The Optical Biometric Measurements In Patients With Previously Received Covid-19 Treatment

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Abstract

Purpose: To determine the comparison of the optical biometric measurements using optical biometry in patients with previously received COVID-19 treatment and the control group.

Methods: In this cross-sectional study, the COVID-19 was diagnosed by polymerase chain reaction test, clinical signs and radiologic findings. Patients with previously received COVID-19 treatment was determined as COVID-19 group and the age and sex-matched healthy subjects were served as control group. The optical biometric measurements including corneal astigmatism, keratometry, astigmatic axis, central corneal thickness, anterior chamber depth and axial length were obtained using Nidek optical biometry (AL-Scan; Nidek Co., Ltd., Japan).

Results: The measurements of keratometry(p=0,47), corneal astigmatism(p=0,42), axial length(p=0,78), anterior chamber depth(p=0,46) and central corneal thickness(p=0,43) were similar between the COVID-19 and control groups. The astigmatic axis type taken from 2.4 mm of the cornea showed statistically significant difference between two groups (p=0,01), while the measurements taken from 3 mm of the cornea were similar(p=0,15). In the subgroup analysis, axial lenght, anterior chamber depth and central corneal thickness measurements were found statistically significantly higher in the male gender of the COVID-19 group (p= 0,03; p= 0,01; p=0,03, Mann Whitney U).

Conclusion: Changing in the optical biometric measurements can be seen as a result of the fact that COVID-19 is more frequent and severe in male gender and SARS-CoV-2 can attach to the cornea via ACE-2 receptors. To our knowledge, there is no study about this subject yet and conducting research with other studies on this issue will provide a better enlightenment about this subject.

Introduction

In December 2019, an epidemic of pneumonia, which first appeared in Wuhan, China and caused by SARS-CoV-2, was declared by the World Health Organization as a global pandemic[1 – 3]. SARS-CoV-2 was reported as the main agent of Coronavirus disease 19(COVID-19) and the most common symptoms of COVID-19 have been reported as fever, dry cough, nausea, muscle and joint pain, breathlessness, and diarrhea[4, 5]. Although it was reported that the disease was mainly transmitted by direct contact of respiratory droplets of infected individuals and mostly affects the respiratory tract, the effect on many other organs and the presence of virus in tears had also been shown[6 – 10]. It has been suggested that the severity of the disease is related not only to viral infection but also to host response[11]. Previous studies reported that Angiotensin Converting enzyme-2 (ACE-2) receptors may be effective in the pathogenesis of COVID-19 related organ failure[8]. As far as we know, the corneal tissue also contains ACE receptors[12 – 13] and SARS-CoV-2 was found in tear samples[6 – 10].

Therefore, in current study, we aimed to compare the optical biometric measurements of the patients who previously received COVID-19 treatment and the healthy control group to show the effect of COVID-19 on

the cornea.

Material And Methods

This study was carried out after the approval of the local ethics committee in accordance with the tenets of the Helsinki Declaration.

Patients and Method

In this study, 102 eyes of 51 patients who previously received COVID-19 treatment and 102 eyes of 51 healthy control group with similar age and gender were examined. The patients in the COVID-19 group were diagnosed according to the clinical and radiological findings and Polymerase Chain Reaction(PCR) test result. All patients were hospitalized and received Favipiravir and Moxifloxacin treatment due to interstitial pneumonia. None of the patients had ocular complaints during COVID-19 infection and none of the patients required for entubation. All patients had a detailed ophthalmic examination including best corrected visual acuity(BCVA), intraocular pressure(IOP, mmHg) measured with applanation tonometry, anterior and posterior segment examination by slit-lamp biomicroscopy, and optical biometric measurements (corneal astigmatism, keratometry, astigmatic axis, central corneal thickness, anterior chamber depth and axial length) using Nidek optical biometry (AL-Scan; Nidek Co., Ltd., Japan). In COVID-19 group, the patients were assessed one month after completion of their treatment. Measurements were performed by an experienced assistant after pupil dilation with 1% Cyclopentolat drop to avoid errors in optical biometric measurements. In both groups, patients with poor tear film stability, high intraocular pressure, > 6.0 diopter refraction, glaucoma, ocular inflammation, cataracts, corneal disease and previous surgical history were excluded from the study. All measurements of the COVID-19 group and the healthy control group were statistically compared.

Statistics

Statistical analysis of this study was performed using SPSS software version 21.0 (IBM Corp., Armonk, NY, USA). Whether the variables were normally distributed was evaluated using Shapiro-Wilk test. While explaining continuous variables, mean standard deviation values were used for normally distributed data and median values were used for non-normally distributed data. The measurements of keratometry, corneal astigmatism, central corneal thickness, axial length and anterior chamber depth were analyzed using the Mann Whitney U test. Values less than 0.05 were interpreted as statistically significant.

Results

In the COVID-19 group, there were 26 male and 25 female patients with a mean age of 47,09 ± 13,32(19-66) years. The PCR test result was (+) in 79% of the patients. All patients had also diffuse interstitial pneumonia. In the healthy control group, 26 male and 25 female patients with a mean age of 47,30 ± 5,9(35-61) years were evaluated. The proinflammatory cytokine values of the patients in the COVID-19 group are shown in table 1.

Table 1

The mean levels of the proinflammatory cytokines in COVID-19.

Parameters (mean ± SD*)	COVID-19 Group	Normal Range
CRP	44.16 ± 52.5 mg/L	0-5 mg/L
Ferritin	727 ± 1113.11 mg/L	30-400 mg/L
D_dimer	0.42 ± 0.69 mg/mL	<0,5 mg/mL

*SD: Standard deviation, CRP; C- reactive protein

The biometrical measurements obtained from the COVID-19 and healthy control groups are shown in table 2.

Table 2

The biometric results of the patients in COVID-19 group and healthy control group.

Parameters	COVID-19 group*	Control group*	P**
Keratometry in 2.4mm	43,29 D	42,57 D	0,47
Keratometry in 3.3mm	43,36 D	42,54 D	0,51
Corneal astigmatism in 2.4mm	0,71 D	0,62 D	0,42
Corneal astigmatism in 3.3mm	0,62 D	0,61 D	0,97
AL	23,47 mm	23,29 mm	0,78
ACD	3,35 mm	3,26 mm	0,46
CCT	558 mm	561 mm	0,43

*Median,**Mann Whitney-U, AL; Axial length, ACD; Anterior chamber depth, CCT; Central corneal thickness

In the COVID-19 group, according to the results of the astigmatic axis which was measured at 2.4 mm of the cornea, 51.2% of the patients had with the rule astigmatism, 16.3% of them had against the rule astigmatism and 32.6% of them had oblique astigmatism. However, the measurements obtained from 3.3 mm of the cornea showed that 53.5% of them were with the rule astigmatism, 9.3% of them were against the rule astigmatism and 37.2% of them were oblique astigmatism. In healthy control group, the astigmatic axis obtained from both 2.4 mm and 3.3 mm of the cornea were same and 67.5% of them were with the rule astigmatism and 32.5% of them were oblique astigmatism. The chi-square relationship test performed to determine the corneal astigmatism type relationship between the COVID-19 group and the control group found that the astigmatic axis type in the 2.4 mm of the cornea was statistically

significantly different (p=0.01), while the measurements obtained from 3.3 mm of the cornea were similar(p=0.15).

The subgroup analysis was performed by gender between two groups, and it was determined that AL, ACD and CCT measurements were statistically significantly higher in the male gender in the COVID-19 group (p= 0.03; p= 0.01; p=0.03, Mann Whitney U), while all parameters were similar between both genders in the healthy control group.

Discussion

Coronaviruses are single-stranded RNA viruses that encode structural and non-structural proteins in their genome. Structural proteins are responsible for viral infection and replication, while non-structural proteins (S protein) provide attachment between the coronavirus and the host cell[14]. The Angiotensin Converting enzyme-2 (ACE) receptor[8],cell surface proteaase enzyme(TMPRSS2) and CD147 transmembrane protein have also been reported to be effective in enabling the SARS-CoV-2 to enter the host cell[15]. Previous studies showed the ACE-2 receptor in conjunctiva, cornea[12, 13], aqueous humor[6, 16], limbus, ciliary body[13], choroid, retina mullerian cell, ganglion cell, retinal vascular endothelial cell, photoreceptor cells[17] and retina pigment epithelium[13], besides that, in the respiratory tract, gastrointestinal system, and endothelial cells[17]. TMPRSS2 has not been demonstrated in tear, cornea and conjunctival epithelium, but association with ACE-2 genes has been demonstrated in some conjunctival cells[18]. Although corneal tissue has a physical barrier against to pathogen entrance, ACE-2 and CD147, also expressed in corneal cells, may make it easier for the virus to enter the cell[19].

We conducted this study based on the hypothesis that COVID-19 can make changes in optical biometric measurements on the cornea via ACE-2 and CD147. According to the current study, we could not find any statistically significant differance in keratometric values, corneal astigmatism values, axial length, anterior chamber depth and central corneal thickness measurements between the COVID-19 group and the healthy control group. In addition, the measurements obtained from 2.4 mm of the cornea showed statistically significant difference in the astigmatic axis type.

These results were thought to be related to the number of ACE-2 receptors in the cornea. In previous studies, although the ACE-2 receptor has been demonstrated in the cornea and conjunctival epithelium[20, 21], it has shown that the number of receptors in the cornea and conjunctival tissue is 5–20 fold lower than in the heart and lung tissue[12, 21]. The results of current study can be explained by the lack of sufficient number of ACE-2 receptors that could make significant keratometric changes in cornea.

The results of subgroup analysis can be attributed to the predisposition of the disease in men, in which some studies reported that severe morbidity and mortality are more common in the male sex[22, 23]. The more viral load and more severe disease may explain the higher AL, ACD and CCT measurements in men.

Consequently, COVID can affect the keratometric values and may be exacerbated the disease of especially in male patients with keratoconus.

To our knowledge, there is no previously report about optical biometric results in COVID-19 patients. Conducting other studies for investigating the corneal involvement by SARS-CoV-2 will provide a better enlightenment on this subject.

Declarations

ACKNOWLEDGEMENT

We have no conflict of interest for this study.

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