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Correspondence: M. Guastalegname, "Jazzolino" Hospital, Vibo Valentia, Vibo Valentia Italy (guama@email.it).

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Self-reported Olfactory and Taste Disorders in Patients With Severe Acute Respiratory Coronavirus 2 Infection: A Cross-sectional Study

To the Editor—We read with interest the article by Wang et al [1] describing the clinical features of 69 patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Wuhan, China. The authors provide a detailed description of major signs and symptoms of overt disease [2, 3], but fail to give an account of minor symptoms that may be present at earlier stages of the infection.

After some patients admitted for coronavirus disease 2019 (COVID-19) at the Infectious Disease Department of L. Sacco Hospital in Milan, Italy, complained of olfactory and taste disorders (OTDs), we performed a cross-sectional survey of the prevalence of these alterations in the context of SARS-CoV-2 infection. On 19 March 2020, a simple questionnaire including questions about the presence or absence of OTDs, their type and time of onset respective to hospitalization were submitted through verbal interview to all SARS-CoV-2–positive hospitalized patients who were able to give informed consent. Of 88 hospitalized patients, 59 were able to be interviewed (29 were nonrespondents, of whom 4 had dementia, 2 had a linguistic barrier, and 23 were on noninvasive ventilation) (Table 1). Of these, 20 (33.9%) reported at least 1 taste or olfactory disorder and 11 (18.6%) both. Twelve patients (20.3%) presented the symptoms before the hospital admission, whereas 8 (13.5%) experienced the symptoms during the hospital stay. Taste alterations were more frequently (91%) before hospitalization, whereas after hospitalization taste and olfactory alteration appeared with equal frequency. Females reported OTDs more frequently than males (10/19 [52.6%] vs 10/40 [25%]; $P = .036$). Moreover, patients with at least 1 OTD were younger than those without (median, 56 years [interquartile range {IQR}, 47–60] vs 66 [IQR, 52–77]; $P = .035$). All patients reported the persistence of OTDs at the time of the interview.

Table 1. Characteristics of Patients With Severe Acute Respiratory Syndrome Coronavirus 2 Infection Assessed for Taste and Olfactory Disorders (N = 59)

Patients	No. (%)
Age, y, median (IQR)	60 (50–74)
Male sex	40 (67.8)
Days from illness onset to hospital admission, median (IQR)	6 (4–10)
Days from illness onset to the interview, median (IQR)	15 (10–21)
Pneumonia at hospital admission	43 (72.8)
Symptoms at hospital admission	
Fever	43 (72.8)
Cough	22 (37.3)
Dyspnea	15 (25.4)
Sore throat	1 (1.7)
Arthralgia	3 (5.1)
Coryza	1 (1.7)
Headache	2 (3.4)
Asthenia	1 (1.7)
Abdominal symptoms	5 (8.5)
No taste or olfactory disorders	39 (66.1)
With olfactory and/or taste disorders	20 (33.9)
Taste disorders only	
Dysgeusia	5 (8.5)
Ageusia	1 (1.7)
Olfactory disorders only	
Hyposmia	3 (5.1)
Anosmia	0 (0)
Mixed taste and olfactory disorders	
Dysgeusia and hyposmia	2 (3.4)
Dysgeusia and anosmia	2 (3.4)
Ageusia and hyposmia	2 (3.4)
Ageusia and anosmia	5 (8.5)

Data are presented as no. (%) unless otherwise indicated. Abbreviations: IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Olfactory and taste disorders are well known to be related with a wide range of viral infections [4, 5]. SARS-CoV has demonstrated in a mice model a transneural penetration through the olfactory bulb [6]. Moreover, angiotensin-converting enzyme 2 receptor, which is used by SARS-CoV-2 to bind and penetrate into the cell, is widely expressed on the epithelial cells of the mucosa of the oral cavity [7]. These findings could explain the underlying pathogenetic mechanism of taste and olfactory disorders in SARS-CoV-2 infection.

Due to limitations related to the diffusivity of the disease and emergency contingencies, it was impossible to perform a more structured questionnaire associated with validated tests (ie, Pennsylvania smell identification test) [8]. However, our survey shows that OTDs are fairly frequent in patients with SARS-CoV-2 infection and may precede the onset of full-blown clinical disease. In a pandemic context, further investigations on nonhospitalized infected patients are required to ascertain if these symptoms, albeit unspecific, may represent a clinical screening tool to orientate testing of pauci-symptomatic individuals.

Notes

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Andrea Giacomelli,[1,2] Laura Pezzati,[1,2] Federico Conti,[1,2] Dario Bernacchia,[1,2] Matteo Siano,[1,2] Letizia Oreni,[1] Stefano Rusconi,[1,2] Cristina Gervasoni,[1] Anna Lisa Ridolfo,[1] Giuliano Rizzardini,[3,4] Spinello Antinori,[1,2] and Massimo Galli[1,2]

[1]III Infectious Diseases Unit, Azienda Socio-Sanitaria Territoriale-Fatebenefratelli-Sacco, Milan, Italy, [2]Luigi Sacco Department of Biomedical and Clinical Sciences, University of Milan, Italy, [3]Department of Infectious Diseases, Azienda Socio-Sanitaria Territoriale Fatebenefratelli Sacco University Hospital, Milan, Italy, and [4]School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

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Correspondence: A. Giacomelli, III Infectious Diseases Unit, Luigi Sacco DIBIC, University of Milan, Via G.B. Grassi 74, 20157 Milano, Italy (andrea.giacomelli@unimi.it).

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Hydroxychloroquine and Chloroquine

To the Editor—The publication by Yao et al [1] in a recent issue of *Clinical Infectious Diseases* investigated the in vitro inhibition of hydroxychloroquine (HCQ) and chloroquine (CQ) against a clinically isolated virus strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and predicted systemic exposure and biodistribution of these compounds in the human body after oral administration using a physiology-based pharmacokinetic modeling approach.

This work is meaningful for the worldwide battle against the pathogenic coronavirus, not only because it introduced a potentially strong and orally administered antiviral agent to the pharmacotherapy of coronavirus disease 2019 (COVID-19) but also because the sister drug, CQ, is known to have a narrow therapeutic window and a steep dose-toxicity relationship in clinical practice [2]. In fact, the fatal dose of CQ [2] is only a couple of folds higher than the therapeutic dose simulated by Yao et al. In comparison, the toxicity profile of HCQ is generally acceptable and monitorable [3], especially for short-term use in patients with COVID-19.

Of note, the authors also reported the in vitro effect of HCQ or CQ with prophylactic use—that is, Vero cells were pretreated 2 hours prior to the propagation of SARS-CoV-2. The results suggested slightly reduced efficacy of both compounds. Given the difference between in vitro and in vivo experimental settings, such findings should be interpreted with caution. On one hand, pretreatment with either of the compounds may impair cellular metabolism [4] and interfere with subsequent virus replication in the cells; on the other hand, the authors did not report the cytotoxic concentration of HCQ or CQ on the Vero cells, thus the selectivity index cannot be calculated [5].

Another remark goes to the "off target" effect of HCQ or CQ. The authors argued that the immunosuppressive effect of HCQ or CQ may lead to additional benefit as they could antagonize the aberrant inflammatory responses aroused by the coronavirus (CoV) infection. However, the use of HCQ or CQ is like a dual-edge sword for animals infected by the pathogenic CoV. Previous study with CQ suggested that in vitro viral inhibition did not translate to antiviral efficacy in SARS-CoV–infected animal models [6]. The explanation may be associated with the role of host innate immunity in viral infection [7]. The inhibition of CQ on type I interferon response counteracts its natural antiviral effect and diminishes the total antiviral activity. The same conflicting mechanism applies to HCQ [8]. Yao et al proposed an HCQ dose similar to its clinical dose for systemic lupus erythematosus. Under this dose, HCQ is supposed to exert both antiviral and immunosuppressive effects. In this perspective, it is necessary to take a second look at the dose of HCQ. According to the simulation, pulmonary exposure of HCQ would be maintained at a plateau more than 5 times higher than its in vitro half-maximal effective concentration (EC50). Therefore, if clinical studies with HCQ do not obtain positive results in COVID-19, a lower HCQ dose might be explored to find the right dose for this new indication.

Notes

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Xia Chen[1,2,3]

[1]China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China, [2]Phase I Unit, Beijing Tiantan Hospital, Capital Medical University, Beijing, China, and [3]Advanced Innovation Center for Human Brain Protection, Capital Medical University, Beijing, China

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