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Research note

More than loss of taste and smell: burning watering eyes in coronavirus disease 2019

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ABSTRACT

Objectives: To evaluate ocular symptoms in European non-hospitalized patients with severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) and to investigate associations with the demographic data as well as nasal and general physical symptoms.
Methods: In this prospective, observational study, 108 non-hospitalized patients with PCR-confirmed SARS-CoV-2 infection not requiring intensive care were asked about disease-associated ocular symptoms, demographic data, as well as general physical and nasal symptoms using a standardized questionnaire. Total ocular symptom score (TOSS) was evaluated during and, retrospectively, before development of coronavirus disease 2019 (COVID-19). Associations between TOSS and demographic data as well as general and nasal symptoms were evaluated.
Results: Seventy-five of the 108 COVID-19 patients (69.4%) had at least one ocular symptom during COVID-19. The most common symptoms included burning sensations in 39 (36.1%), epiphora in 37 (34.3%) and redness in 28 (25.9%), compatible with conjunctivitis. These symptoms occurred 1.96 ± 3.17 days after the beginning of COVID-19 and were mild. TOSS was significantly higher during COVID-19 (1.27 ± 1.85) than before the infection (0.33 ± 1.04; $p < 0.001$). There were no significant associations between TOSS and gender (β coefficient −0.108; p 0.302), age (−0.024; p 0.816), rhinorrhoea (−0.127; p 0.353), nasal itching (−0.026; p 0.803), sneezing (0.099; p 0.470), nasal congestion (−0.012; p 0.930), cough (−0.079; p 0.450), headache (0.102; p 0.325), sore throat (0.208; p 0.052), or fever (0.094; p 0.361).
Conclusions: Ocular involvement in European non-hospitalized individuals with COVID-19 seems to be highly underestimated. Overall, these ocular symptoms, including burning sensations, epiphora and redness, seem to be mild and to not need treatment. **Alexander C. Rokohl, Clin Microbiol Infect 2020;26:1560.e5–1560.e8**

Introduction

The rapid spread of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has encouraged clinicians and researchers to analyse SARS-CoV-2 and to characterize the symptoms of COVID-19 [1]. Previous studies reported the expression of angiotensin-

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converting enzyme 2, the entry receptor of SARS-CoV-2, on the human conjunctiva and cornea potentially resulting in conjunctivitis and keratitis [2–5]. SARS-CoV-2 existed in COVID-19 patients' tears and ocular involvement was present in 1%–32% of hospitalized individuals [3,6]. Ocular involvement included chemosis, epiphora, secretion and conjunctival hyperaemia [6]. There are some studies regarding ocular manifestations in individuals with COVID-19, but most of them evaluated hospitalized patients in China retrospectively [3,5]. Therefore, the objectives of this study included the evaluation of ocular symptoms in European non-hospitalized individuals infected with SARS-CoV-2 and investigation of associations with the demographic data as well as nasal and general physical symptoms.

Methods

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration. Institutional Review Board approval was obtained. Inclusion criteria were COVID-19 confirmed by PCR test on a throat swab and age over 18 years. On eight consecutive days, these patients were identified by the records of the University Hospital of Cologne, Germany and all of them were called by phone. Exclusion criteria were hospitalization at any time-point caused by COVID-19. A standardized three-section questionnaire was used. Section Introduction requested demographic data, general symptoms including fever, cough, headache and sore throat as well as dates of the positive PCR test and of the first symptoms associated with COVID-19. Nasal symptoms, which might potentially influence ocular symptoms, were evaluated for nasal congestion, sneezing, nasal itching and rhinorrhoea using a four-point scale (0–3), respectively [7]. A score of 0 indicated no symptoms, 1 documented mild symptoms that were easily tolerated, 2 described awareness of symptoms that were bothersome but tolerable, and 3 matched severe symptoms that were hard to tolerate and interfered with daily activities or sleep.

Section Methods asked about ocular symptoms during COVID-19 including burning sensations, itching, watering, mucoid and purulent discharge, photophobia, foreign body sensation, conjunctival swelling, eyelid swelling, feeling of pressure, double images, metamorphopsia, redness, reduced visual acuity, and pain for the right and the left eye, respectively. Furthermore, the date of the beginning of each symptom was noted. Total Ocular Symptom Score (TOSS) was evaluated for two different time-points: retrospectively before coronavirus infection and during COVID-19. TOSS included ocular itching, redness, epiphora and eye swelling. Each symptom was graded analogous to nasal symptoms and TOSS was then calculated by adding the four scores to a total score between 0 and 12. Section Results requested information about pre-existing eye conditions, topical ocular medication and ophthalmologist's visits during COVID-19. All statistical analyses were performed with SPSS version 26.0 for Mac. Shapiro–Wilk tests were performed to analyse normal distribution. To compare ocular symptom scores before infection and during COVID-19, Wilcoxon tests were performed. To investigate factors related to TOSS, a general linear model including analysis of variance was used with explanatory variables of gender, age, rhinorrhoea, nasal itching, sneezing, nasal congestion, cough, headache, fever and sore throat. The threshold for statistical significance was set at $p < 0.05$.

Results

In all, 115 non-hospitalized individuals with COVID-19 were called and 109 of them responded; 108 agreed to participate, one declined. Of these 108 individuals, 51 were men and 57 were women with a mean age of 37.9 ± 13.7 years (range 18–87 years). Mean time since PCR-confirmed COVID-19 was 6.8 ± 1.5 days (range 3–9 days), and mean time since first symptoms occurred was 13.2 ± 3.8 days (range 6–23 days). Eighty-two of the 108 COVID-19 patients (75.9%) suffered from cough, 80 (74.1%) from headache, 63 (58.3%) from sore throat and 47 (43.5%) from fever.

Mean scores were 1.02 ± 1.13 (range 0–3) for nasal congestion, 0.57 ± 0.74 (range 0–3) for sneezing, 0.16 ± 0.39 (range 0–2) for nasal itching and 0.70 ± 0.85 (range 0–3) for rhinorrhoea.

Seventy-five of the 108 COVID-19 patients (69.4%) had at least one ocular symptom during COVID-19. The most common symptoms included burning sensations (36.1%), epiphora (34.3%) and redness (25.9%), compatible with conjunctivitis (Table 1). These ocular symptoms occurred mostly in the first 3 days after any symptom of COVID-19 was noticed. All scores were significantly higher during COVID-19 than the scores before infection ($p \leq 0.022$, respectively; Table 2). Before COVID-19, two individuals had previously had dry eye disease diagnosed and one had ocular allergy, while six individuals sometimes used artificial tears if needed and one patient used antihistamines. During COVID-19 only one individual bought artificial tears and none was seen by an ophthalmologist. None of the investigated explanatory variables including gender, age, rhinorrhoea, nasal itching, sneezing, nasal congestion,

Table 1
Ocular symptoms of 108 European non-hospitalized patients (216 eyes) with COVID-19

Ocular symptoms	Right and left eyes with symptoms, *no. (%)*	Patients with bilateral symptoms, *n* (%)	Duration of occurrence since first symptom was noted (days), mean ± SD (range)
Burning sensations	76 (35.2%)	37 (34.3%)	1.89 ± 3.26 (range 0–13)
Itching	38 (17.6%)	18 (16.7%)	2.53 ± 3.72 (range 0–13)
Epiphora (watering eyes)	71 (32.9%)	34 (31.5%)	1.91 ± 3.59 (range 0–13)
Mucoid discharge	18 (8.3%)	9 (8.3%)	0.78 ± 1.09 (range 0–13)
Purulent discharge	0 (0.0%)	0 (0.0%)	—
Photophobia	44 (20.4%)	22 (20.4%)	1.77 ± 3.41 (range 0–13)
Foreign body sensation	15 (6.9%)	7 (6.5%)	2.25 ± 2.12 (range 0–6)
Conjunctival swelling	16 (7.4%)	8 (7.4%)	1.14 ± 1.46 (range 0–3)
Eyelid swelling	30 (13.9%)	15 (13.9%)	2.00 ± 2.88 (range 0–10)
Feeling of pressure	45 (20.8%)	22 (20.4%)	2.04 ± 2.40 (range 0–7)
Double images	4 (1.9%)	2 (1.9%)	3.50 ± 2.12 (range 2–5)
Metamorphopsia	0 (0.0%)	0 (0.0%)	—
Redness	54 (25.0%)	26 (24.1%)	2.07 ± 2.67 (range 0–10)
Reduced visual acuity	19 (8.8%)	9 (8.3%)	3.10 ± 2.60 (range 0–7)
Pain	22 (10.2%)	11 (10.2%)	2.09 ± 2.12 (range 0–7)

Table 2
Graded ocular symptoms and total ocular symptom score of 108 European COVID-19 non-hospitalized patients before versus during COVID-19 infection

Graded ocular symptoms	Before COVID-19	During COVID-19	p value
Ocular itching, mean ± SD (range)	0.05 ± 0.25 (range, 0–2)	0.30 ± 0.67 (range, 0–3)	0.001
None, *n* (%)	104 (96.3%)	88 (81.5%)	—
Mild, *n* (%)	3 (2.8%)	9 (8.3%)	—
Moderate, *n* (%)	1 (0.9%)	10 (9.3%)	—
Severe, *n* (%)	0 (0.0%)	1 (0.9%)	—
Ocular redness, mean ± SD (range)	0.06 ± 0.27 (range, 0–2)	0.33 ± 0.64 (range, 0–3)	<0.001
None, *n* (%)	103 (95.4%)	80 (74.1%)	—
Mild, *n* (%)	4 (1.9%)	22 (20.4%)	—
Moderate, *n* (%)	1 (0.9%)	4 (3.7%)	—
Severe, *n* (%)	0 (0.0%)	2 (1.9%)	—
Epiphora, mean ± SD (range)	0.17 ± 0.42 (range, 0–2)	0.45 ± 0.72 (range, 0–3)	<0.001
None, *n* (%)	92 (85.2%)	71 (65.7%)	—
Mild, *n* (%)	14 (13.0%)	27 (25.0%)	—
Moderate, *n* (%)	2 (1.9%)	8 (7.4%)	—
Severe, *n* (%)	0 (0.0%)	2 (1.9%)	—
Eye swelling, mean ± SD (range)	0.06 ± 0.31 (range, 0–2)	0.19 ± 0.51 (range, 0–3)	0.022
None, *n* (%)	103 (95.4%)	93 (86.1%)	—
Mild, *n* (%)	3 (2.8%)	11 (10.2%)	—
Moderate, *n* (%)	2 (1.9%)	3 (2.8%)	—
Severe, *n* (%)	0 (0.0%)	1 (0.9%)	—
Total Ocular Symptom Score, mean ± SD (range)	0.33 ± 1.04 (range, 0–8)	1.27 ± 1.85 (range, 0–12)	<0.001

cough, headache, fever and sore throat was associated with TOSS during COVID-19 (analyses of variance p 0.559; $p \geq 0.05$, respectively).

Discussion

This prospective study showed for the first time the high prevalence of burning sensation, redness and watering in non-hospitalized European individuals with COVID-19. The consecutively enrolled individuals were much younger than in previous studies including mostly inpatients in China [3,6]. Younger patients without any pre-existing conditions normally have a mild course of disease and therefore need not be hospitalized. Approximately one-third of the outpatients in this study had epiphora or burning sensations, respectively, and one-quarter reported ocular redness. Therefore, the incidence of conjunctivitis, especially in outpatients, seems to be highly underestimated. Ocular symptoms occurred mostly in the first 3 days of COVID-19, but were usually mild. However, in some rare cases moderate or severe courses including subconjunctival bleeding, keratitis, or even vitreous haemorrhages may occur [8,9].

The reasons why patients had no ophthalmologist's visit, despite a high incidence of symptoms, remain unclear. The mild disease, fear of infection and/or the home quarantine order by the health authorities might be reasons.

Ocular symptoms were not associated with nasal symptoms, cough, headache, fever or sore throat, so these concomitant COVID-19 symptoms seem to have no significant impact on the ocular symptoms. Therefore, SARS-CoV-2 might have a significant causative influence on these ocular symptoms, making further prospective studies comparing the clinical ocular involvement of outpatients and inpatients a high priority. Eventually, the presence of clinical ocular manifestations in individuals with COVID-19 might be a negative predictor of outcome [10].

Nevertheless, there are some limitations of this study. First, TOSS before infection was evaluated retrospectively and second, all ocular symptoms were not confirmed by clinical examinations but only reported subjectively by patients on average 13 days after the first symptom occurred, that is during or, in a few individuals, shortly after COVID-19.

As these complaints were not associated with nasal symptoms, there is a high priority to evaluate the causative factors by prospective studies including clinical examinations.

Transparency declaration

The authors declare that they have no conflicts of interest. All authors have full control of all primary data and they agree to allow review of their data upon request.

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Authors' contributions

ACR and LMH conceptualized the study. NL, PAWM and SZ collected the data. ACR conducted the data analyses. ACR and NL wrote the first draft of the manuscript. MA, FD, RSG, FK, CL and LMH revised the manuscript. All authors approved the final version. LMH had the overall responsibility.

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