

Olfactory and Gustatory Dysfunction Associated with SARS-CoV-2 Infection

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Abstract

Background: The coronavirus disease (COVID-19) outbreak has become a global pandemic. COVID-19 patients with olfactory loss and taste disorders have received considerable attention.

Objective: To explore the incidence and prognosis of olfactory and gustatory dysfunction in patients with COVID-19.

Methods: A questionnaire was given to each patient, and endoscopic nasal examination was performed on every patient. CT scan of nasal cavity was performed in seven cases and Cerebrospinal Fluid (CSF) was tested in one case. Olfactory and gustatory visual analogue scales were completed to evaluate the recovery rate of olfactory and gustatory dysfunction by patients on the 1st, 7th and 21st day of hospitalization.

Results: The self-reported prevalence of olfactory and gustatory dysfunction was 39.4% (28/71) and 35.2% (25/71), respectively. Anosmia was the initial onset symptom in 15.49% (11/71) patients, 5 of them had anosmia as the only complaint. No purulent mucus or new organism was found in the nasal cavity of any patients. No obvious obstruction was found in the CT scan of paranasal sinuses and the olfactory cleft. Three weeks after admission to the hospital, all patients had different degrees of olfactory and gustatory improvement.

Conclusions: Olfactory and gustatory dysfunction can be an initial symptom of COVID-19, and even be the only complaint. The appearance of anosmia may serve as a practical warning sign, indicating the individual is likely to be infected with SARS-CoV-2, especially in patients without any other symptoms.

Keywords: COVID-19; SARS-CoV-2; olfactory and gustatory dysfunction; Anosmia/Hyposmia; Coronavirus infections

Abbreviations: COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome-Coronavirus 2

Introduction

The coronavirus disease (COVID-19) outbreak has become a global pandemic. In addition to common respiratory manifestations of COVID-19, such as fever, cough, fatigue and dyspnea, olfactory loss and taste disorders have received considerable attention. The WHO has warned that a large number of confirmed COVID-19 patients have developed anosmia or hyposmia [1,2]. The aim of the present work is to explore the incidence and prognosis of olfactory and gustatory dysfunction in patients with COVID-19.

Methods

Study participants

A total of 71 patients including 28 males and 43 females with confirmed COVID-19, who had been admitted to Beijing Ditan Hospital, Capital Medical University, from March 1 to March 27, 2020 were investigated continuously for their olfactory and taste sensation. All patients had been tested for COVID-19 using a reverse transcription polymerase chain reaction (RT-PCR)-based test, and all patients met the diagnostic criteria of COVID-19 [3]. Exclusion criteria included previous long-term anosmia, acute attack of nasal disease, diabetes, epilepsy, anxiety and depression. Patient who were in intensive care units or who were deceased were excluded. The study was approved by the medical ethics committee of Beijing Ditan Hospital, and written informed consent was obtained from each participant prior to study entry.

Study design

Demographic characteristics of the participants-age, sex, smoking history, and histories of allergic rhinitis, chronic rhinosinusitis, and asthma were collected. A questionnaire was given to each patient, and endoscopic nasal examination was performed on every patient. The questionnaire covered time of occurrence, severity, duration, and accompanying nasal symptoms of olfactory and gustatory hypoesthesia. CT scan of nasal cavity was performed in seven cases and Cerebrospinal Fluid (CSF) was tested in one case with headache. Olfactory and gustatory visual analogue scales (0 for anosmia, 10 for normal) were completed by patients under the guidance of doctors on the 1st, 7th and 21st day of hospitalization.

Statistical analysis

Statistical analysis was conducted using SPSS version 19.0 (IBM SPSS, Armonk, NY, USA). The quantitative data were described by median (25th-75th percentile), the differences between groups were analyzed by nonparametric test. For qualitative variables, frequency and percentage were used as descriptive statistics.

Results

The self-reported prevalence of olfactory and gustatory dysfunction was 39.4% (28/71) and 35.2% (25/71), respectively (Table 1) from the first day of testing when hospitalized. The incidence of olfactory dysfunction accompanied by concurrent taste loss was 89.3% (25/28). Of these 28 patients, the median age was 23.5 (17-62) years; 9 males and 19 females. All patients had returned from abroad. In 17 cases, smell dysfunction occurred before positive detection of SARS-CoV-2 and in 11 cases, smell loss occurred after the patient entered the hospital. Anosmia was the initial on set symptom in 15.49% (11/71) patients, 5 of them had anosmia as the only complaint and did not have other symptoms like fever or cough. 21 cases had complete loss of smell and 7 cases had partial hyposmia. Seven patients reported a decrease in smell and taste on the first or the second day after taking Lopinavir/Ritonavir tablets, which is a HIVPI for the treatment of HIV infection and has recently been recommended for the treatment of

COVID-19 in China. They were not receiving any other medications at that time. Few patients complained of obvious nasal symptoms such as congestion or runny nose. No purulent mucus or new organism was found in the nasal cavity of any patients. No obvious obstruction was found in the CT scan of paranasals and the olfactory cleft (Figure 1). No abnormality was found in CSF. Detection of SARS-CoV-2 RNA in CSF specimens was performed using a real-time quantitative fluorescence polymerase chain reaction (RT-qPCR), and results were negative. We tested the CSF for IgM and IgG antibodies against SARS-CoV-2 using the colloidal gold method, and results were negative. Three weeks after admission to the hospital, all patients had different degrees of olfactory and gustatory improvement, including 11 cases of complete and 17 partial recovery of olfactory function, and 12 cases of complete and 13 partial recovery of taste sensation (Table 2).

Discussion

There is strong evidence that a large number of patients with confirmed COVID-19 have developed anosmia/hyposmia. A growing number of reports are showing a significant increase in the number of patients with anosmia without other symptoms [1-2]. These patients may be some hidden carriers, promoting the rapid spread of COVID-19. The self-reported prevalence of anosmia in patients with COVID-19 in this study is 39.4%, compared with 5.1% in Wuhan. Ling M, et al. explained that the symptoms of taste and smell impairment might not be recorded if they are too mild [4]. Although the patients in this study are ethnic Chinese, they had all recently returned from visits outside mainland China. Leurs and colleagues noted that the reported prevalence of olfactory and gustatory symptoms seems to be substantially higher in European COVID-19 cohorts than in East Asian cohorts [5]. The possibilities were informed by the hypothesis that there are differences in ACE2 receptor expression and in the virus itself between East Asian and European populations [6].

Olfactory decline often occurs before admission to a hospital, corresponding to a positive viral load in the nasopharynx early during the disease [7]. Considering that there may be anosmia in COVID-19, especially during the early stage, during which the average viral load in the early and advanced stage of the disease is significantly higher than during the recovery stage [7], it is here suggested that any person with sudden anosmia and ageusia is likely to be infected with SARS-CoV-2, and further viral testing is necessary. Anosmia was the initial symptom in 15.49% (11/71) of our patients. 5 patients listed anosmia as the only complaint and said they did not have other symptoms, like fever or



Figure 1: Coronal CT image of the paranasal sinuses in a 24-year-old male patient with COVID-19 and anosmia. There was no obvious obstruction of the olfactory cleft or nasal cavity.

Table 1: Clinical characteristics of olfactory and gustatory dysfunction in patients with COVID-19.

Characteristics	Olfactory dysfunction (n=28)	Gustatory dysfunction (n=25)
Gender, Male: Female	9:19	8:17
Age, median (25 th -75 th percentile)-years	23.5 (17-62)	24.3(17-62)
Symptoms (Percent and Number)		
Fever	60.7% (17/28)	60.0% (15/25)
Cough	42.9% (12/28)	48.0% (12/25)
Sore throat	21.4% (6/28)	24.0% (6/25)
Headache	17.9% (5/28)	16.0% (4/25)
Myalgia	17.9% (5/28)	20.0% (5/25)
Diarrhea	14.3% (4/28)	16.0% (4/25)
Abnormal Chest CT (%)	89.3% (25/28)	88.0% (22/25)

Table 2: Visual scores of olfactory and taste sense and recovery rate.

	N	VAS (25 th -75 th percentile)			Recovery rate (%)	
		Initial	1 Week	3 Weeks	1 Week	3 Weeks
Olfactory sense	28	0(0,0.5)	3.5(0.5,6.5)	7.5(5,10)	4(14.29)	11(39.29)
Gustatory sense	25	1(0,3)	5(3,7)	9(7,10)	5(20.00)	12(48.00)

Abbreviations: VAS=Visual Analogue Scale

cough. This is a clear and definite alert that patients with anosmia, especially olfactory dysfunction alone need to be tested.

Most of the cases in the study were returned from Europe. As in European patients, women were more profoundly affected than men, and there was a significant association between anosmia and ageusia [2]. Unlike in European cases, in which facial pain and nasal obstruction were the most common disease-related otolaryngological symptoms [2], our patients did not have readily visible symptoms of nasal inflammation such as congestion or runny nose, which is similar to previous reports [3-4]. Twenty-five patients with ageusia also had anosmia, 7 of whom saw these symptoms appear after taking lopinavir/ritonavir. It is necessary to determine whether Lopinavir/Ritonavir can cause olfactory changes other than the known taste changes. As with the loss of sense of smell caused by other viruses [8], the olfactory decline in COVID-19 patients showed a tendency to self-resolve. 39.29% and 48% of these patients recovered complete olfactory and gustatory sense within the 3 weeks after admission. Other patients also showed different degrees of olfactory improvement.

The mechanism by which anosmia occurs in patients with COVID-19 remains unclear. Not all the patients accepted CT scan of nasal cavity, because the olfactory sensation gradually recovered within a few days, and without nasal congestion or runny nose and else. We performed the concurrent endoscopic nasal examination and CT scans on the patients, both the objective assessments, suggesting that nasal inflammation and related obstruction were not considered as the main etiological factors underlying the olfactory dysfunction in patients with COVID-19. Yet a study has shown elevated levels of the proinflammatory cytokine TNF- α were seen in the olfactory epithelium in patients with COVID-19 [9]. This suggests that direct inflammation of the olfactory epithelium could play a role in the acute olfactory loss described in many patients with COVID-19. CSF examination showed little evidence of brain involvement or direct presence of SARS-CoV-2 in the central nervous system. The current results do not suggest that SARS-CoV-2 invades the brain through retrograde neuronal route. We should be aware of the limitation of the CSF results as they were from only one patient. SARS CoV could enter the nervous system through the olfactory bulb in mice [10], so the neurotropic potential of SARS-CoV-2 in patients of COVID-19 remains to be confirmed. Single-cell sequencing performed by Brann et al. revealed that ACE2 is expressed in support cells, stem cells, and perivascular cells and less important in neurons. Immunostaining confirmed these results. These findings suggest that SARS-CoV-2 infects the non-neuronal cell types, leading to anosmia and related disturbances in odor perception in COVID-19 patients [11].

There are some limitations in this study. These include the small sample size, the lack of objective evaluation of olfactory dysfunction, and the exclusion of patient's hospitalized in the Intensive Care Unit of our institution.

Conclusion

Olfactory and gustatory dysfunction can be an initial symptom of COVID-19, and they may even be the only complaint. The appearance of anosmia may serve as a practical warning sign, indicating the individual is likely to be infected with SARS-CoV-2, especially in patients without any other symptoms. This could also have public health implications in terms of instructing people with anosmia to self-isolate immediately, alert medical personnel when they must stop providing clinical care in person, and inform those in institutional settings, such as elder care facilities or prisons, when they must seek quarantine.

Potential Conflicts of Interest

All authors: No reported conflicts of interest.

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