

# Can Topical Nasal Steroid Prevent the Loss of Smell in Covid-19?

Mustafa Timurkaan (✉ [eseda61@hotmail.com](mailto:eseda61@hotmail.com))

Elazığ Fethi Sekin City Hospital: Elazığ Fethi Sekin Şehir Hastanesi

Yavuz Sultan Selim Yıldırım

Elazığ Fethi Sekin City Hospital: Elazığ Fethi Sekin Şehir Hastanesi

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## Research

**Keywords:** SARS-CoV-2, COVID-19, Nasal Steroid, Loss of Smell

**Posted Date:** July 13th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-672443/v1>

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# Abstract

**Purpose:** The purpose of this study is to evaluate the effects of nasal steroid use on the loss of smell in patients diagnosed with Covid-19.

**Material and Method:** 211 patients diagnosed with Covid-19 with positive PCR tests between April 2020 and December 2020 and followed up and treated in the Elazig City Hospital Pandemic Clinic were included in this cross-sectional study. The demographic data, comorbidities and drug use histories of the patients were interviewed face-to-face and recorded.

**Findings:** The average age of the patients was  $53.55 \pm 17.81$  (129 men, 82 women). Regarding the age, gender and comorbidities of the patients, there was no difference between the groups with and without loss of smell in terms of average age and gender. Anosmia developed in 50 patients (23.5%) and hyposmia developed in 84 patients (40%). No decrease or loss of sense of smell was observed in 77 patients. 26 of these patients were using nasal steroids at the time of diagnosis, and none of them had a decrease or loss in sense of smell.

**Results:** With the results of the study, it has presented for the first time to the literature that the use of nasal steroids can prevent the loss of smell, which is one of the common neurological symptoms in Covid-19. The results of our study suggest that the nasal steroid, which plays an immunomodulatory role, can be a shield against loss of smell by creating a local anti-inflammatory effect in the nasal mucosa and around the olfactory nerve.

## Background

The SARS-CoV-2 virus, which causes COVID-19 disease, is a single-stranded RNA virus and is transmitted via droplets. After the disease was first seen in China, it was declared as a pandemic by the World Health Organization (WHO) as it spread rapidly throughout the world. The SARS-CoV-2 virus has significant morbidity and the mortality rate is estimated at approximately 3.4%. Especially in geriatric patients, mortality reaches 6.5–10% (1). The characteristic infection caused by the SARS-CoV-2 virus is the interstitial lung disease in which diffuse chronic inflammation occurs. Dyspnea, muscle-joint pain, fever and cough are the most common symptoms in patients. In some patients, it becomes more severe, developing Acute respiratory distress syndrome (ARDS), which can lead to acute lung failure and death afterward (1).

The sudden onset anosmia seen in COVID-19 patients is a distinctive feature from other viral infections, and its incidence has been reported to be between 30–88% (2, 3). It is pointed out that isolated sudden onset anosmia may be the only sign of COVID-19 infection without any other symptoms and these patients can transmit the disease to a large number of people. Recently, it has been reported that smell and taste disorders may be the first and sometimes additional symptoms of the disease. (4). Although it is stated that different cranial nerves may also be retained due to the possible neurotropic properties of

the SARS-CoV-2 virus, the number of SARS-CoV-2 positive patients presenting with cranial nerve neuropathy in the literature is very low (4).

## Material And Method

211 patients who were applied to the Elaziğ Fethi Sekin City Hospital pandemic polyclinic between April 2020 and December 2020 and were hospitalized with a pre-diagnosis of Covid-19 and confirmed to be Covid-19 in PCR tests were included in this cross-sectional study. The ages, genders, comorbidities and drug uses of the patients were questioned face to face and recorded. All patients were informed about the study and written informed consent was obtained. Ethical approval from Firat University Ethics Committee (Document No 2021 / 01–30). and the Ministry of Health Covid – 19 study permission (Study Permission No: 2021-01-13T\_07\_43) were obtained for the study. The data were analyzed using Microsoft Excel and SPSS version 21.

## Findings

A total of 211 patients (129 men, 82 women) were included in the study and the average age of them was  $53.55 \pm 17.81$ . The average age of male patients was  $55.24 \pm 17.21$  while it was  $50.90 \pm 18.50$  for women. The average hospitalization period of the patients was 19.3 days. In both women and men the group with multiple diseases constituted the majority and hypertension and diabetes were the most common comorbidities in patients, respectively (Table 1). When age, gender and comorbid diseases were considered, no significant difference was found between the groups with and without loss of smell. Anosmia developed in 50 (23.5%) patients, and hyposmia developed in 84 patients (40%).

Table 1  
The distribution of the ages, genders and comorbidities of the patients

Gender	Age	Hypertension	DM	COPD	Multiple Disease	No Additional Disease
Male	$55,24 \pm 17,21$	20 % 9.5	19 %9	7 %3.3	58 %16.6	25 %11.8
Female	$50,90 \pm 18,50$	16 %7.6	5 %2.4	3 %1.4	35 %27.5	23 %10.9

No decrease or loss of sense of smell was observed in 77 patients in total. It was concluded that 26 (12.3%) of these patients used nasal steroids during the diagnosis (Table 2). It was found out that there was no decrease in sense of smell during and after Covid-19 infection. 14 of these patients were female (6.6%) and 12 were male (5.7%). (Table 1–2).

Table 2  
Nasal preparations of the patients (according to the number of people)

Gender	Triamcinolone Acetonide	Fluticasone	Beclometasone
Male	9	4	3
Female	4	4	2
	13	8	5

## Discussion

SARS-CoV-2 virus, which is a member of the Coronaviridae family, contains 4 structural proteins consisting of S (spike), M (membrane) and N (nucleocapsid, containing the RNA genome) proteins. S protein attaches to the cell membrane by the angiotensin-converting enzyme-2 (ACE2) receptor in the host (2, 3). SARS-CoV-2 has genetic sequences that are highly similar to MERS-CoV and SARS-CoV coronaviruses, which are potentially lethal to humans. The fact that neuroinvasive properties of these viruses were detected in individuals with MERS and SARS and in experimental animal studies conducted for these viruses suggests that the SARS-CoV-2 virus may also have similar properties (4, 5).

SARS-CoV-2, enters cells via ACE-2 receptors, which are an important component of the renin-angiotensin system in the brain, such as SARS-CoV (6, 7).

The olfactory nerve pathway begins with bipolar neurons; their axons and dendrites go to the olfactory bulb and synapse in this area. In addition, this pair of cranial nerves are divided into two branches and heads towards the olfactory nucleus located in the piriform cortex (8). In the animal models examining coronavirus infection pathways, it has been shown that the olfactory nerve pathways are used by the virus after the virus is occluded into the nasal passage (9, 10). It has been proven that the virus reaches the olfactory bulb approximately 60 hours after its exposure to SARS-CoV-2; it reaches the dorsal nucleus of the raffin in the piriform cortex and brain stem on the 7th day (9). The most important aspect of this spreading route is that there is a possibility that the virus may affect respiratory centers after it has settled in regions in the brainstem. (9–11).

In their study including 214 patients, Mao et al. evaluated neurological symptoms in 3 categories as peripheral, central and musculoskeletal. In this study, neurological symptoms were detected in 77 patients and it was reported that the symptoms correlated with the severity of the disease. Imbalance was found in 16.8% and headache was found in 13.1% in the patients with central nervous system (CNS) symptoms. The most common symptoms of the peripheral nervous system (PSS) (8.9%) were hypogusia with 5.6% and hyposmia with 5.1% (4). In the study conducted by Yan and his team, it was also reported that 71% of COVID-19 positive patients had loss of smell and taste (12). Menni et al. found that the rate of loss of smell and taste was 59% in 1702 patients with positive PCR tests. They also stated that the loss of smell may be one of the sensitive symptoms for the diagnosis of Covid-19, together with major symptoms such as fever, cough and shortness of breath (13). In our study, anosmia developed in 50 (23.5%) patients and

hyposmia developed in 84 (40%) patients. In 3 patients (1.40%), only loss of taste developed without loss of smell.

Although it is well known that various viruses can damage the olfactory neuroepithelium, the cause of loss of smell due to SARS-CoV-2 is not exactly known. Indeed, these acute viral upper respiratory viral infections that damage the epithelium are the major cause of chronic olfactory dysfunction, and it is known that a large number of viruses enter the brain via cellular and pericellular transport through this epithelium (14). In North America, the highest period of non-flu-related loss of smell, including those possibly due to coronaviruses, occurs in April, May, and June while flu-associated loss of smell peaks in December, January, and February. It is thought that some of the viruses taken into the body through droplets settle in the lungs through the respiratory system and form an infection focus while some may settle in the olfactory epithelium. Also some of the viruses that settle in the olfactory epithelium are thought to be transported to the central nervous system via the olfactory bulb by replicating here (10, 14).

In our study, of the patients with nasal steroid 13 patients were using preparations containing triamcinolone acetonide, 8 were using preparations containing fluticasone, and 5 patients were using preparations containing beclomethasone dipropionate (Table 2). Remarkably, it was observed that the symptoms related with loss of smell did not develop in patients using all three preparations. Nasal steroids prevent the effects of inflammatory cytokines on the nasal mucosa by suppressing the allergic-inflammatory process both in the early and late stages. Thus, they prevent the cytokine exposure of olfactory nerve cells. In addition, since they also suppress the release of mediators such as histamine that can cause congestion, they mechanically prevent nasal obstruction. The effects of nasal steroids on loss of smell have not been clarified yet. We think that nasal steroids prevent the loss of smell seen in Covid-19.

We believe that this protective effect occurs due to the fact that the nasal steroid used plays an immunomodulator role with a local anti-inflammatory effect on the nasal mucosa and around the olfactory nerve.

Although in many studies, loss of smell has been reported based on the patient's declaration, Moein et al. compared 60 covid-19 patients with 60 healthy individuals in their UPSIT objective smell test studies and reported that 58% of patients developed hyposmia (20/60, 33%) or anosmia (15/60, 25%) (16). As well as our findings are similar to the results of Moei et al.'s studies with an objective smell test, we criticize ourselves and our limitations as these findings are based on data obtained according to subjective patient statements. However, considering that the primary transmission route of covid-19 is the droplets, the objective smell test is not recommended at this stage, as it will increase the risk of contamination of the virus.

## Conclusion

Although the loss of smell and taste, which can sometimes be the first symptom in Covid-19, is stimulating, it is an extremely disturbing situation for patients. In our study, when we examined the drug

use histories of 211 patients we followed up, we found that 26 patients had been using nasal steroids for a long time. The fact that none of these patients developed a decrease or loss of sense of smell suggested that nasal steroids may have a preventive effect on the loss of smell in Covid-19 patients. We believe that the loss of smell due to Covid-19 can be prevented by nasal steroid administration, which was presented to the literature for the first time through our study. However, in order to reach a definite conclusion, there is a need for randomized studies in which larger series and objective smell tests are applied.

## Abbreviations

World Health Organization (WHO)

Acute respiratory distress syndrome (ARDS)

S (spike), M (membrane), N (nucleocapsid)

Central nervous system (CNS)

Peripheral nervous system (PSS)

## Declarations

**Acknowledgements:** Ethics approval and consent to participate: Ethical approval from Firat University Ethics Committee (Document No 2021 / 01-30). and the Ministry of Health Covid -19 study permission was obtained (Study Permission No: 2021-01-13T\_07\_43) for the study.

**Consent for Publication:** Not applicable

**Availability of data and material:** The data were made readily reproducible materials described in the manuscript.

**Funding Details:** The authors received no financial support for the research, authorship, and/or publication of this article.

**Disclosure Statement:** The authors have no conflicts of interest to declare.

**Authors' contributions:** MT: Conception or design of the work. Data analysis and interpretation. Critical revision of the article. Final approval of the version to be published.

YSSY: Data collection. Data analysis and interpretation. Drafting the article.

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