Assessing Corneal Changes in Age-Related Macular Degeneration

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ABSTRACT

Purpose: This study aimed to assess the central corneal thickness (CCT) and cornea specular microscopy values in patients with age-related macular degeneration (ARMD).

Materials and Methods: In total, 60 eyes of 30 patients with wet macular degeneration (Group 1) in one eye and dry macular degeneration (Group 2) in the other eye were compared with 50 eyes of 50 healthy people (Group 3) for CCT, endothelial cell density (CD), coefficient of variation (CV) and hexagonality (HEX) values. Patients who had undergone ocular surgeries or used ocular or systemic medication were excluded from the study.

Results: The ARMD group comprised 17 men and 13 women (average age,71.76±5.26 years), whereas the healthy group comprised 27 men and 23 women (average age,70.14±2.14 years); the difference between these groups was not statistically significant (p=0.96 and p=0.11, respectively). Groups 1, 2 and 3 had CCT of 534.0±20.34, 528.46±24.26 and 513.04±33.47 µm, an CD of 2312.43±740.81, 2451.40±587.42 and 2414.22±379.91 cells/mm^2, a CV of 33.60%±7.08%, 34.30%±5.65% and 33.74%±4.78% and a HEX of 52.80%±9.57%, 51.96%±7.06% and 52.74%±9.16%, respectively. Regarding CCT, no statistical difference was observed between Groups 1 and 2 (p=0.34), whereas a statistical difference was observed between Groups 1 and 3 (p=0.003) and between Groups 2 and 3 (p=0.031). There were no differences among groups regarding other parameters (p>0.05).

Conclusion: While there were no differences among the CCT values of patients with wet ARMD in one eye and dry ARMD in the other eye, their CCT values were higher than those of the control group. There was no difference among other parameters.

Key Words: Macular degeneration, Specular microscopy, Cornea.

INTRODUCTION

Age-related macular degeneration (ARMD) was first defined by Otto Haab in 1885 as a clinical scenario characterised by pigmentary and atrophic changes in the macula and by progressive decrease in the visual acuity in patients aged>50 years. Currently, ARMD is defined as a macular neurodegenerative disease[1,2] that manifests as a complicated degeneration affecting the photoreceptors, retina pigment epithelium (RPE), Bruch membrane and choriocapillaris in the macula. It is the most common cause of central visual loss among people aged ≥65 years in developed countries. Its prevalence is 10% in individuals aged 65-75 years and 25% in those aged >75 years, making it an important public health problem.[3,4] Neovascular/exudative/wet-typeARMD is observed in 10%-15% of all ARMD cases but is responsible for 88% of severe visual losses related to ARMD. Conversely, the non-neovascular/atrophic/dry-type is observed in 85%-90% of ARMD cases. With slowly progressing, dry ARMD, severe visual loss occurs in 10%-12% of the cases.[5]

Since the cornea is a transparent tissue, it represents one of the most important steps of the visual function. An intense metabolic activity is maintained for ensuring the continued transparency of the cornea, and oxygen is an important parameter for this metabolic activity.[6] In patients with wet ARMD in one eye and dry ARMD in the other eye, changes in corneal endothelium and thickness can occur due to factors that play a role in ARMD a etiology, such as increasing age, hypoxia and oxidative stress.[7] In the present study, we compared cornea specular microscopy and central cornea thickness (CCT) parameters between eyes with dry or wet ARMD and healthy eyes.

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MATERIALS AND METHOD

After obtaining an approval from the ethics committee of the Karabuk University Faculty of Medicine, patients admitted to the eye clinic of the Karabuk Training and Research hospital were prospectively evaluated. Among the 60 eyes of 30 patients with dry ARMD in one eye and wet ARMD in the other eye, the eyes with wet ARMD were categorised into Group 1 and those with dry ARMD were categorised into Group 2. The control group (Group 3) comprised 50 eyes of 50 patients who were admitted to the clinic for refraction defects. Patients who underwent any type of ocular surgery or who had a history of ocular or systemic medication use were excluded from the study. Evaluations were performed at the time of first admission of the patients. CCT was performed using an ultrasonic pachymetry device (Quentel Medical Clermont-Fernand, France), and corneal examination was performed using a specular microscopy device (Topcon SP-1P, Japan). Endothelial cell density (CD), coefficient of variation (CV) and hexagonality (HEX) values were determined.

Data was statistically analysed using the SPSS 22 (Statistical Package for Social Sciences-SPSS, Inc., Chicago, Illinois) package programme, and the results were presented as mean±standard deviation. The comparison of the treatment groups regarding gender was performed using the chi-square test. Numerical variables were evaluated using the independent *t*-test in independent groups and using the paired *t*-test in dependent groups. $P<0.05$ was accepted as the level of significance.

RESULTS

There were 17 men and 13 women in the ARMD group with an average age of 71.76±5.26 years, whereas there were 27 men and 23 women in the control group with an average age of 70.14±2.14 years, and the difference between these groups was not statistically significant (p=0.96 and 0.11, respectively). Groups 1, 2 and 3 had CCT of 534.0±20.34, 528.46±24.26 and 513.04±33.47 µm, an CD of 2312.43±740.81, 2451.40±587.42 and 2414.22±379.91 cells/mm^2, a CV of 33.60±7.08%, 34.30±5.65% and 33.74±4.78% and a HEX of 52.80±9.57%, 51.96±7.06% and 52.74±9.16%, respectively (Table 1). In terms of CCT, no statistical difference was noted between Groups 1 and 2 (p=0.34), whereas a statistical difference was observed between Groups 1 and 3 (p=0.003) and between Groups 2 and 3 (p=0.031). In terms of CD, there was no statistical difference between Groups 1 and 2, Groups 1 and 3 and Groups 2 and 3 (p=0.48, p=0.41 and p=0.73, respectively). In terms of CV, there was no statistical difference between Groups 1 and 2, Groups 1 and 3 and Groups 2 and 3 (p=0.64, p=0.91 and p=0.63, respectively). Moreover, no statistical difference was noted regarding HEX between Groups 1 and 2, Groups 1 and 3 and Groups 2 and 3 (p=0.70, p=0.97 and p=0.69, respectively).

DISCUSSION

ARMD, RPE and photoreceptor degeneration are characterized by lipofuscin accumulation in RPE, chronic inflammation and drusen accumulation. It is also related to the pathogenesis of chronic oxidative stress disease. It is believed that in wet ARMD, the immune reaction resulting on the tissue due to cellular stress and/or RPE damage promotes proangiogenic factor production and causes choroidal neovascularisation.[7,8]

Corneal CD decreases significantly until the early puberty period, especially during the first few years after birth. Previous studies demonstrated a decrease in the average number of endothelial cells and a significant increase in pleomorphism in the population, particularly people aged >50 years.[9] The average age-related endothelial loss is 0.5% per year.[10] Contradictory to this study, a study conducted by Wilson et al. on 275 normal human eyes emphasised that the number of endothelial cells decrease until the age of 50 years and that there is no significant decrease after the age of 50 years.[11] In the present study, no difference was observed with respect to CD, CV and HEX values among the ARMD groups and between the ARMD groups and control group. However, CD was found to be lower in patients in Group 1 than that in patients in

Table 1. *Central corneal thickness (CCT) cell density (CD), coefficient of variation (CV), hexagonality (HEX) values in groups.*

	GROUP 1	GROUP 2	GROUP 3
CCT	534.0±20.34 µm	528.46± 24.26 µm	513.04±33.47 µm
CD	2312.43±740.81 cells/mm^2	2451.40±587.42 cells/mm^2	2414.22±379.91cells/mm^2
CV	% 33.60±7.08	% 34.30±5.65	% 33.74±4.78
HEX	% 52.80±9.57	% 51.96±7.06	% 52.74±9.16

other groups, although this difference was not statistically significant. This result demonstrated that there is a need to conduct studies with a larger number of patients. This may be an important result for preoperative, perioperative and postoperative periods in intraocular surgeries such as cataract, especially in patients with wet ARMD.

Another study conducted by Faragher et al. clinically and experimentally examined age-related changes associated with the corneal endothelium. Based on the results, they determined that the annual decrease in cell density between the ages of 20 and 80 years is approximately 6% and that this was also accompanied by an increase in polymegathism and pleomorphism. Moreover, the Descemet's membrane was found to have increased in thickness. It is believed that the loss of endothelial cells during ageing may be due to environmental factors such as hormonal changes, ultraviolet rays and chemical toxicities.[12] A study by Murphy et al. assessed the thickening and morphing of the human Descemet's membrane from the 12th week until the 98th week of pregnancy using a light microscope and electron microscope. Based on the result of the study, it was considered that age-related thickening in the Descemet's membrane is related to the continuous synthesis of this membrane by the corneal endothelium.[13] The ability of endothelial cells to undergo mitosis is very low or non-existent. When the number of cells decreases due to the natural cell death caused by ageing or a small trauma in a region of the endothelium, neighbouring endothelial cells without the ability to undergo mitosis try to fill the gap by changing their sizes and shapes.[14] Loss of or damage to endothelial cells disrupts the functioning of the endothelial layer and indirectly provides information regarding the corneal endothelium function.[15] In a previous study, 100 eyes (100 patients,1 eye of each patient) were included in the ARMD group, whereas 116 eyes (116 patients, 1 eye of each patient) were included in the control group. Half of the 100 eyes exhibited wet ARMD and the other half exhibited dry ARMD. The difference in CCT was not statistically significant between eyes with wet and dry ARMDs and the control eyes.[16] In our study, CCT was significantly higher among the patients with ARMD than that in patients in the control group. It was also higher in eyes with wet ARMD than that in eyes with dry ARMD, although the difference was not statistically significant.

The increase in intraocular pressure (IOP) is considered to be the most important risk factor for the development and progression of glaucoma.[17] In many studies, a positive relationship has been shown between IOP measurements and CCT values. When a patient is being evaluated for glaucoma, it is extremely important to determine the CCT value along with assessing IOP.[18,19] Based on the results of our study, we recommend that increased CCT values should be taken into consideration in the IOP evaluation of patients with ARMD, especially those with wet ARMD.

In conclusion, oxidative, immunologic and/or inflammatory mechanisms in patients with ARMD can, for a variety of reasons, lead to significant changes in corneal thickness and also cause other changes in the corneal endothelium that are not statistically significant.

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