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Evaluation of nasal function in patients with COVID-19: nasal secretion, nasal clearance, and SNOT-22 score

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ABSTRACT

Objective: This study aimed to investigate the nasal findings in patients who tested positive for the coronavirus disease 2019 (COVID-19) and objectively evaluate the amount of nasal secretion and nasal clearance.

Methods: The study included 40 patients who tested positive and 40 volunteers who tested negative for COVID-19 infection. The self-administered Turkish version of the sinonasal outcome test -22 (SNOT-22) questionnaire was used to evaluate the sinonasal findings, the nasal Schirmer test was used to evaluate the amount of nasal secretion, and the saccharin test was used to evaluate nasal clearance. The results of both groups were compared.

Results: The SNOT-22 score averages were 23.3±14.5 and 11.2±11.7 for the COVID-19-positive group and COVID-19-negative controls, respectively. In the COVID-19 positive group, SNOT-22 results were statistically significantly higher than those of the controls ($p \leq 0.001$). The nasal Schirmer and nasal saccharin test results in the COVID-19-positive group were statistically significantly higher than those of the controls ($p \leq 0.002$ and $p \leq 0.001$).

Conclusion: In patients who tested positive for COVID-19 infection, increased amounts of nasal secretion and prolonged nasal clearance time were observed. They also had higher SNOT-22 scores than those of the negative controls. Although these findings demonstrate that there may be changes in nasal functions in patients positive for COVID-19 infection, new studies are needed to elucidate the nasal effects in detail.

Keywords: COVID-19, schirmer test, saccharin test, SNOT

Introduction

The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects the human respiratory epithelial cells. The clinical features of patients infected with SARS-CoV-2 include fever, dry cough, and shortness of breath with lower respiratory tract infection (1). In severe cases, infections cause viral pneumonia, which can lead to severe acute respiratory distress syndrome and even death (2). The nasal cavity plays an important role in the entry of SARS-CoV-2 into the human body and in proliferation of the virus (3). In addition, epidemiological studies have also reported that some patients might have upper respiratory tract infection findings (nasal congestion, rhinorrhea, and pharyngodynia) (4, 5).

Foreign particles and pathogenic agents in the inhaled air are filtered out by the mucociliary function, which works together with cilia, mucous membranes, and mucus-producing glands (6). Nasal secretions protect the airway epithelium against the harmful effects of the external environment and maintain normal physiology by keeping the mucosa moist (7, 8). Many environmental and individual factors affect the amount of nasal secretion (9, 10). Changes in the amount and content of the nasal secretion affect mucociliary clearance (11). The nasal clearance time is prolonged after viral infections, and this leads

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to various infections in the lower and upper respiratory tract (12-14). Otorhinolaryngological findings are frequently seen in patients with COVID-19 infection as are rhinological findings, such as olfactory dysfunction, rhinorrhea, and nasal congestion (15).

To date, there are no literature data on the effects of COVID-19 on nasal secretion and clearance. In addition, the effects of nasal findings caused by COVID-19 on the quality of life of the patient are not sufficiently known. This study aimed to determine the amount of nasal secretion, nasal clearance, and sinonasal outcome test -22 (SNOT-22) results of patients with COVID-19 infection and compare these with COVID-19-negative controls.

Methods

In this study, 40 patients with COVID-19 infection and 40 COVID-19-negative controls underwent standard rhinological examination and nasal endoscopic examination. All the participants were tested for COVID-19 using a reverse transcription-polymerase chain reaction (RT-PCR)-based test. Patients who presented to the hospital with complaints of fever and cough were tested for the presence of the COVID-19 with the PCR test. The control group included individuals without upper respiratory symptoms and who had a negative COVID-19 PCR test. Patients and controls with allergic rhinitis and rhinosinusitis, nasal septal deviation, nasal polyps, nasal mucosal abnormalities, and other structural abnormalities of the nose, a history of sinonasal surgery, diabetes, hypertension, liver disorder, chronic renal failure, hypo-hyperthyroidism, asthma, topical or systemic drug use (topical or oral decongestant, antihypertensive, antidepressant, antipsychotic, and so on), smoking, and alcohol consumption were excluded from the study. In addition, patients and controls with recent head trauma, psychiatric disorder, autoimmune disease, neurodegenerative disease and who had previously received radiotherapy in the head and neck region were excluded. Participants who had a history of olfactory and taste dysfunction or complained of olfactory and taste dysfunction on the day of the test were also excluded from the study.

The nasal Schirmer test, nasal saccharin test, and the SNOT-22 were conducted to patients before treatment. The same tests were conducted in the control group after the PCR test. Consent was obtained from all the participants. This study was approved by the Ümraniye Training and Research Hospital ethics committee (protocol number: 122, date: 28/04/2020).

Main Points:

- Coronavirus disease 2019 (COVID-19) infection can affect nasal physiology.
- Nasal Schirmer test can reveal whether nasal secretion is affected in COVID-19 infection.
- The saccharine test can reveal whether nasal clearance is affected in COVID-19 infection.
- The sinonasal outcome test can reveal whether these results will be useful in clinical use.

Nasal Schirmer Test

After the patients were adapted to the hospital environment for 15–30 minutes, they were taken to the Schirmer test room. The environmental temperature was recorded as 20.25°C±0.87°C (18.3°C–21.9°C), and humidity was recorded as 45.34±14.26 (23%–68%). For the nasal Schirmer test, a standard Schirmer test paper of 35 millimeter (mm) length and 5 mm width was used (ERC SCHIRMER Tear Test Strip, Turkey). The nasal Schirmer test paper was folded at an angle of 45° from an area of approximately 5 mm from one end and then placed bilaterally with the help of speculum and bayonet in parallel with the nasal dorsum and anterior nasal septum after the anterior rhinoscopic examination. The 5 mm portion of the test paper was placed in contact with the anterior nasal mucosa and the rest of the test paper overflowing from the nostril. During this period, care was taken not to touch the turbinates on the lateral nasal wall. After 10 minutes, the amount of wetting of the paper was recorded in mm.

Nasal Saccharin Test

The saccharin test was used to measure the mucociliary clearance time. Half an hour before the test, all the participants were rested in the environment where the test would be performed. The test was performed at room temperature with the participants in a sitting position with their heads up. The patients were asked to clear the secretions in their noses, and 1/4 saccharin tablet (1×1×1 mm^3), the lower turbinate, was placed in the front. The participants were asked to sit calmly (without sneezing, sniffing, eating, drinking, or bending) until they get the first sense of taste. They were asked to swallow frequently and report as soon as they felt the taste. The time between the insertion of saccharin and when the taste was felt was considered the duration of mucociliary clearance.

Sinonasal Outcome Test-22 Scale

The clinical effects and quality of life of the participants were evaluated using the Turkish version of the SNOT-22 scale. Participants who reported olfactory or taste dysfunction in the SNOT-22 scale were excluded from the study.

Statistical Analysis

Data were analyzed using the The Statistical Package for Social Sciences version 22.0 software (IBM Corp.; Armonk, NY, USA). Power analysis was performed to determine the minimum sample width required to compare 2 groups and 2 ratios. The chi-square test was used for comparison of sexes between groups. The Mann-Whitney U test was used for age comparison between groups. The normal distribution suitability of the parameters was evaluated by the Shapiro-Wilks test. Descriptive statistical methods (mean and standard deviation) were calculated. The Mann-Whitney U test was used to compare non-parametric data. Significance was assessed at $p<0.05$ level.

Results

This study included 40 patients with COVID-19 infection and 40 COVID-19-negative controls. There were 15 male and 25 female patients in the COVID-19 group. The age of the men and women in the COVID-19 group was 22–49 and 24–52 years, respectively, with the mean age being 37.3±7.9 and 34.8±8.1 years, respectively. There were 21 men and 19 women in the

control group with their ages ranging between 18–54 and 18–57 years, respectively, and their mean ages were 40.9±10.6 and 36.9±10.1years, respectively (Table 1). No statistically significant difference was found between the patient and control groups in terms of sex and age (p=0.178 and p=0.143).

The mean saccharin test results for the COVID-19-positive group were 16.3±6.5 minutes (range: 7–28), whereas those for the controls were 8.6±4.6 minutes (range: 2–18). There were statistically significant differences in the saccharin test results between both groups (p≤0.001) (Table 2).

The mean Schirmer test results for the COVID-19-positive group were 11.3±6.5 mm (range: 4–30), whereas those for the controls were 8.1±4.1 mm (range: 4–25). There were statistically significant differences in the Schirmer test results between both the groups (p≤0.002) (Table 2).

The mean SNOT-22 scale results for the COVID-19-positive group were 23.3±14.5 (range: 0–70), whereas those for the controls were 11.2±11.7 (range: 4–36). There were statistically significant differences in the SNOT-22 scale results between both the groups (p≤0.001) (Table 2). According to the SNOT-22 results in the patient group, 19 (47.5%) patients had a nasal obstruction and 16 (40%) had rhinorrhea. In the control group, 12 (30%) patients had nasal obstruction and 6 (15%) had rhinorrhea.

Table 1. Demographic data

		Age (years)	
	N	Min-Max	Mean±SD
COVID-19-positive group			
Men	15	22–49	37.3±7.9
Women	25	24–52	34.8±8.1
Control group			
Men	21	18–54	40.9±10.6
Women	19	18–57	36.9±10.1

N: Number of patients; SD: Standard deviation
Min: Minimum, Max: Maximum

Table 2. Comparison of the COVID-19-positive and control groups

	N	Min-Max	Mean±SD	p
Saccharin test				
COVID-19 group	40	7–28	16.3±6.5	0.001
Control group	40	2–18	8.6±4.6	
Schirmer test				
COVID-19 group	40	4–30	11.3±6.5	0.002
Control group	40	4–25	8.1±4.1	
SNOT-22				
COVID-19 group	40	0–70	23.3±14.5	0.001
Control group	40	0–36	11.2±11.7	

Mann-Whitney U test, p≤0.05
N: Number of patients; SD: Standard deviation; SNOT-22: Sinonasal Outcome Test-22

Discussion

Nasal mucociliary clearance plays a key role in the defense mechanism of the upper and lower airways. Respiratory mucosa, mucus structure, and epithelial ciliary activity play an important role in the formation of sinonasal pathologies (16). The nasal epithelium is one of the first areas where SARS-CoV-2 caused the infection. Expression of the SARS-CoV-2 host cell surface receptor, angiotensin-converting enzyme 2, is highly expressed in the nasal mucosa, particularly the ciliated epithelium and goblet cells (17). It has been approved to bind to the SARS-CoV-2 spike protein and promote the internalization of the virus into human cells (18). Moreover, viral replication appears to be the highest in the nasal cavity, as demonstrated by the maximum viral titers shed from the nose (19). Viruses that infect the upper respiratory tract disrupt their function by causing changes in the nasal mucosa cilia cells (20). SARS-CoV-2 may multiply in the nasal epithelial cells, causing changes in the structure and function of these cells. In this study, the Schirmer test evaluated the nasal secretion, and the saccharin test evaluated the nasal clearance values qualitatively in patients with COVID-19 infection and in the control group. Increased secretion and clearance values were determined in the COVID-19-positive group. In addition, a statistically significant increase was detected in the sinonasal quality of life measurements performed with the SNOT-22 scale.

The nasal mucosa is rich in vascular and glandular structures that are vital in the mucous layer and for the mucociliary movement. Any factor affecting the mucous layer affects mucociliary clearance. Nasal glandular secretion is important for nasal mucociliary clearance (21). Nasal Schirmer test is an inexpensive, easy-to-apply, objective, and simple method to determine the amount of nasal secretion and does not cause any discomfort to the patient (22). Server et al. (23) have also revealed that the intranasal Schirmer test can be used in the Turkish population to determine the amount of nasal secretion. In our study, a statistically significant increase in the nasal Schirmer test values was detected in the COVID-19-positive group than in the controls.

Nasal clearance is impaired in patients with a viral upper respiratory infection (24). Patients who have had rhinovirus, influenza A, and influenza B infections have damaged nasal mucosal epithelium and consequently prolonged clearance time (25, 26). Degeneration of ciliated cells in the sinonasal mucosa was detected after viral infection (27). In a study where nasal symptoms of 18 (5 men, 13 women) patients with positive COVID-19 test results were observed, 6 patients had rhinorrhea, 6 had a nasal obstruction, and 12 had olfactory dysfunction. The nasal cytology examinations of all the patients revealed increased mild nasal inflammation and changes consistent with cellular distress. They suggested that the nasal symptoms in patients with COVID-19 infection were related to the findings they found in the nasal cytology examination (28). In our study, prolongation of nasal clearance was detected in the COVID-19-positive group. In patients with COVID-19 infection, prolongation of clearance time may be related to increased distress on nasal epithelial cells.

Health-related quality-of-life (HRQL) surveys are frequently used in daily medical practice to understand how an individual senses his/her disease. These questionnaires are also useful for the assessment of patients with rhinological complaints. The use of HRQL questionnaire plays a critical role in understanding the patient's perspective concerning disease-related issues (29, 30). Therefore, HRQL measurements are often used during diagnosis and post-treatment clinical follow-up (31). The SNOT-22 is a broadly used, validated, patient-reported, and disease-specific questionnaire to assess the quality of life in patients with sinonasal diseases (32). In patients with sinonasal complaints, the Turkish version of the SNOT-22 is a reliable, consistent, and valid test for the Turkish community (33); therefore, we used the SNOT-22 scale in our study.

Patients with COVID-19 infection can present with a wide range of clinical findings. The most common findings are fever, cough, shortness of breath, fatigue, and muscular joint pain. Less often, headache, sore throat, nausea, vomiting, and diarrhea are also observed (34, 35). In a study evaluating the sinonasal findings of 103 patients with COVID-19 infection, 61.2% had olfactory dysfunction, 65% had taste dysfunction, 49.5% had nasal congestion, and 35% had rhinorrhea (36). In addition, 54% patients with olfactory dysfunction were found to have nasal obstruction, and 34.9% of them had rhinorrhea (36). In another study investigating the findings of taste and olfactory dysfunction in patients with COVID-19 infection, sinonasal complaints were evaluated retrospectively with the SNOT-22 scale, and the total score was 21 (range 0–73) (37). Of all the patients evaluated, 55.4% had taste dysfunction, 41.7% had olfactory dysfunction, 35% had rhinorrhea, 34.3% had nasal congestion, 23% had postnasal discharge, and 14.2% had dark viscous discharge (37). In our prospectively planned study, higher SNOT-22 scores were observed in patients with COVID-19 infection than in the controls. According to the test results in the patient group, 19 (47.5%) had nasal obstruction and 16 (40%) had rhinorrhea. In addition, it was found that the amount of nasal secretion and nasal clearance time increased in the COVID-19-positive group.

One of the limitations of our study was that we did not investigate whether the results of patients with COVID-19 infection returned to normal after treatment. Another limitation is the lack of objective tests evaluating other nasal functions. To completely study the effects of COVID-19 infection on the nasal mucosa, studies involving a large number of patients may be required along with tissue-level research.

In conclusion, there was an increase in the nasal Schirmer and nasal clearance test results in COVID-19-positive group than in the control group. In addition, higher SNOT-22 results were observed in the COVID-19-positive group. Further studies can elucidate the effects of increased nasal secretion and prolonged nasal clearance caused by COVID-19 on the nasal mucosa and paranasal sinuses.

Ethics Committee Approval: This study was approved by Ethics committee of Umraniye Training and Research Hospital (Approval No: 122)

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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