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Original Article

How does rheumatoid arthritis affect corneal biomechanical properties?

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Abstract: The aim of this study was to investigate the corneal alterations occurring in rheumatoid arthritis (RA) patients compared with healthy subjects and to define the presence of biomechanical alterations in cornea accompanying dry eye disease, the most common ocular manifestation of RA. Forty-seven RA patients and 40 control cases without any known systemic or ocular diseases were included in this prospective, cross-sectional study. All subjects underwent a complete ophthalmologic examination. For the diagnosis of dry eye disease; the symptoms were asked, Break up Time and Schirmer tests were applied. The Ocular Response Analyzer (Reichert Ophthalmic Instruments, Buffalo, NY) was used to measure the biomechanical properties of the cornea. In RA group, 19 (40.4%) patients had the diagnosis of dry eye disease, but it was present in only one of the control cases (P=0.001). There was a significant difference between groups regarding the mean intraocular pressure (IOP) (P=0.04) but not the mean central corneal thickness values (P=0.56). Although there was not a statistically significant difference between RA group and control cases regarding corneal hysteresis and corneal resistance factor, IOPcc and IOPg were statistically significantly lower in RA group (P=0.03 and P=0.04, respectively). There is conflicting data in the literature about the effects of RA on the biomechanical properties of the cornea. Clinicians should be aware of these alterations since it may cause underestimated IOP readings in RA eyes. Larger prospective studies are warranted to determine the alterations on biomechanical properties of the cornea among RA patients, annually.

Keywords: Rheumatoid arthritis, corneal biomechanics, corneal hysteresis, corneal resistance factor, ocular response analyzer, dry eye, cornea

Introduction

Rheumatoid arthritis (RA) is a chronic progressive, autoimmune disease that primarily affects small joints. It is the progressive, destructive joint disease leading to reduced physical function, and impaired quality of life with its extraarticular involvements [1, 2]. Substantial ophthalmic involvement is frequently reported in RA cases, causing varying degrees of ocular morbidity [3, 4]. Recently Vignesh et al studied 392 eyes of 196 RA cases and reported that 135 eyes of 77 patients (39%) had ocular manifestations of RA including dry eye, episcleritis, scleritis, peripheral ulcerative keratitis and sclerosing keratitis [5]. Since severe ocular manifestations such as peripheral ulcerative keratitis and necrotizing scleritis may accompany RA, it is important to determine the ocular alterations in RA patients to define the treatable ones.

In this study, we aimed to investigate the corneal alterations occurring in RA patients compared with healthy subjects and we also aimed to define the presence of biomechanical alterations in cornea accompanying dry eye disease, the most common ocular manifestation of RA.

Material and method

Forty-sevenRA patients and 40 control cases without any known systemic or ocular diseases were included in this prospective, cross-sectional study that was conducted in Bagcilar Training and Research Hospital, Istanbul, Turkey. The exclusion criteria were defined as having an ocular or corneal operation history,

presence of any scars or opacities on cornea, having a refractive error of lower than -3.0 and above than +3.0 and presence of pterygium. The study was approved by the local ethics committee and informed consent was obtained from each patient before the study.

RA patients were further subgrouped into 3 as mild, moderate and severe, using a Disease Activity Score (DAS)-28 that measures the RA activity, by physical medicine and rehabilitation specialist. DAS-28 score has four components which are tender joint count, swollen joint count, erythrocyte sedimentation rate (ESR) and visual analog score (VAS). Disease activity was calculated by DAS-28 score as follows: score <2.6: remission, >2.6 and ≤3.2: low disease activity (mild), >3.2 and ≤5.1: moderate disease activity, >5.1: High disease activity (severe) [6].

All of the subjects underwent a complete ophthalmological examination, including visual acuity testing, slit lamp examination, intraocular pressure (IOP) measurement with Goldmann applanation tonometer, and fundus examination.

For the diagnosis of dry eye disease; the symptoms (burning sensation and itching) were asked, Break Up Time was determined (<10 sec was suspicious for dry eye), and Schirmer test was applied (<5 mm: dry eye disease, 5-10 mm: suspicious for dry eye disease; >10 mm: normal). If 2 of those 3 tests were positive or suspicious for dry eye disease; the diagnosis was made. Intraocular pressure (IOP) measurements were performed with Goldmann applanation tonometer, at daytime (between 10:00-16:00). Central corneal thickness (CCT) was measured with AccuPach (Accutome Ultrasound Inc.) at daytime (between 10:00-16:00) and the mean of 3 consecutive measurements was obtained.

The Ocular Response Analyzer (Reichert Ophthalmic Instruments, Buffalo, NY) was used to measure the biomechanical properties of the cornea with a standard technique [7]. Corneal biomechanical properties, including corneal hysteresis (CH), corneal resistance factor (CRF), corneal compensated IOP (IOPcc), and Goldmann-correlated IOP (IOPg) can be measured using this instrument. Corneal hysteresis shows the corneal viscoelasticity, and CRF demonstrates the overall resistance of the cornea. All subjects were asked to look at a target light with the same room temperature and light level. At least 3 consecutive measurements, having a Waveform Scores ≥7, were obtained for each eye, and the average value of these measurements was calculated. In fact, only one eye of each participant, which had the better Waveform Scores were included in the study.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences software version 21.0 (SPSS Inc, Chicago, IL). All continuous variables were tested for normality. Chi-square test was used for comparison of 2 groups (RA and control groups). The analysis of variance (ANOVA) was carried out to compare mean values of continuous variables among groups. The Tukey HSD test was used to make post hoc comparisons after ANOVA. The Levene test for equal variances was performed before the comparison of groups by ANOVA test. The Pearson correlation analysis was used to test bivariate correlations among variables. All the results were given as mean ± standard deviation. *P* value ≤0.05 was regarded as statistically significant.

Results

The study included 47 RA patients with a mean age of 49.70±11.07 years (range: 26-72 years) and 40 control cases with a mean age of 45.82±14.11 years (range: 25-73 years). There was not a statistically significant difference between groups regarding age (P=0.16). All participants were women.

The mean BCVA values were 0.95±0.17 in RA group and 0.98±0.09 in the control group. The difference between groups regarding BCVA was not statistically significant (P=0.24). Biomicroscopic evaluation revealed that 3 (6.4%) of the RA patients were having cataract, but cataract was not present in any of the control cases (P=0.29).

Dry eye symptoms were present in 16 (34.0%) patients in RA group but only 1 of the control cases had dry eye symptoms. In the evaluation of Break up time; in RA group; it was <10 sec in 16 (34.0%) patients but it was >10 sec in all

Table 1. Results of ORA examinations, comparison of 4 groups

	Mild RA (n:15)	Moderate RA (n:27)	Severe RA (n:5)	Control (n:40)	P
CH (mm-Hg)	10.50±1.24	9.80±1.37	9.82±1.74	10.18±1.41	0.58
CRF (mm-Hg)	10.48±1.69	9.90±1.64	9.94±2.31	10.55±1.47	0.82
IOPcc (mm-Hg)	15.86±2.33	16.69±3.44	16.62±3.50	18.20±3.60	0.03
IOPg (mm-Hg)	15.46±3.06	15.47±3.55	15.54±4.35	17.31±3.69	0.04
IOP (mm-Hg)	14.73±2.55	15.33±4.11	14.40±2.70	16.32±2.64	0.63
CCT (μm)	554.27±32.76	546.67±29.67	561.80±19.91	554.93±29.94	0.21

CH: Corneal hysteresis, CRF: Corneal resistance factor, IOP: Intraocular pressure, IOPcc: corneal compensated IOP, IOPg: Goldmann-correlated IOP and CCT: Central corneal thickness.

Table 2. Results of ORA examinations, IOP and CCT, comparison of RA patients with or without dry eye disease with control group

	RA patients with dry eye disease (n:19)	RA patients without dry eye disease (n:28)	Control cases (n:40)	P
CH (mm-Hg)	9.57±1.35	10.34±1.34	9.79±1.32	0.12
CRF (mm-Hg)	9.55±1.31	10.46±1.86	10.44±1.50	0.12
IOPcc (mm-Hg)	16.43±3.73	16.40±2.63	18.20±3.60	0.09
IOPg (mm-Hg)	14.97±3.52	15.81±3.35	17.31±3.69	0.08
IOP	15.52±2.95	14.71±3.86	16.70±3.10	0.09
CCT (μm)	552.42±26.49	549.54±32.22	554.93±29.94	0.80

CH: Corneal hysteresis, CRF: Corneal resistance factor, IOP: Intraocular pressure, IOPcc: corneal compensated IOP, IOPg: Goldmann-correlated IOP and CCT: Central corneal thickness.

control cases. On the other hand; Schirmer test was diagnostic for dry eye disease in 11 (23.4%) patients and it was suspicious in 7 (14.9%) patients of RA group. However, none of the control cases had a diagnostic value for dry eye disease in Schirmer test but 5 (18.5%) had suspicious results. In the light of these data; in RA group, 19 (40.4%) patients had the diagnosis of dry eye disease but the dry eye was present in only 1 of the control cases (P=0.001).

Examination of fundus was normal in all participants. The mean IOP determined by Goldmann applanation tonometer was 15.04±3.51 mmHg and 16.32±2.64 mmHg in RA and control groups, respectively. There was a statistically significant difference between groups regarding IOP values (P=0.04). The mean CCT values were 550.70±29.76 mm and 555.07±31.51 mm in RA and control groups, respectively. The difference between groups regarding CCT was not statistically significant (P=0.56).

In RA group; the mean disease duration was 5.98±5.05 years (range: 1-20 years). According to DAS-28 assessment; 15 patients were having mild, 27 patients were having moderate and 5 patients were having severe disease.

In RA group; CH, CRF, IOPcc and IOPg values were 10.03±1.38, 10.09±1.71, 16.42±3.09 mm-Hg and 15.47±3.41 mmHg, respectively. The results of ORA examinations of 4 groups are summarized in **Table 1**. In one way ANOVA test, although there was not a statistically significant difference between groups regarding CH and CRF values, IOPcc and IOPg were statistically significantly lower in all RA groups compared with the control cases.

The patients with or without dry eye disease were also compared with the control cases regarding corneal biomechanical findings as well as the IOP and CCT (**Table 2**). There was not any statistically significant difference between groups regarding ocular biomechanical parameters, IOP or CCT.

Discussion

In this study, we have evaluated the corneal biomechanical alterations in RA patients together with the presence of dry eye disease. Interestingly, in RA patients IOP, IOPcc and IOPg values were statistically significantly lower compared with the control cases; however CH, CRF or CCT values did not show any variances. Dry

eye disease was present in about 40% of the RA patients. When patients were sub-grouped according to the presence of dry eye disease; there was not any statistically significant difference between groups regarding ocular parameters. In that aspect, we can suggest that dry eye disease was not the cause of alterations in intraocular pressure in RA patients.

Zlatanović et al [8] examined 691 RA patients and reported that ocular manifestations were present in 27.2% of patients while Vignesh et al [5] found the incidence of ocular manifestations in RA to be 39% in a population of 196 patients. Dry eye was the most common ocular manifestation of RA whereas keratoconjunctivitis sicca, episcleritis, scleritis, corneal changes, and retinal vasculitis are the other main ocular manifestations of RA [9, 10]. However, the data about the biomechanical values of eyes of RA patients is limited in the literature. Prata et al reported lower corneal hysteresis values in RA patients (n:20 eyes) when compared with healthy subjects (n:36 eyes). However, similar with our results they also defined statistically significantly lower IOP values in RA group compared with control cases [11]. Taş et al compared the corneal biomechanical properties of 39 RA patients with those of 55 healthy controls and determined that corneal hysteresis and corneal resistance factor were significantly lower in the RA group with higher corneal-compensated intraocular pressure values than healthy controls [12]. Very recently, similar with our study, Can et al investigated the variations in biomechanical properties of the cornea in RA patients and determined a decrease in the mean corneal hysteresis measurements indicating ultrastructural changes in the cornea that may occur in the active phase, and persist in the remission period [13]. We did not determine any alterations in CH or CRF values in patients with RA. But all IOP, IOPcc, and IOPg values were determined to be decreased in RA patients. The differences in biomechanical properties reported in literature among RA patients may depend on the differences on disease period of patients in those studies.

In this study, we also evaluated the presence of dry eye disease among RA patients and in about 40% of cases, dry eye was accompanying RA. Cingü et al evaluated the corneal parameters of RA with Scheimpflug camera and reported that RA patients had thinner corneas compared to control subjects that may be affected by disease duration. Moreover, they also defined that coexistence of dry eye and RA seems to aggravate the thinning of cornea as well [14]. On the other hand Tuominen et al reported that average corneal thickness was lower as well as the mean intraocular pressure in patients with Sjögren's syndrome [15]. Villani et al also defined a statistically significant decrease in CCT values of patients with Sjögren's syndrome [16]. However we did not determine any alterations in CCT values of RA patients; moreover CCT values of RA patients with dry eye disease were also not different significantly from that of RA patients without dry eye disease or control cases.

Small sample size was the main limitation of this study. In RA group; the mean disease duration was 5.98±5.05 years in this study. This may be regarded as not a long period for a chronic disease and this may be one of the reasons for un-altered CCT or CH values in RA group. Larger studies with RA patients having extended disease duration periods may elucidate this condition. Moreover, annual follow-up of RA patients may show different alterations in those parameters and may elucidate the effects of disease on cornea more exactly. All of our patients were female and this was a power of the study since it eliminates the effects of gender on ocular biometric findings. However accompanying diseases and drugs used for the disease may also change the corneal findings.

In conclusion, we have determined lower IOP, IOPcc, and IOPg values without any alterations in CH, CRF or CCT in RA patients compared with healthy subjects. There is conflicting data in the literature about the effects of RA on the biomechanical properties of the cornea. Clinicians should be aware of these alterations since it may cause underestimated IOP readings in RA eyes. Larger prospective studies are warranted to determine the alterations on biomechanical properties of the cornea among RA patients, annually.

Disclosure of conflict of interest

None.

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