.183
K2 (D)	44.026±0.529	44.238±0.639	1.068	0.320
Nasal iris area (mm^2)	1.161±0.051	1.086±0.054	2.793	0.115
Temporal iris area (mm^2)	0.968±0.043	0.999±0.059	0.503	0.490
Nasal Schlemm's canal length (µm)	255.9±27.4	245.4±24.2	0.323	0.580
Temporal Schlemm' canal length (µm)	282.2±18.6	241.3±20.5	2.155	0.165
Nasal Schlemm's canal area (mm^2)	0.007±0.001	0.006±0.001	0.069	0.798
Temporal Schlemm's canal area (mm^2)	0.007±0.001	0.006±0.001	0.228	0.640

Data are given as mean ± standard error of mean, *F*: Linear mixed models IOP: intraocular pressure; HVID: Horizontal Visible Iris Diameter; CCT: central corneal thickness; HACD: horizontal anterior diameter

There was no statistically significant difference in corneal tomography parameters, iris area, or Schlemm's canal parameters between the affected and unaffected eyes of FUS patients (Table 1).

Among the FUS patients, 11 (68.7%) had heterochromia while 6 (37.5%) had glaucoma. For glaucoma treatment, 5 patients were on beta-blockers, while 1 patient was receiving a beta-blocker plus an alpha-2 agonist. There was also posterior subcapsular cataracts in 4 patients but their visual acuity was greater than 0.7 on the Snellen scale in these patients. When patients were divided into subgroups based on the presence or absence of heterochromia or glaucoma, no statistically significant difference was found in the nasal iris area, temporal iris area, nasal Schlemm's canal length, temporal Schlemm's canal length, nasal Schlemm's canal area, or temporal Schlemm's canal area (Table 2 and Table 3).

DISCUSSION

In our study, we found no significant differences in the iris area, Schlemm's canal length, or area when we compared

Table 2: *Comparison of subgroups based on heterochromia.*

	Heterochromia		Test Statistics	
	No *n*=5	Yes *n*=11	*t* value	*p* value
Nasal iris area (mm^2)	1.038±0.169	1.107±0.238	0.580	0.571
Temporal iris area (mm^2)	0.970±0.104	1.040±0.264	0.561	0.584
Nasal Schlemm's canal length (µm)	186.7±63.3	266.8±96.2	1.528	0.150
Temporal Schlemm' canal length (µm)	205.7±67.1	254.0±82.4	1.044	0.315
Nasal Schlemm's canal area (mm^2)	0.005±0.003	0.007±0.003	0.931	0.369
Temporal Schlemm's canal area (mm^2)	0.003±0.002	0.008±0.004	2.055	0.061

Data are given as mean±standard deviation, *t*: Independent samples t test

Tablo 3: *Comparison of subgroups based on glaucoma.*

	Glaucoma		Test Statistics	
	No *n*=10	Yes *n*=6	*t* value	*p* value
Nasal iris area (mm^2)	1.086±0.265	1.085±0.119	0.010	0.992
Temporal iris area (mm^2)	1.032±0.266	0.988±0.107	0.345	0.736
Nasal Schlemm's canal length (µm)	242.7±109.2	251.0±62.9	-0.186	0.855
Temporal Schlemm' canal length (µm)	237.2±106.8	169.0±73.3	1.274	0.225
Nasal Schlemm's canal area (mm^2)	0.006±0.004	0.007±0.003	-0.241	0.813
Temporal Schlemm's canal area (mm^2)	0.007±0.005	0.005±0.003	0.786	0.446
Data are given as mean±standard deviation, *t*: Independent samples t test				

the affected and unaffected eyes of FUS patients based on measurements taken from both the nasal and temporal quadrants. Similarly, no significant differences were observed when patients were stratified by the presence or absence of heterochromia or glaucoma. It was found that the keratometry values and central corneal thickness were also comparable between the two eyes.

In FUS, thinning in all layers of the iris including the stroma and iris pigment epithelium leads to heterochromia. Iris atrophy typically starts from areas adjacent to the pupil and progresses through iris. Ivernizzi et al. assessed iris thickness and found that only the temporal iris was thinner in eyes with FUS when compared to healthy eyes.[12] In a study by Ruiz-Cruz et al., it was found that both the nasal and temporal iris areas as well as subfoveal choroidal thickness were lower in FUS patients compared to the healthy control group.[13] In the study Başarır et al. a statistically significant difference was found in the thickest part of the iris between eyes with and without FUS and that iris was thinner in the affected eyes.[14] However, authors found no significant difference in other regions of iris (at the center and 500 µm); suggesting that it may be due to the presence of iris crypts in these measurement areas. Özer et al. reported that the iris stromal thickness was comparable with unaffected eyes in both nasal and temporal quadrants.[11] As similar to our study, they concluded that iris stromal thickness is not a sensitive index in cases with suspected unilateral FUS. In the subgroup analysis based on the presence of heterochromia, it was found that the iris area was similar between the affected and unaffected eyes in our study. Zarei et al. suggested that it could be more helpful to asses the relative flatness of the anterior iris surface in FUS-affected eyes compared to unaffected eye might help in the diagnosis of unilateral FUS cases with subtle heterochromia.[15]

Glaucoma is a common complication of the syndrome, which is considered the leading cause of vision loss in FUS.[8] Many potential causes for glaucoma have been proposed, including neovascularization in the iris stroma and anterior chamber angle, trabeculitis, trabecular sclerosis, collapse of Schlemm's canal, and steroid treatment.[16, 17] Kagemann et al. reported that Schlemm's canal parameters, as imaged by SD-OCT, were smaller in glaucoma patients compared to control subjects.[18] Similarly, Shi et al. reported that Schlemm's canal area and diameter were smaller in both newly diagnosed glaucoma patients and those already on glaucoma medications.[19] However, it was found that the Schlemm's canal length and area were found to be similar between the FUS-affected and unaffected eyes in our study. In addition it was found that there was no significant difference in Schlemm's canal parameters in the subgroup analysis according to the presence of glaucoma. This finding supports the idea that the mechanism of glaucoma in FUS may be due to changes in the angle structures rather than the Schlemm's canal itself.

Although it was found that the central corneal thickness was higher in the affected eyes of FUS patients in our study, the difference did not reach statistically significant. Keratometry values were also similar between the affected and unaffected eyes. In 2 studies from Turkey, it was found that central corneal thickness and keratometry values were similar between FUS patients and control groups in agreement with our study.[20, 21] Cai et al. reported that central corneal thickness and keratometry values were similar in the affected and unaffected eyes of FUS patients, but corneal volume was higher in the affected eyes, suggesting that this could be due to repeated intraocular pressure spikes.[22] Ortega-Larrocea et al. found that the average keratometric value was higher in FUS patients (2.2±1.19 diopters) compared to the control group.[23] Faramarzi et

al. reported that the average SimK astigmatism value was higher in the affected eyes (1.65±1.27 diopters) compared to the unaffected eyes (0.88±0.52 diopters).[24] Authors suggested that an immunological reaction against corneal epithelial and stromal antigens could lead to subclinical structural changes and remodeling of the corneal stroma and epithelium, which may lead increased corneal astigmatism.

This study has some limitations including the small sample size and the use of SD-OCT for measurements. All measurements were taken between 8:00 and 12:00, thus, we failed to assess the 24-hour variations in Schlemm's canal. Additionally, the evaluations of Schlemm's canal parameters were restricted to the nasal and temporal quadrants in order to obtain the best quality images and minimize discomfort during imaging.

In conclusion, iris atrophy is one of the most prominent features of FUS, manifesting virtually in all patients. However, in our study, iris area measurements at a distance 3 mm from the pupillary margin were found to be similar between the affected and unaffected eyes. These results suggest that iris area measurements obtained via AS-OCT may not be sensitive enough to differentiate between affected and unaffected eyes in unilateral FUS. It is striking that the changes in Schlemm's canal anatomy reported in studies on glaucomatous eyes were not observed in FUS-affected glaucomatous eyes in our study.

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