

Coronavirus Disease 2019 (COVID-19): Current Date on Ophthalmological Problems

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The first date on a novel severe acute respiratory syndrome (SARS) were reported in Wuhan, China at the end of 2019. Since that time, the disease caused by the SARS-Coronavirus (CoV) 2 has become a global pandemic COVID-19 [1,2]. SARS-CoV2 spread mainly due to contact with infected patients (also those asymptomatic and PR symptomatic carriers), after exposure to respiratory droplets (talking, sneezing, coughing, breathing) [2,3]. Moreover, contact with infectious particles can be established through surfaces and contaminated objects. Stable virus particles were found on the surface after up to 72 hours, and greater stability on plastic and stainless steel than on copper and cardboard was noted [2,4].

SARS-CoV2 belongs to beta coronavirus family, the same family as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome-related coronavirus (MERS-CoV), which were responsible for previous SARS pandemics in 2002 and 2012 respectively [5-7]. The virus is described as: enveloped positive-sense unsegmented single-strand RNA virus, which genome consists of 29,891 nucleotides in size, encoding 9860 amino acids. Besides, SARS-CoV2 genome is similar to those of batSARS-like-CoVZXC21 and SARS-CoV (nucleotide identity 89% and 82% respectively) [5,8].

The mechanism of viral cell entire depends on the viral spike S proteins binding to cellular receptors and on S protein priming by the host cell proteases. With regard to this model, for SARS-CoV2 those are: angiotensin-converting enzyme 2receptor (ACE2) and transmembrane serine protease 2 (TMPRSS2) [5,9-10]. ACE2 and TMPRSS2 receptors have been found in the eye both on the ocular surface (cornea, conjunctiva) and also in choroid and retina [5,10-12]. Some studies revealed the presence of ACE2 in corneal and conjunctival epithelial cells, others suggested that located under epithelium dendritic cells and fibroblasts express more ACE2. High vascularity of the conjunctiva and the expression of ACE2 on the endothelial cells surface can be probable reason of local transient vasculitis [2,5,10,12]. The presence of SARS-CoV19 RNA was confirmed in conjunctival swabs and tears though those results were not significant (small group, test limitations). However, the presence of SARS-CoV-2 RNA in ocular samples highlights the role of the eye as a possible route of disease transmission [5,13]. The presence of viral ribonucleic acid (RNA) of SARS-CoV-2 in human corneas(both anterior and posterior), conjunctiva, vitreous and retina in deceased patients with confirmed novel coronavirus disease 2019 (COVID-19) has been detected [14,15].

The majority of reports describing ocular findings in patients with COVID-19 infection comes from small-case studies and case reports. Larger-scale studies are focused on the lung, cardiac or gastrointestinal effects of the virus and ocular manifestation is not documented. Furthermore, studies usually analyze symptoms not patients' signs [10]. Conjunctival manifestation is the most common ocular finding. It has been reported at rates 0.8%, 6%, 32%, 66% in various studies [14,16-18]. Previous studies on animal models of coronaviruses in general pathogenicity reported such complications as conjunctivitis, anterior uveitis, retinitis and optic neuritis [2,11]. It is not clear how often SARS-CoV2 reveals severe complications – patients with a high viral load usually develop severe or critical illness, are treated in intensive care units for life-threatening conditions and their ocular problems are unnoticed [2]. In published case-reports keratoconjunctivitis [10,19], anterior uveitis [20], pan uveitis and optic neuritis [21] were described. One study reported retinal findings in patients examined after COVID-19 symptom onset. All patients had no visual disturbances, no intraocular inflammation signs and symptoms, but during

fundus examination subtle cotton-wool spots and microhemorrhages along the retinal arcades were observed. OCT examination showed hyperreflective lesions at the level of ganglion cell and inner plexiform layers (especially at the periglomerular bundle) [23]. Moreover, patients with ocular symptoms had more often higher levels of white blood cells, neutrophil counts, procalcitonin, C-reactive protein and lactate dehydrogenase. Those markers strongly correlate with severity of the disease. That is why future studies probably estimate the correlation between ocular symptoms and the course of the COVID-19 [10,16,22].

As we mentioned above, viral transmission is due to exposure to respiratory droplets, to through contact with infected patient or contaminated surface or object. Nevertheless, SARS-CoV2 transmission through the eye should be considered. The nasolacrimal system is a natural linkage for SARS-CoV2 entry (as other respiratory viruses, e.g. adenoviruses or influenza virus) from the respiratory tract to the eye [24,25]. On the other hand, SARS-CoV2 can colonize ocular surface because of ACE2 and TNFRSS2 presence. Wherefore eye manifestation may evolve [2,24]. Based on the literature, exposure of the ocular surface to SARS-CoV2 might be the reason for infection, probably by reason of the drainage of the viral particles with tears via nasolacrimal duct to the respiratory tract [2,24,26].

Understanding SARS-CoV2 transmission is important for prevention during ophthalmological examination. In ophthalmological practice, the working distance at the slit lamp examination is between 20 and 40 cm. Moreover, there is unavoidable contact with tears and ocular discharges. That is why ophthalmologists are high-risk personnel for SARS-CoV2 infection. To prevent viral spreading as respiratory droplets from infected or possibly infected patients, wearing face coverings by both patients and healthcare workers is recommended. Basing on clinical experience, eye protection (protective glasses and shields, both individual and attached to the slit lamp) is also suggested. To minimize influence of ocular secretions single-use gloves and proper disinfection is necessary. Many ophthalmic instruments (e.g. gonioscopy and laser lenses, ultrasound probes, tonometry prisms) requires direct or close contact with patients eye. Non-contact tonometry creates aerosol when measure intraocular pressure. All of those situations increase risk of viral transmission, therefore they should be used only where it is necessary [2,5,10,27-28]. Many surgical procedures (nasolacrimal surgery, phacoemulsification, lasers, electrical cutting, coagulation) are connected with aerosol generation. Because of that, it is important to adjust the equipment, surgical techniques and work protocols to reduce exposure as much as possible [5, 29-30].

SARS-CoV2 is a highly contagious virus, responsible for worldwide pandemic with high morbidity and mortality. To reduce the further spread of pandemic it is important to understand its transmission. The eyes represent crucial route of infection both through lacrimal drainage into the respiratory and gastrointestinal tract or because of ophthalmic involvement. Further large, controlled studies are required to evaluate the role and the precise rate of ocular changes in COVID-19, to elucidate the clinical value of tear and conjunctival testing, to connect results of tests with the risk and the severity of infection.

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