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Original Article

Anterior segment parameters and corneal specular microscopy findings in rheumatoid arthritis

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Abstract

Aim: To compare the anterior segment parameters and specular microscopy findings between patients with Rheumatoid arthritis (RA) and healthy controls.

Material and Methods: In this prospective study, 55 patients diagnosed with RA and age and matched 55 control subjects without any systemic diseases were enrolled. Central corneal thickness (CCT), corneal endothelial cell density (cells/mm2) (ECD), percentage of hexagonal cells of corneal endothelial cells (HEX), and cell size variability (CV%) of endothelial cells were measured using noncontact specular microscopy (CEM-530 Specular Mıcroscope, NIDEK).

Anterior chamber depth (ACD), Axial Length (AL), white to white limbus length and keratometry were measured using an ocular biometry system. In all patients of RA group, disease activity severity was assessed with The Disease Activity Score in 28 joints diseases activity score (DAS28 rate).

Results: There were statistically significant differences between RA patients and control subjects regarding ACD (3.06±0.43 vs 3.24±0.31; p: 0.001), white to white limbus length (11.63±0.45 vs 11.76±0.38; p: 0.02), CV% (35.49±5.96 vs 32.02±5.22, p: 0.001) and hexagonality (67.31±4.66 vs 71.35±11.02; p: 0.001). In correlation analysis, there was a negative correlation between disease periods and both ACD and CCT; while there was a negative correlation with the number of cells and endothelial cell density and DAS 28 score.

Conclusion: Although there was not a significant difference regarding endothelial cell density values in RA group compared with healthy controls; there was a negative correlation between the disease activity and endothelial cell density. Moreover, CV% was significantly higher and hexagonality % was significantly lower in RA group; indicating the endothelial damage and increase in the expected compensatory response.

Further, larger studies are warranted to define the exact pathological mechanisms and clinical outcomes of this corneal endothelial damage in RA patients.

Keywords: Anterior Segment Parameters; Specular Microscopy Findings; Rheumatoid Arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a common systemic autoimmune disorder that is characterized by polyarticular synovial inflammation, antibody production and cartilage and bone destruction (1). Non-steroidal anti-inflammatory drugs for pain relief, corticosteroids and disease modifying anti-rheumatic drugs (DMARDs) and biological agents are the mainstay of the treatment (2).

RA has some systemic features including cardiovascular, pulmonary and psychological disorders (3). Dry eye, peripheral ulcerative keratitis and scleritis are the major ocular complications associated with RA (4). Some ultrastructural changes in the cornea were also reported in RA patients (5,6).

To the best of our knowledge the data about the ocular findings in RA patients is limited. In this study, we aimed to compare the anterior segment parameters and specular microscopy findings between patients with RA and healthy controls.

MATERIAL and METHODS

In this prospective study, patients diagnosed with RA in Erzincan Binali Yildirim University Mengucekgazi Training and Research Hospital, Physical Therapy and

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Rehabilitation Department between 11/2017 - 04/2018 and age and matched control subjects without any known systemic diseases were enrolled. The patients under 18 years of age, with central corneal scar, previous ophthalmic surgery, pregnancy and lactation, and history of herpes simplex keratitis, were excluded from the study. The study was approved by local ethics committee (Ethics Committee number: E.49936 date: 31/10/2017) and informed consent was obtained from all patients who agreed to participate the study.Signed waivers of consent received.

A complete ophthalmologic examination was performed in all participants. Central corneal thickness (CCT), corneal endothelial cell density (cells/mm2) (ECD), percentage of hexagonal cells of corneal endothelial cells (HEX), and cell size variability % (CV%) of endothelial cells were measured using noncontact specular microscopy (CEM-530 Specular Microscope, NIDEK,Japan).

Axial Length (AL) and keratometry were measured using an ocular biometry system (AL-Scan Optical Biometer NIDEK, Japan). Minimal K (K1) and maximal K (K2) were determined and the two values were averaged to obtain K. Anterior chamber depth (ACD) was defined as the distance from the anterior corneal surface to the anterior lens surface, and it was also measured with ocular biometry system.

Adult patients (aged ≥18 yr), who were under follow-up for RA were included in the study. Rheumatoid arthritis diagnosis was performed based on the ACR/European League Against Rheumatism (ACR/EULAR) 2010 criteria (3).

In all patients in RA group, disease activity severity was assessed with The Disease Activity Score in 28 joints (DAS28) by utilizing total joint count, swollen joint count, visual analogue scale and erythrocyte sedimentation rate (7).

Statistical analysis

The statistical analysis was performed with SPSS version 21 (SPSS Inc., Chicago, IL). The significance between parameters was assessed by Student's t-test for paired values and Chi-square test for nonparametric variables. For calculating the difference between the values of the two groups, two sample t-test was applied. Spearman correlation was used to assess correlation between disease duration or DAS28 score and ophthalmologic findings in RA group. Significance was set at $P < 0.05$.

RESULTS

Totally 110 eyes of 55 patients diagnosed with RA (8 male, 47 female) with a mean age of 55.45 ± 10.03 years and 110 eyes of 55 control patients without any known rheumatologic disease or symptoms (11 male, 44 female) with a mean age of 54.71 ± 9.99 included in the study. There was not any statistically significant difference between two groups regarding age (p:0.71) or gender (p:0.37).

The results of ophthalmological analysis of 2 groups are summarized in Table 1. There were statistically significant differences between two groups regarding ACD, white to white limbus length, number of cells, CV%, and hexagonality.

Table 1. Comparison of RA patients with control group regarding the ophthalmologic findings

	RA (n: 55)	Control (n:55)	P
IOP (mmHg)	13.68±3.21	13.94±1.34	0.43
Axial length	22.84±0.82	22.73±2.34	0.64
Keratometry	44.27±1.67	44.23±1.59	0.85
Central corneal thickness (µm)	517.78±42.87	523.39±27.98	0.25
Anterior Chamber Depth	3.06±0.43	3.24±0.31	0.001
White to White Limbus Length	11.63±0.45	11.76±0.38	0.02
Number of cells	145.97±36.04	164.89±46.61	0.001
Corneal endothelial cell density cell/mm^2	2524.12±213.46	2539.74±332.89	0.68
Cell size Variation (%)	35.49±5.96	32.02±5.22	0.001
Hexagonality (%)	67.31±4.66	71.35±11.02	0.001

IOP: Intraocular pressure

The mean duration of the disease was 8.58 ± 6.31 (range: 1-30 years) in RA group. DAS28 score was calculated for all RA patients. The mean DAS28 score of the patients was 3.02 ± 0.90 (range: 1.58 -5.17). In correlation analysis, there was a negative correlation between disease period and ACD and CCT; while there was a negative correlation with the number of cells and endothelial cell density and DAS 28 score. On the other hand there was a positive correlation between AL and DAS 28 score (Table 2).

Table 2. Results of correlation analysis performed in RA group

	Disease period		DAS28	
	r	p	R	P
IOP	0.10	0.28	0.15	0.12
Axial length	0.06	0.55	0.20	0.034
Keratometry	-0.19	0.06	-0.16	0.09
Central corneal thickness	-0.26	0.006	0.11	0.27
Anterior Chamber Depth	-0.26	0.006	-0.02	0.82
White to White Limbus Length	-0.19	0.84	0.02	0.80
Number of cells	-0.009	0.92	-0.33	0.001
Corneal endothelial cell density cell/mm^2	-0.13	0.18	-0.20	0.03
Cell size Variation %	0.008	0.93	-0.08	0.41
Hexagonality (%)	-0.15	0.10	0.07	0.47

IOP: Intraocular pressure; disease period: time passed since the diagnosis of the disease, r: correlation coefficient

DISCUSSION

In this study we analyzed the anterior segment parameters and specular microscopy findings in RA patients and we determined that there was not any statistically significant difference between RA patients and control group regarding IOP, AL, keratometry and CCT values; while Anterior Chamber Depth and White to White Limbus Length, number of cells, percentage of hexagonality were significantly lower and cell size variation was significantly higher in RA patients. In correlation analysis, there was a negative significant correlation between disease period and CCT and ACD; while there was a negative correlation between DAS28 score and number of cells and corneal endothelial cell density.

Rheumatoid arthritis has a female preponderance thus women are affected 3 to 4 times more commonly than men (8). In our study, women were also more commonly involved compared with men.

We did not determine any difference between RA patients and control cases regarding IOP values although many of our patients were under treatment for a long time including oral glucocorticoids. Similar with our results Graf et al (9) evaluated IOP among RA patients who were chronic oral glucocorticoid users in low to moderate doses and reported that, although there was an about 5% increase in IOP in RA patients compared with the control cases, the difference was not statistically significant. Similarly, Tas et al (6) also did not determine a significant difference in RA patients regarding IOP or CCT values compared with controls.

In this study we determined that mean ACD values and white to white corneal length were significantly lower in RA group compared with the control cases. In a recent study, Anayol et al reported that there was not a significant difference in RA patients compared with the control cases regarding ACD, CCT and keratometry values (10). In our study, we also did not determine any significant difference between RA and control groups regarding CCT or K values. Ozcura et al (11) reported that there was not any statistically significant difference between RA patients and control cases regarding the CCT values and K readings; moreover CCT values and K readings were also not associated with RA activity and RA duration. Similarly, Atalay et al (12) also did not determine any difference in CCT values in RA patients compared with the control cases. However Sevimli et al (14) reported a significant moderate negative correlation with CCT and disease duration in RA patients treated with DMARDs and biologic agents together. Interestingly, in this study we also determined a negative correlation with CCT and disease duration in RA patients but there was not a significant correlation between CCT and DAS 28 score. We can suggest that, in RA patients, in time, a decrease in CCT may be expected.

Markovitz et al (14) reported that corneal damage found in RA patients takes place only on the external layer and does not affect the endothelial layer. We also did not determine any significant difference between 2 groups regarding endothelial cell density. Heinke et al (15) reported that there was not any statistically significant difference regarding CCT or ECD between RA patients and control cases. We also did not determine any significant difference regarding CCT or ECD in RA patients compared with the controls. However, number of cells was significantly lower in RA group in this study. We also determined a negative correlation between number of cells and ECD with DAS 28 score in RA group. With those results, we can suggest that, more severe disease was associated with a more severe endothelial damage.

Unfortunately, corneal endothelial cells have a very weak regeneration capacity and healthy but older cells get larger in time to provide the integrity of the endothelium causing an increase in CV% in specular microscopy (16). An increase in CV% was reported in some previous studies with aging (17,18). In our study, CV% was also significantly higher in RA patients compared with the control group indicating an augmented damage and recovery in the endothelial healing response. Although the data about the CV% in RA patients is limited in literature, in some chronic inflammatory diseases such as diabetes mellitus, CV% was reported to be significantly lower compared with the healthy controls (19). Together with a decrease in ECD, a significant increase in CV% in patients with RA is important; since it shows an increase in the expected compensatory response.

As mentioned above, a reduction in corneal endothelial cell density is compensated by enlargement of the older cells causing an increased cellular pleomorphism and a decrease in the percentage of hexagonal cells (20). In this study we also determined a significant decrease in hexagonality in RA group indicating this compensatory response.

There are some limitations of this study that should be mentioned. The main limitation of this study is that, the patients were under different treatments for RA which may also affect the results of these evaluations. Secondly, since our patient population was not very large we could not analyze the ocular alterations in RA patients with different stages or time periods of the disease in subgroup analyses.

CONCLUSION

In conclusion, we determined that in patients with RA, although there was not a significant difference in ECD compared with healthy controls; there was a negative correlation between the disease activity and both number of cells and ECD. Moreover, CV% was significantly higher and hexagonality % was significantly lower in RA group; indicating the endothelial damage and augmented compensatory response. Further, larger studies are warranted to define the exact pathological mechanisms and clinical outcomes of this corneal endothelial damage in RA patients.

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