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ORIGINAL ARTICLE – OPEN ACCESS

Assessment of Anterior Segment Parameters and Specular Microscopy Findings in Patients with COPD

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ABSTRACT

Objective: The aim of the present study was to assess the anterior segment parameters of patients with chronic obstructive pulmonary disease (COPD) by corneal specular microscopy and biometry and to compare the results with healthy controls.

Materials and Methods: Our prospective study consisted of 122 eyes of 61 patients with COPD and 110 eyes of 55 patients without any systemic diseases. A comprehensive medical history was obtained, and corrected visual acuity, bio microscopic and fundus examination, intraocular pressure (IOP) measurement with applanation tonometry, and non-contact specular microscopy were performed in all participants.

Results: The endothelial cell density was lower in the COPD group than in the control group ($p<0.001$). The coefficient of variation (CV) was higher, central corneal thickness was significantly higher, and hexagonal cell ratio (HEX) was lesser in the COPD group than in the control group ($p<0.001$). Any significant difference between the control and the COPD groups was not determined in comparison with IOP, mean axial length keratometry (Kmean), anterior chamber depth (ACD), and white-to-white limbus length (WTW) measurements. Patients were grouped into two regarding the disease severity as mild–moderate (group 1, n=20), and moderate–severe (group 2, n=41) according to the Global Initiative for Chronic Obstructive Lung Disease criteria. The number of endothelial cells was lesser, the CV was higher, and the HEX was lower in the moderate–severe COPD group than in the mild–moderate COPD group ($p<0.001$). The duration of smoking was significantly longer in the moderate–severe group than in the mild–moderate COPD group ($p<0.001$).

Conclusion: We suggest that in patients with COPD, due to the reduction of endothelial functional preserve, the risk of corneal endothelial damage is increased in intraocular surgery. In patients with end-stage COPD, caution should be exercised with regard to endothelial decompensation, frequent disease in the general population, corneal parameters, and to define the alterations that the ocular surgeons should be cautious about. Data regarding the alterations in anterior segment parameters in patients with COPD are highly limited in the previous literature.

Keywords: Specular microscopy, chronic obstructive pulmonary disease, corneal endothelial cell

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common health issue defined by permanent airflow limitation and respiratory symptoms due to alveolar abnormalities that develop as a result of significant exposure to harmful particles or gases (1). COPD is a preventable and treatable disease, yet COPD is a leading cause of morbidity and mortality worldwide. The prevalence is generally associated with direct tobacco use, but in many countries the main risk factors are occupational exposure, external, and internal air pollution (1).

Hypoxia associated with COPD can have an impact on many organs and tissues in the body. Tissue hypoxia and oxidative stress are the main mechanisms responsible for the general effects of COPD (2, 3). Like other organs, ocular structures are also influenced by the systemic alterations associated with COPD. There are many studies indicating that the eye layers, such as the retina and the choroid, are affected in COPD patients (4, 5).

Corneal endothelial cells avoid the formation of edema in the cornea by preventing the passage of fluid into the stroma through the active pump function and play a vital role in maintaining normal corneal transparency (6). Corneal endothelial cells are highly sensitive to hypoxia (7). Since corneal endothelial cells have limited mitotic capacity, in response to cell loss, neighboring endothelial cells expand and compensate. As a result, the coefficient of variation (CV) increases and the hexagonal cell ratio decreases. In clinical practice, non-contact specular microscopy is used to evaluate corneal endothelial cell density (ECD) and morphology. Data about corneal endothelial specular microscopy findings in COPD patients remain very limited. Significantly, the results of one study showed that the preoperative corneal endothelial reserve was weak in patients with respiratory diseases, including COPD (8).

This study was a comparison of corneal endothelial measurements in a group of COPD patients categorized according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria and a control group. The ob-

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

	COPD (n=61)	Control (n=55)	p
Age (years)	62.11±8.94	63.71±10.00	**0.233**
Gender (M/F)	40/21	35/20	0.541
IOP (mmHg)	13.68±3.21	13.94±1.34	0.438
Number of cells	161.60±33.11	145.97±36.04	**0.001**
Corneal endothelial cell density (cell/mm^2)	2367.32±341.78	2561.35±144.02	**0.001**
Cell size variation (%)	34.30±6.49	31.20±4.63	**0.001**
Hexagonality (%)	59.80±4.89	67.18±8.14	**0.001**
Central corneal thickness (µm)	552.20±36.27	523.39±27.99	**0.001**
Keratometry	44.20±1.68	44.23±1.60	0.890
Axial length	22.82±0.85	22.94±0.83	0.280
Anterior chamber depth	3.13±0.31	3.15±0.32	0.370
White-to-white limbus length	11.64±0.46	11.67±0.39	0.218

COPD: Chronic obstructive pulmonary disease; M: Male; F: Female; IOP: Intraocular pressure

jective was to analyze the effects of COPD on corneal parameters, to examine changes that could have a significant impact on ocular surgery and to make a contribution to the existing data regarding alterations in anterior segment parameters in patients with COPD.

MATERIALS and METHODS

Our prospective study consisted of 61 patients aged between 40 and 85 years who were diagnosed with COPD in Erzincan Binali Yıldırım University, Medical Faculty, Mengücek Gazi Training and Research Hospital, Chest Diseases Clinic and 55 age- and gender-matched non-smoker control cases. The COPD diagnosis was performed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.

The study was approved by the ethics committee of Erzincan Mengücek Gazi Training and Research Hospital (date: 10/16/2018, no.: 32/07). Informed consent was obtained from all participants. Medications, disease duration, and smoking history (pack/year) were recorded in all patients. Patients with COPD were further grouped into two as mild to moderate and moderate to severe COPD groups according to the GOLD criteria.

Patients with a history of corneal disease, intraocular surgery, glaucoma, uveitis, or ocular trauma, contact lens users, ocular diseases that may affect the corneal endothelium, and patients with systemic diseases, such as diabetes or renal failure, were excluded from the study. A comprehensive medical history was obtained, and visual acuity determination, bio microscopic, and fundus examination, and IOP measurement with applanation tonometry were performed in all patients. Corneal endothelial measurements were performed with non-contact specular microscopy device (CEM-530 Specular Microscope; NIDEK, Japan) in all patients, and control cases. Central corneal thickness (CCT), corneal endothelial cell density (ECD) (cell/mm^2), percentage of corneal endothelial hexagonal cell ratio (HEX), and coefficient of variation (CV) were recorded. Axial length (AL) and keratometry were measured using an ocular biometry system (AL-Scan Optical Biometer; NIDEK). ACD is the distance between anterior corneal and lens surfaces, and it was also determined by ocular biometry system. Biometrical measurements and specular microscopy findings were compared between patients with COPD and the control group; moreover, patients with COPD were further sub grouped into two according to the GOLD criteria, and those two groups were compared.

Statistical Analyses

IBM SPSS Statistics 22 program (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. The chi-square test was used for comparing nominal data. The independent t-test was used as a parametric test to compare normally distributed data, and the Mann–Whitney U test was performed for non-normally distributed data. Pearson correlation analysis was used for evaluating the data correlations between specular microscopy findings and smoking status. A p value <0.05 was considered significant.

RESULTS

The study included 122 eyes of 61 patients with COPD and 110 eyes of 55 patients without any systemic diseases. The mean ages of the patients were 62.11±8.9 years in the patient group and 64.71±10.0 years in the control group (p=0.233). Demographic features of the two groups were not significantly different. The ECD and the HEX were lesser, whereas the CV was higher in the COPD group than in the control group (p<0.001) (Table 1). IOP, mean axial length keratometry (Kmean), ACD, and WTW evaluations were not significantly different between the control and patient groups. When the COPD and control groups were compared, CCT was significantly higher in the patient group (p<0.001) (Table 1).

Patients with COPD were further divided into two subgroups as mild–moderate (group 1) and moderate–severe (group 2) according to the GOLD criteria. The specular microscopy findings of patients with COPD sub grouped according to the GOLD criteria are shown in Table 2. Group 1 consisted of 20 individuals; group 2 consisted of 41 age- and gender-matched patients. When the ECD was compared between the groups, it was found that

Table 2. Findings of specular microscopy according to the GOLD criteria

	GOLD 1-2	GOLD 3-4	p
Mean age (years)	62.11±8.94	62.71±10.00	0.340
Gender (M/F)	21/20	10/10	0.544
Smoking (pocket/year)	29.23±15.91	43.65±22.23	**0.001**
IOP (mmHg)	13.88±3.21	13.62±1.34	0.43
Number of cells	163.05±32.61	157.85±34.57	**0.002**
Corneal endothelial cell density cell/mm^2	2459.97±303.18	2327.53±322.29	**0.001**
Cell size Variation (%)	33.87±4.48	36.56±6.73	**0.001**
Hexagonality (%)	62.08±4.50	55.50±4.30	**0.001**
Central corneal thickness (µm)	550±29.44	558.38±49.27	0.090
Keratometry	44.37±1.65	43.76±1.70	0.180
Axial length	22.84±0.88	22.77±0.79	0.523
Anterior chamber depth	3.10±0.33	3.10±0.28	0.820
White-to-white limbus length	11.61±0.46	11.62±0.47	0.640

COPD: Chronic obstructive pulmonary disease; M: Male; F: Female; IOP: Intraocular pressure

Table 3. Correlation analysis of smoking with ocular parameters in patients with COPD

	R	P
Number of cells	-0.112	0.403
Corneal endothelial cell density (cell/mm^2)	-0.171	0.184
Cell size variation (%)	0.151	0.249
Hexagonality (%)	-0.228	0.081
Central corneal thickness (µm)	0.089	0.499
Keratometry	0.055	0.678
Axial length	0.088	0.503
Anterior chamber depth	0.034	0.795
White-to-white limbus length	0.151	0.249

COPD: Chronic obstructive pulmonary disease; r: Correlation coefficient

the number of endothelial cells in patients with moderate–severe COPD was less than that in patients with mild–moderate COPD ($p<0.001$) (Table 2). The CV was higher in the moderate–severe COPD group ($p<0.001$). The HEX was lower in the moderate–severe group than in the mild–moderate group ($p<0.001$) (Table 2).

When subgroups of patients with COPD were compared, CCT, AL, mean keratometry value, ACD, WTW, and IOP measurements were not different significantly (Table 2).

In patients with COPD, correlation analysis was performed between specular microscopy findings and smoking status (Table 3). We did not determine any significant correlation between any specular microscopy parameters and smoking.

DISCUSSION

In the present study, in the COPD group, there were a decrease in ECD, and hexagonal cell numbers and an increase in the CV showing the compensatory response compared with the control group. We found that alterations in corneal endothelial morphology augmented with the increased severity of the disease.

COPD is a systemic disease affecting many organs and systems. Difficulties in breathing and eliminating CO_2 from the lungs result in hypercapnia, hypoxia, and respiratory acidosis, exacerbating oxidative stress and inflammatory responses in patients with COPD (9, 10). This oxidative stress and inflammatory response are responsible for the systemic alterations determined in COPD.

Data regarding the alterations in corneal endothelial cells in patients with COPD are limited. Soler et al. (11) analyzed the alterations in corneal endothelial cells in 172 patients (110 with COPD and 62 control) and reported that patients with COPD have significant decrease in corneal thickness, ECD, and hexagonality and a significant increase in CV. Moreover, they showed that there is a direct association between ECD and an antioxidant enzyme paraoxonase-1. In another prospective study, the authors reported that in patients with COPD, cell density, and hexagonal cell percentage were lower, whereas CV was higher in the preoperative period before cataract surgery with an increase in susceptibility to intraocular surgical stress (12).

Margo et al. (13) also reported decreased corneal endothelial cell count in patients with COPD who were investigated for being corneal donors. In the same way, chronic pulmonary disease was reported as a significant threat for decreased ECD before cataract surgery (8). The results of all these studies were compatible with our results. In addition, as the severity of the disease increased, the percentage of ECD, and hexagonal cells decreased, and CV increased. Recently, hypoxia was shown to reduce the expression of vascular endothelial growth factor in human corneal epithelial cells, which may play a role in the pathophysiological mechanisms of decreased ECD in patients with COPD (14). Although the endothelium is an avascular tissue and does not resemble the epithelial tissue, hypoxia may also alter the expression of some other growth factors.

Unfortunately, the corneal endothelial cells are not capable of mitosis and regeneration. With the expansion of cell size, the compensatory mechanism is filled with the missing cells. This results in increased cellular pleomorphism and decreased percentage of hexagonal cells. The result of chronic hypoxia in COPD explains this compensatory mechanism of change in endothelial cells. We found that this change increased with the severity of the disease.

Smoking is one of the main etiological factors in COPD. Among our patients, smoking was significantly more common, defined as pack/years, in the moderate–severe COPD group. Golabchi et al. reported that smoking results in an increased CV and decreased ECD (15). Ilhan et al. (16) reported that smoking does not affect the CCT, CV, and percentage of hexagonality values, but there was a significant reduction in ECD in smokers. However, Kara et al. (17) did not determine any significant difference between smokers and non-smokers regarding the mean ECD or parameters of endothelial cell morphology. In our study, we determined a significant difference regarding the smoking status between two subgroups of patients with COPD; moreover, number of cells, ECD, and hexagonality were significantly lower, and CV was significantly higher in the smoking group. However, we did not determine any significant correlation between specular microscopy findings and smoking. Very recently, Cankurtaran et al. (18) reported that neither only diabetes mellitus nor only smoking has a significant effect on corneal endothelial measurements, but the coexistence of diabetes, and smoking results in a significant reduction in ECD. Smoking is clearly known to cause an oxidative stress burden in all tissues of the body (19). However, since there was no any correlation between the smoking status and alterations in ocular structures in patients with COPD, it can be concluded that the only mechanism in those alterations is not the oxidative stress burden associated with smoking. COPD is defined as the premature aging of the lungs associated with chronic inflammation. It should be emphasized that only 15%–20% of smokers develop clinically significant COPD, not all smokers directly become patients with COPD (20). Genetic factors and previous exposure of the individuals to the pathogens also play a role in COPD development. For those reasons, we did not determine any significant correlation between smoking status and ocular alterations.

CONCLUSION

In conclusion, COPD reduces the endothelial functional reserve and increases the risk of corneal endothelial damage in intraocular surgery. Therefore, in patients with COPD, the augmented risk of corneal decompensation, which increases as the severity of the disease increases, should be kept in mind. In end-stage COPD disease, caution should be exercised with regard to endothelial decompensation. To minimize endothelial damage during cataract surgery and other surgeries, endothelial protective maneuvers should be performed if necessary, and preoperative specular microscopy findings should be examined carefully in these patients.

Ethics Committee Approval: Ethics Committee of Erzincan Mengücekgazi Training and Research Hospital approved the study (date: 16.10.2018, number: 32/07).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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