COVID-19: Transmission Through the Ocular Surface and Implications on Clinical Practice in Cornea, Cataract and Refractive Surgery Patients

M. Cuneyt OZMEN[1], Bahri AYDIN[2], Fikret AKATA[2]

ABSTRACT

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is responsible for the coronavirus disease-19 (COVID-19) pandemic, which has affected ophthalmology among other medical specialties. The virus is transmitted by person-to person contact, exposure to contaminated surfaces, or via aerosols carrying infective particles usually originating from respiratory tract. Furthermore, there is evidence suggesting that the ocular surface may be a site for infection. The purpose of this review is to examine transmission of COVID-19 through the ocular surface and review the major guidelines regarding the management of cornea, the ocular surface, cataract and refractive surgery patients.

Keywords: COVID-19, Coronavirus, SARS-CoV-2, Pandemic, Cornea, The ocular surface, Cataract, Refractive surgery.

INTRODUCTION

Since December 2019, the world has been dealing with severe acute respiratory syndrome (SARS) corona virus-2 (CoV-2) disease (COVID-19), which was declared a pandemic by the World Health Organization (WHO) on March 11th, 2020.[1] As of May 2020, COVID-19 has affected more than 5 million people and caused more than 300,000 deaths.[2] One of the earlier deaths from COVID-19 was an ophthalmologist from Wuhan Central Hospital, who reportedly contracted the SARS-CoV-2 from a glaucoma patient.[3] Peking University reported that a member of the national expert panel on pneumonia was infected by SARS-CoV-2 even though he was wearing an N-95 mask.[4] Authors suggest that exposure of the eyes to SARS-CoV-2 might have allowed the virus to infect the body.[4,5] Recently Wu et al.[6] showed that although only 2 out of 38 patients were positive for SARS-CoV-2 in their conjunctival specimens, 31.6% of patients had ocular findings. Further, they conclude that transmission of the disease through ocular secretions may be possible.[6] However, SARS-CoV-2 infection through ocular transmission has not been well studied.

Ophthalmology, among other specialties, strongly relies on biomicroscopic examination for diagnosis from a short distance from the patient. Center for Disease Control describes close contact as being less than 2 meters from a patient for a prolonged duration (any contact longer than 1-2 minutes).[7] Although ophthalmologists do not perform aerosol-generating procedures during examination, close contact and prolonged duration during ophthalmic examinations could increase the risk of exposure and transmission of SARS-CoV-2. Thus, many countries, government organizations, and ophthalmological associations proposed examination and surgery guidelines for ophthalmologists.

The purpose of this review is to assess the recent literature regarding the potential transmission of SARS-CoV-2 to and from the ocular surface as well as to report the latest guidelines on the management of cornea, the ocular surface, cataract and refractive surgery patients.

Literature Search

A literature search was conducted on 28/05/2020 in the SCOPUS database using the search terms: “COVID” AND “ophthalmology” OR “ocular surface” OR “cornea”

1- MD., FICO, Gazi University Medical School, Ophthalmology Department, Ankara, Turkey

2- MD., FICO, Gazi University Medical School, Ophthalmology Department, Ankara, Turkey

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Correspondence Adress:
Mehmet Cuneyt OZMEN
Gazi University Medical School, Ophthalmology Department, Ankara, Turkey

Phone: +90 532 242 0367
E-mail: mcozmen@gmail.com

OR "cataract" OR "refractive surgery" with a filter of publication date within 1 year. Abstracts of these documents were read and those pertinent to the purpose of this review were downloaded and examined. Any related documents to these were also downloaded regardless of their publication date. Latest guidelines for ophthalmology practice from American Academy of Ophthalmology (AAO), Royal College of Ophthalmologists (RCOphth), Turkish Ministry of Health, and Turkish Ophthalmological Association were obtained and reviewed.

Transmission of COVID-19 via Ocular Surface

SARS-CoV-2 is a beta corona virus.[8] From a genetic standpoint SARS-CoV-2 is 70% similar to SARS-CoV. Therefore, it is capable of using the same receptor (ACE2) to infect human cells.[9,10] However, it has been shown that SARS-CoV-2 binds to human ACE2 receptors with 10 to 20 times higher affinity than SARS-CoV.[11] Once inside a human body SARS-CoV-2 causes severe, life-threatening pneumonia.[10] Respiratory tract should not be considered as the only route of infection. It is known that SARS-CoV-2 can be transmitted through direct or indirect contact with conjunctiva, mucous membranes (e.g. mouth and nose).[5,12,13] Proposed ocular involvement include; direct inoculation of conjunctiva with infected aerosols, migration through nasolacrimal duct during an upper respiratory tract infection, and endogenous infection of the ocular surface through conjunctival vessels. [8,14]

A recent study showed that one third of clinically confirmed COVID-19 patients (n=38) showed ocular manifestations similar to conjunctivitis including hyperemia, chemosis, epiphora, or increased secretions.[6] Seah et al.[14] studied viral shedding and infectivity of tears in COVID-19 patients and showed that all samples were negative for SARS-CoV-2 on viral isolation and real time polymerase chain reaction (RT-PCR).[14] The authors conclude by stating that the risk for SARS-CoV-2 transmission via tears is low.[14] However, this study has many limitations, such as the tear collection method (Schirmer's strip), low sensitivity of RT-PCR to detect small quantities of viral particles, and missing the viral particles in the ocular surface cells, which are not secreted in the tear.[15]

Another study examined conjunctival swabs from lower fornix and sputum samples, which were obtained at the same time (n=30, two samples were obtained 3 days apart). Viral RNA was positive in 96.6% of sputum samples in contrast to 3% positive results in conjunctival swabs.[12] The only conjunctival swab positive patient had conjunctivitis, however, the virus could not be isolated and cultured from this patients conjunctival secretions.

Studies suggest very low risk of infection through the ocular surface. The evidence regarding SARS-CoV-2 transmission through the ocular surface is anecdotal.[3-5] Some authors even propose that eye itself is unlikely to be a route for transmission.[8] Even if there is a very low risk of transmission through tears, ophthalmologists and other specialist who work in close proximity of patients should protect their eyes (e.g. goggles, protective sheets mounted on biomicroscopes) until further research is done.

Management of Cornea, the Ocular Surface, Cataract and Refractive Surgery Clinics

During the COVID-19 pandemic, many countries restricted elective examinations and surgeries to reduce the transmission of the virus. Turkish Ministry of Health has proposed performing only the urgent and emergent surgical procedures and Turkish Ophthalmological Association has published urgent and emergent ophthalmic surgical procedures (Table 1).[16] AAO,[17] RCOphth,[18] and many other ophthalmological associations have published guidelines for ophthalmologists. We have summarized these guidelines to be specific about the ocular surface and anterior segment of the eye. We further expanded the section with additional information from studies and personal experience.

During the COVID-19 pandemic, everyone (patients, physicians, and health care workers) should protect themselves by using the appropriate personal protective equipment (PPE) and obeying social distancing rules. At-risk patients should be detected by COVID-19 symptom analysis by triage personnel before getting in the ophthalmology department.[18,19] Keep in mind that our knowledge about SARS-CoV-2 and COVID-19 is changing rapidly. Please refer to the latest guidelines.

Cornea and the Ocular Surface

Patients with scheduled routine follow-up appointments for corneal and ocular surface pathologies should continue their medications unless otherwise is suggested by their ophthalmologist and postpone their appointments until further notice. If the symptoms deteriorate, patients should contact their ophthalmologist to decide whether an appointment is necessary.[7,18,19]

New patients with symptoms of reduced visual acuity, red eye, and/or pain should be seen immediately. This is especially important to rule out keratitis, chemical injury, penetrating ocular injury, and acute angle closure glaucoma among many other ophthalmic emergencies.[19]

Table 1 summarizes clinical and surgical patient risk stratification, urgent and emergent surgical procedures.[16-19]

We believe, itching and keratoconus should be prioritized and treated, especially in children under 18-years old. Keratoconus can progress rapidly in the setting of eye

Table 1. *Urgent and emergent surgical procedures for cornea, cataract and refractive surgery patients.[16-19] (CXL: corneal collagen crosslinking).*

Cornea and Cataract Clinic	**Indication**
● **Low risk: Book 4-6 months ahead**	● Blepharitis ● Dry eye disease ● Keratoconus with previous CXL ● Cataract
● **Medium risk: Phone consultation with visit rebooked accordingly**	● Minor trauma ● Abrasions ● Foreign body ● Patients on topical steroids ● Therapeutic contact lens patients ● Routine 1 month follow-up cataract surgery
● **High risk: Face to face visit**	● Microbial keratitis ● Major trauma ● Corneal transplant within 1 month ● Corneal graft rejection ● Complex postoperative cataract complications
Cornea and Cataract Surgery	**Indication**
● Tissue adhesive application ● Repair of corneal perforation ● Tectonic keratoplasty	● Corneal perforation ● Severe corneal thinning
● Amniotic membrane application ● Corneal collagen crosslinking ● Intrastromal antibiotic injection ● Tectonic keratoplasty	● Keratitis/Chemical Trauma
● Keratoplasty	● Pediatric patients with corneal blindness in both eyes in their amblyopic period
● Anterior chamber wash out	● Traumatic hyphema
● Cataract surgery	● Congenital Cataract ● Phacolytic/Phacomorphic glaucoma ● Acute lens complications ● Monocular patients with documented vision loss precluding driving ● Severe anisometropia of fellow eye post recent lens extraction in first eye

rubbing and reduce visual acuity. [20] Furthermore, corneal collagen crosslinking (CXL) for progressive keratoconus, especially in children, may be considered as an urgent ophthalmic surgical procedure.

Cataract and Refractive Surgery

According to many ophthalmological associations in the world, cataract and refractive surgery is elective and should be postponed, aside from the urgent and emergent indications shown in Table 1.[16-18] However, Shih et al.[21] propose to continue elective eye surgeries, specifically cataract surgery that cause morbidity, which can be performed under local anesthesia in areas where community transmission of new infections is kept low.[21] In their correspondence, additional infection control measures are described: 1) prescreening through phone (several days before surgery) and on the day of the surgery, 2) The use of PPE, 3) Social distancing (reducing number of people in the waiting room, limiting accompanying person to 1, increased spacing between patients). Prescreening is described as checking for fever and respiratory symptoms, in addition to history of recent overseas travel and possible contact or exposure to COVID-19 cases.[21] They report performing 136 cataract surgeries with the above defined precautions, without any cases of COVID-19 among the clinical staff and patients.

Phacoemulsification is not classified as an aerosol generating procedure (AGP) in a review by Tran et al,[22] however, Darcy et al.[23] showed that phacoemulsification is an AGP, which may increase the risk for SARS-CoV-2 transmission.[23] They have demonstrated that 2.75 mm phacoemulsification tip generates visible aerosol during

phacoemulsification, however, no visible aerosol were noted with 2.2 mm tip. It is also worth noting that the presence of visible aerosol is regardless of corneal wetting. Coating the cornea with hydroxypropyl methylcellulose (HPMC) annuls visible aerosol production for 67 seconds.[23]

Although elective cataract surgery is currently not recommended, it is wise to use smaller incisions and copious use of HPMC during urgent and emergent cataract surgery.

CONCLUSION

The relationship between COVID-19 and the ocular surface as a potential portal of entry and as a transmission mechanism is currently under discussion. Further research is needed to conclude whether the ocular surface should be considered as a route for transmission of COVID-19. All clinics and ophthalmologists should carefully follow the guidelines and organizational advice. Ophthalmologists should not risk health care workers and patients by exposing them to SARS-CoV-2 unnecessarily, however patients should be seen face to face or operated on whenever necessary. A good communication between patients and ophthalmologists is crucial to navigate through this pandemic.

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