The Frequency of Hand-to-Eye/Nose Contact can Increase the Risk of Ocular Symptoms in SARS-CoV-2-Infected Patients

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Research Article

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Abstract

Purpose

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has the capacity to use the eye for transocular entry. The characteristics of lacrimal drainage remind us to pay attention to the transmission route passing through the nasolacrimal ducts and then into the respiratory tract. The aim of this study was to assess ocular symptoms and hand-to-eye/nose contact behaviour in SARS-CoV-2-infected patients.

Methods

A questionnaire was designed by brain storing method according to practical requirements, then the survey of ocular symptoms and hand-to-eye/nose contact behaviour in SARS-CoV-2-infected patients was administered in person. The patients answered the items under the guidance of a nurse. The data of ocular symptoms and basic information was collected analysed. The correlation between ocular symptoms and hand-to-eye/nose contact behaviour was evaluated.

Results

The most common ocular symptoms were increased discharge (in 53.19% of patients), foreign body sensation (44.68%), tearing (44.68%), conjunctival congestion (40.43%) and mild eye pain (40.43%). In total, 61.7% of patients had nasal obstruction and running. A total of 40.4% of patients blew their nose more frequently than usual because of nasal symptoms. A total of 63.8% of patients rubbed their eyes with their hands 1-5 times per day. Only 44.68% of patients washed their hands immediately when arriving at home more than 6 days per week. Increased frequencies of blowing noses ($p=0.032$), washing hands ($p=0.025$), and rubbing eyes ($p=0.005$) can affect ocular symptoms. The frequency and the way of face washing had no correlation with ocular symptoms.

Conclusions

Ocular symptoms in SARS-CoV-2-infected patients are much more common than currently reported but nonspecific. This prompts us to pay more attention to the true incidence of conjunctivitis in SARS-CoV-2-infected patients. The frequency of hand-to-eye/nose contact can increase the risk of presenting ocular symptoms. However, hand washing can decrease the risk. These results provide direct evidence of behaviour change and smooth the concerns for many people.

Introduction

The coronavirus 2019 (COVID-19) pandemic was caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is a positive single-stranded RNA beta coronavirus. Since its emergence in December 2019, COVID-19 has posed a tremendous threat to global public health. According to the World Health Organization (WHO, <https://www.who.int/>), there were 111,928,777 confirmed cases and 2,474,572 deaths due to COVID-19 worldwide as of February 22, 2021. Respiratory droplets and direct contact are considered the main transmission routes of SARS-CoV-2. Additionally, SARS-CoV-2 can be transmitted by aerosols. Whether the virus is airborne remains unclear. Because the human conjunctiva and cornea can express the angiotensin-converting enzyme 2 (ACE2) receptor, which is the key target for SARS-CoV-2 entry into host cells, the ocular mucous membrane is suspected to be a portal of entry as well as a reservoir for person-to-person transmission of this virus [1, 2]. Several studies and clinical observations further suggested that SARS-CoV-2 has the capacity to use the eye for transocular entry and as a potential reservoir [3–5]. On the other hand, SARS-CoV-2 can survive for several hours or more on some environmental surfaces, such as plastic and stainless steel [6, 7]. A mathematical modelling approach by Furuya H showed that SARS-CoV-2 infection can occur through hand-to-face contact via a contaminated environment [8]. Hence, the behaviour of hand contact with facial membranes (i.e., ocular, nasal and oral) should be seriously considered as a mode of transmission. In this study, we performed a survey of hand contact with nose/eyes and relative behaviours in SARS-CoV-2-infected patients. We hope this study can clarify how our daily hand-to-eye/nose behaviour affects ocular-related symptoms and provide guidance to reduce the risk of transmission of COVID-19 via this route.

Materials And Methods

Survey on ocular symptoms and hand-to-eye/nose behaviour

The questionnaire was designed by two ophthalmologists and one doctor who specialized in the management of nosocomial infections. All the items in this survey were selected by the brain storing method according to practical requirements, which allowed the questionnaire to truly reflect the survey situation. We administered this survey through an online questionnaire to COVID-19-infected patients who were transferred to the intensive care unit (ICU) department in Eastern District of Renmin Hospital, Wuhan University. The infection of these patients was confirmed by a positive result from high-throughput sequencing or real-time reverse transcriptase polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens or bronchoalveolar lavage fluid. To obtain high quality and credibility of the survey, a nurse showed the two-dimensional code of this online questionnaire to the patients face to face. Then, the patient used their smartphone to scan the two-dimensional code to finish the questionnaire. In this process, if the patient had any question, they could ask the nurse, and the nurse would explain the item to them. Additionally, the nurse could show the patient some pictures depicting typical ocular symptoms, for example, conjunctival congestion and discharge, to help the patient understand the items and finish the questionnaire efficiently and correctly. However, the nurse was not allowed to give any guidance to the patients. This part of the work was completed by the second author (X. G), who worked as a nurse in the medial rescue department of the ICU at Renmin Hospital of Wuhan University from February 12 to April 7. Only the patients who remained conscious and could independently finish the questionnaire by smart phone were surveyed.

This study was approved by the Research Ethics Committee of the Hospital Authority of West China Hospital, Sichuan University and adhered to the tenets of the Declaration of Helsinki. Informed consent was presented as the first item of the electronic questionnaire. Only after the patients chose the “YES” response could the survey proceed. The questionnaire included 3 parts and 29 items. In the first part, basic information was assessed, including hospital admission number, sex, age, occupation, inhabited environment, family composition, and telephone number (this item is of the patient’s own free will). Part one also assessed whether the patient had confidence in themselves to self-report and recover from the disease. In the second part of the questionnaire, the ocular symptoms were assessed, such as blurred vision, conjunctival congestion, eye pain, photophobia, tearing, secretion, opening the eyelid freely and foreign body sensation. In the third part, the behaviours of the hand to the eye/nose were assessed. For example, do patients have a streaming nose or stuffy nose? How many times did they rub their eyes or blow their nose each day? Did they wash their hand and face immediately after arriving at home in the week before they were diagnosed with COVID-19? When they washed their face, did they clean their nasal cavity simultaneously? Which part was first cleaned? Did they share a basin and towel with others?

Data analysis

All the results and patient data were automatically input to an Excel worksheet and then analysed by SPSS statistical software (v17.0) (Chicago, IL, USA). Continuous variables such as age were expressed as medians $\pm$ standard deviation. Most of the variables were categorical variables, which were summarized as counts and percentages. Each ocular symptom or sign was given a weighed score of 1; hence, the seriousness of the ocular symptoms can be reflected by the sum of the scores. Fisher’s exact test for cross tables was performed to analyse whether hand-to-eye/nose behaviour was correlated with ocular symptoms. P values less than 0.05 were considered statistically significant.

Results

Demographic data

After removing the invalid data, we finally obtained 47 valid questionnaires. The participants included 27 males (57.4%) and 20 females (42.6%). The mean age of all the patients was 53.09 ± 15.72 years. Thirty-four infected patients (72.3%) lived together with 2–3 family members, while 11 (23.4%) infected patients lived together with 4–6 family members. Only 2 (4.3%) infected patients lived together with more than 6 family members. The data showed that retirees were more likely to be infected with COVID-19, accounting for 34.4% (16/47) of all the patients. Nearly all of the patients (97.87%, 46/47) had confidence that they would recover from this infection.

Ocular symptoms

The ocular symptoms included blurred vision, conjunctival congestion, eye pain, photophobia, tearing, secretion, foreign body sensation, and inability to open the eyelid freely because of secretion or sticky feelings. The most common ocular symptom was secretion, which was present in 25 (53.19%) patients. Other symptoms that were also very common in the COVID-19-infected patients included foreign body sensation (21 patients, 44.68%), tearing (21 patients, 44.68%), conjunctival congestion or reddish eye (19 patients, 40.43%) and mild eye pain (19 patients, 40.43%). Fewer individuals presented with blurred vision (17 patients, 30.17%) and photophobia (13 patients, 27.66%). Additionally, 11 patients (23.4%) could not open their eyelid freely because of secretion or sticky feelings. We listed all the detailed data in Table 1.

As each of the self-reported symptoms or signs was given a weighted score of 1, 12 patients (25.5%) received a score of 0, which means they did not have any ocular symptoms. Conversely, 3 patients (6.4%) had scores of 8, which means that the individual had all the ocular symptoms listed above. Detailed information on the weighted scores is presented in Fig. 1.

These ocular symptoms can occur at any stage of the disease course, varying from 5 days before to 20 days after obtaining a confirmed diagnosis of COVID-19 infection by PCR. However, most of the patients presented with ocular symptoms in the early stage of infection, with a median of 1.35 (lower quartiles 0.25, upper quartiles 2.25) days after identification of the infection. However, this question was only answered by 30 patients.

Nasal symptoms and hand-to-eye/nose contact behaviour

Twenty-nine (61.7%) patients had nasal obstruction and running. Nineteen (40.4%) patients blew their nose more frequently than usual because of nasal symptoms. Direct hand-to-eye contact behaviour was evaluated by the number of times the eye was rubbed in one day. Most infected patients (63.8%, $n = 30$) rubbed their eyes 1–5 times with their hands in one day. In addition, 10.64% (5 patients) rubbed their eyes 6–10 times a day. A total of 2.13% of patients rubbed their eyes more than 10 times a day. Only 23.4% (11) of individuals denied hand-to-eye contact behaviour.

Additionally, we found that most patients did not wash their hands and face immediately after returning home in the week before diagnosis. Only 44.68% (21 patients) washed their hands immediately upon returning home more than 6 days per week. A total of 40.43% (19 patients) achieved this process 1–3 days per week. A total of 12.77% (6 patients) washed their hands immediately 4–5 days per week. One patient (2.13%) never washed his hands after returning home in the week before infection confirmation.

Compared to hands, much fewer people paid attention to washing their face immediately after returning home. Only 25.53% (12 patients) washed their faces immediately after returning home more than 6 days per week. Most infected individuals (23 patients, 48.94%) washed their face after returning home 1–3 days a week. Additionally, 21.28% (10 patients) of patients never washed their faces when they returned home. When they washed their faces, 38.3% (18 patients) also washed or cleaned their nasal cavity. Among these 18 patients, 11 (61.11%) preferred to clean their nasal cavity before washing the ocular

portion of their face. When washing faces, 10.64% (5 patients) of patients shared towels with other family members. In addition, 48.94% (23 patients) used a basin to wash their face. Among them, 78.26% (18/23) shared the basin with others.

Correlation between ocular symptom grades and hand-to-eye/nose contact behaviour

Fisher's exact test for cross table showed that only the increased frequency of blowing noses ($p = 0.032$, two sided), the frequency of washing hands ($p = 0.025$, two sided), and the frequency of rubbing eyes ($p = 0.005$, two sided) affected the ocular symptom grades. Other factors, including the frequency of washing faces, the way faces were washed, the use of a basin/towel or not, and the presence or absence of nasal obstruction/running, had no correlation with ocular symptom grades (Table 2).

Discussion

Presence of Ocular Symptoms

To date, the frequency of ocular symptoms presented in SARS-CoV-2-infected patients is relatively low, and the data vary greatly. One study containing 1,099 patients showed that approximately 0.8% showed conjunctival congestion. [9] Other studies with smaller sample sizes demonstrated a higher rate of conjunctival congestion, ranging from 5% (27/535) to 31.6% (12/38) [5, 10–11]. However, our survey of SARS-CoV-2-infected patients found that approximately 40.43% (19/47) had conjunctival congestion or reddish eyes at least once during the infection. Although a nurse showed a typical picture of ocular signs and explained them distinctly to the patients, our data obtained from this survey were self-reported by patients. Hence, the rate of ocular symptoms and signs in this research may be slightly overestimated. We thought several reasons caused this discrepancy. First, these patients were often initially admitted to the Respiratory Department or Infections Diseases Department, and both the physicians and patients were mainly concerned about severe systemic signs, such as fever, cough, dyspnoea, myalgia or fatigue. The ocular symptoms and signs were ignored. Second, the signs and symptoms of SARS-CoV-2-related conjunctivitis are not specific. Almost all the published papers concerned conjunctival congestion or reddish eye. Some studies also paid attention to conjunctival chemosis, epiphora, increased secretions, foreign body sensation, itching or tearing [3–5, 10, 12]. The incidence of these symptoms is also very common in people. By comparison, the rate of some ocular symptoms, such as foreign body sensation, blurred vision, and itching, showed no difference in infected patients with and without conjunctival congestion [10]. Third, the timing of ocular manifestations during the evolution of COVID-19 infection is not clear [13]. Ocular symptoms may present as the initial and only symptom of infection but can also present in the late stage of infection. As in our study, one patient reported that he presented with these symptoms 5 days before obtaining a positive PCR test result for the virus. Some individuals had ocular symptoms in the very late stage of infection (20 days after obtaining a confirmed diagnosis). However, the median time of symptom presentation was 1.35 days after receiving a confirmed diagnosis (lower quartiles 0.25, upper quartiles 2.25 days). Fourth, the proportion of patients with evidence of viral particles in tears or conjunctiva remained low because of the timing sample acquisition, low sample concentration for RT-PCR detection of the virus and the collection techniques used [13–15]. Patients with or without the presence of viral conjunctivitis can show positive RT-PCR results for the virus [3, 5, 16]. Hence, the diagnostic criteria and true incidence of conjunctivitis in SARS-CoV-2-infected patients should be re-evaluated by additional research.

Hand to eye/nose behaviour

Whether exposed mucous membranes can be the direct inoculation site and the portal of entry of SARS-CoV-2 is unclear. When the COVID-19 epidemic began in Wuhan, China, many specialists shared their perspective on the possible transmission of the virus via mucous membranes. The possible hypotheses include direct inoculation of the ocular tissues from respiratory droplets or aerosolized viral particles, migration through the nasolacrimal ducts and then into the respiratory tract, or even haematogenous spread through the lacrimal gland [17–19]. In support of the theory of the conjunctival mucosa acting as an entrance route for the virus is the case of the nurse who wore a medical N95 respirator and dislocated goggles that presented with conjunctivitis as initial symptoms of infection [4]. Further, in this study, we investigated hand-to-eye/nose behaviour and found that the total score of ocular symptoms was only correlated with an increased frequency of rubbing eyes, blowing noses and washing hands. As the item was a categorical variable, we could not perform linear regression to calculate the related coefficient. However, Table 2 clearly shows that the infected patients who were free of ocular symptoms had a lower frequency of rubbing eyes and blowing noses and a higher frequency of washing hands. Deng et al. inoculated rhesus macaques with SARS-CoV-2 conjunctively, and the animals displayed mild interstitial pneumonia with detectable viral RNA in the nasolacrimal system, nasal system, and throat [20]. Their research verified that infection via the conjunctival route was possible. Combined with our research, these results implied that a high frequency of hand-to-eye behaviours, such as rubbing eyes, can increase the risk of transocular transmission from environmental matrices and surfaces, causing infection in the respiratory system through the nasolacrimal duct. However, we believe that infection via this route also depends on the viral load in the ocular surface, which needs more research.

Our research found that whether the patient had nasal symptoms (obstruction and running) had no correlation with ocular symptoms. However, hand-to-nose contact behaviour—the frequency of blowing nose—showed a significant correlation with ocular symptoms. Therefore, we think that the transmission route from the nasolacrimal duct to the conjunctiva is possible. However, the chance is very low, except under tremendous pressure, for example when blowing the nose.

Another conclusion in our research was the importance of hand washing. In the patients free of ocular symptoms (total score was 0), 11/12 washed their hands immediately after returning home more than 4 days per week. Hand washing with running water and soap is a fundamental way to reduce viral load and to reduce transmission of SARS-CoV-2 [21]. For contact lens users, the epidemic of COVID-19 caused extreme anxiety. Our research provided evidence that an increased frequency of hand washing may decrease the risk of eye transmission from the environment. The importance of hand washing for contact lens users is emphasized and promoted by Jones et al [22].

Other behaviours, including whether to wash face, how to wash face, using basin or not, and using towels, had no correlation with ocular symptoms. These results can smooth the concerns for many people.

Conclusions

In conclusion, this survey of SARS-CoV-2-infected patients found that the proportion of ocular symptoms and signs may be much higher than is currently reported. The frequency of hand-to-eye/nose contact can increase the risk of ocular symptoms. However, hand washing should be suggested because it can decrease the risk of transmission and thus ocular symptoms.

There are some limitations in our study. The items on the survey were all self-reported by the patients, so bias was inevitable. The limited sample size also constrained our further analysis of the data. However, our research provided direct evidence on the correlation of hand-to-eye/nose contact behaviour and ocular symptoms, which provides direct evidence of behaviour change. More behavioural science methods and investigations should be applied to provide solid evidence on this.

Declarations

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Competing interests

There is no conflict of interest to declare.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable.

Authors' contributions

G.Y, X.W and L.L. conceived the study. X.G performed this survey. X.H and J.Z provided suggestions on questionnaire design and contributed to data analysis. The manuscript was drafted by G.Y. and critically revised by L.L and X.W.

Ethics approval and consent to participate

This research was approved by Institutional Review Board of West China Hospital, Sichuan University (NO.2020 (195)) and performed with firm adherence to the tenets of the Declaration of Helsinki. Informed consent was obtained from all the participants.

Consent for publication

Not applicable.

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None.

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Tables

Table 1
Ocular symptoms of COVID-19 infected patients by self-reporting (patients/proportion)

Response	blurred vision	conjunctival congestion	eye pain	photophobia	tearing	increased discharge	cannot open the eyelid freely	foreign body sensation
yes	17(30.17%)	19(40.43%)	19(40.43%)	13(27.66%)	21(44.68%)	25(53.19%)	11(23.4%)	21(44.68%)
no	30(63.83%)	28(59.57%)	28(59.57%)	34(72.34%)	26(55.32%)	22(46.81%)	36(76.6%)	26(55.32%)

Table 2. Correlation between ocular symptom grades with hand to eye/nose contact behaviour													
Ocular symptoms grades	Frequency of washing hands immediately after returning home						Frequency of rubbing eyes with hands in one day						Increase in symptoms
	0 day/week(n)	1–3 days/week(n)	4–5 days/week(n)	6 days/week(n)	Total (n)	P value	0(n)	1–5 times (n)	6–10 Times (n)	≥10 times (n)	Total (n)	P value	
8	0	1	1	1	3		1	1	1	0	3		3
6	0	2	1	0	3		0	2	1	0	3		3
5	0	9	1	5	15		0	13	2	0	15		7
4	0	1	0	1	2		1	1	0	0	2		1
3	0	0	0	2	2		0	1	0	1	2		1
2	0	4	0	1	5		0	5	0	0	5		1
1	0	2	0	3	5		2	3	0	0	5		1
0	1	0	3	8	12		7	4	1	0	12		2
Total	1	19	6	21	47		11	30	5	1	47		19
						P ₁ = 0.025							P ₂ = 0.005
n = number of patients; Y = yes, N = no; P value was determined by Fisher's exact test (two tailed).													

Figures

Figure 1

Weighted scores of ocular symptoms of COVID-19 patients. The horizontal and longitudinal axes indicate the weighted score and number of patients, respectively.

Supplementary Files

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- [rawdataforcovid2019.xlsx](#)