Original Article

Role of Topical Intranasal Corticosteroid for Treatment of Post-COVID Olfactory Dysfunction – Our Experiences

Santosh Kumar Swain, Swaha Panda, Ansuman Sahu, Somya Ranjan Pani

Department of Otorhinolaryngology and Head and Neck Surgery, IMS and SUM Hospital, Siksha "O" Anusandhan University, Bhubaneswar, Odisha, India

Abstract

Background: The coronavirus disease 2019 (COVID-19) is a highly contagious acute respiratory disease caused by a novel virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 infection presents with respiratory illness and even respiratory failure and death. Olfactory dysfunction is an important clinical manifestation that has an impact on quality of life. **Objective:** This study is designed to analyze the role of the topical nasal corticosteroid in post-COVID olfactory dysfunction. **Materials and Methods:** This is a prospective and descriptive study on 72 COVID-19 patients who were administered topical intranasal corticosteroids and olfactory training. All of them were diagnosed with COVID-19 infection by reverse transcription–polymerase chain reaction of the nasopharyngeal swab. The detailed clinical examination and treatment with intranasal corticosteroid and its outcome were analyzed. **Results:** In this study, 46 (63.88%) patients were male and 26 (36.11%) were female with a male-to-female ratio of 1.76:1. The age ranges from 18 to 58 years. There were 30 (41.66%) patients in the age range of 18–30 years and 42 (58.33%) patients in the age range of 31–58 years. Out of 72 patients, 11 (15.27%) patients recovered after 2 weeks, 34 (47.22%) patients recovered after 3 weeks, and 20 (27.77%) recovered after 4 weeks. Three patients lost to follow-up during the treatment period. **Conclusion:** COVID-19 infection is spreading quickly all the continents of the world. Olfactory dysfunction is an important symptom of the COVID-19 infection. Intranasal mometasone spray and olfactory training are useful treatment options for post-COVID olfactory dysfunction.

Keywords: Coronavirus disease 2019, intranasal steroid spray, olfactory dysfunction, olfactory training, severe acute respiratory syndrome coronavirus 2

Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] By March 2021, approximately 117 million people worldwide have been affected with COVID-19 infection with more than 2.6 million deaths.[2] SARS-CoV-2 is a heterogeneous virus that manifests itself with a wide range of the spectrum, from asymptomatic to life-threatening and fatal diseases. The symptoms of COVID-19 range from fever, dry cough, throat pain, myalgia, fatigue, gastrointestinal symptoms, loss of smell, loss of taste to severe acute respiratory distress syndrome and respiratory failure.[3] Currently, COVID-19 patients keep on coming to the hospital with sudden onset of olfactory dysfunction. Olfactory dysfunction in COVID-19 patients might be caused by upper respiratory tract infections. SARS-CoV-2 is one of many pathogens which cause postinfectious olfactory dysfunction. Angiotensin-converting enzyme 2 (ACE2) receptors are more expressed on nasal epithelial cells which are needed for entry of SARS-CoV-2.[4] In the course of COVID-19 disease, many patients present with anosmia or hyposmia and mostly after recovery from SARS-CoV-2 infection. Oral corticosteroids have been prescribed to exclude an inflammatory component in patients with postinfectious olfactory dysfunction. However, oral corticosteroids are not recommended currently for postinfectious olfactory dysfunction as the benefit is lacking and with a potential risk of mucormycosis.[5] Here, this study

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Address for correspondence: Prof. Santosh Kumar Swain, Department of Otorhinolaryngology and Head and Neck Surgery, IMS and SUM Hospital, Siksha "O" Anusandhan University, K8, Kalinga Nagar, Bhubaneswar - 751 003, Odisha, India.
E-mail: santoshvoltaire@yahoo.co.in

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is aimed to evaluate the role of topical intranasal steroids along with olfactory training for post-COVID olfactory dysfunction.

Materials and Methods

This is a prospective study conducted at a tertiary care teaching hospital between November 2020 and December 2021. This study was approved by the Institutional Ethical Committee (IEC) with reference number IEC/IMS/SOAU//21/12.08.2020. The patients who recovered from proven COVID-19 infection and complained of anosmia or hyposmia were enrolled in this study. The proven COVID-19-positive patient was based on the positive reverse transcription polymerase chain reaction (RT-PCR) where samples were obtained from the nasopharyngeal swab. The recovery was defined as a negative report of RT-PCR. The patients who participated in this study were above the age of 18 years. All of them had complained of decreased smell sensation. Patients with previous sinonasal disease, already using topical nasal steroids, pregnancy, and patients with hyposmia/anosmia improved before COVID-19 recovery were excluded from this study. All the enrolled patients have signed their written informed consent for this study. All participants underwent a detailed medical examination and past relevant history documented such as age, sex, duration, the severity of the COVID-19 infection, and place of isolation/treatment. The risk factors such as diabetes mellitus, hypertension, and if any steroid taken by the patient during the treatment period were documented. The clinical examinations of the participants were done with the use of appropriate protective measures. Diagnostic nasal endoscopy was done in all cases to rule out any obstructive pathology in the nasal cavity. Magnetic resonance imaging (MRI) was done in all cases with olfactory dysfunction to rule out any lesions at the olfactory neuroepithelium. All the participants received topical corticosteroid nasal spray (mometasone furoate) with one puff in each nostril twice daily for 4 weeks. The direction of the tip of the nasal spray was toward the olfactory area at the time of spray. All the participants were advised to sniff the rose, clove, and lemon for 20 s each, twice a day (olfactory training) during the treatment period. The assessment of smell was done after 1 week, after 2 weeks, after 3 weeks, and after 4 weeks for all patients. The duration of decreased smell was documented from the onset of hyposmia/anosmia till full recovery of the sensation. The Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 20, was used for all statistical analyses (IBM-SPSS Inc., Chicago, IL, USA).

Results

In this prospective study, 72 (23.07%) patients presented with olfactory dysfunction out of the 312 COVID-19 patients. Out of 72 patients, 46 (63.88%) were male and 26 (36.11%) were female with a male-to-female ratio of 1.76:1. The age ranges from 18 to 58 years with a mean age of 28.4 years. There were 30 (41.66%) patients in the age range of 18–30 years and 42 (58.33%) patients in the age range of 31–58 years [Table 1]. Out of 72 patients, 44 (61.11%) patients were managed in-home isolation and 28 (38.88%) were managed in hospital. In this study, 14 (19.44%) patients were diabetic, 10 (13.88%) were hypertensive, and 12 (16.66%) were taking systemic steroids during their treatment period. Out of 72 patients, 11 (15.27%) patients recovered after 2 weeks, 34 (47.22%) patients recovered after 3 weeks, and 20 (27.77%) recovered after 4 weeks [Table 2]. Three patients lost to follow-up during the treatment period. Four (5.55%) patients persisted with olfactory dysfunction even after 4 weeks of the use of intranasal steroid spray [Table 2]. All of the patients underwent olfactory training during the treatment period. These four patients underwent intranasal steroid spray and olfactory training for the next 2 weeks, and they recovered with olfaction.

Discussion

COVID-19 is a viral pandemic that originated from Wuhan, China, and rapidly spread to the whole world.[6] COVID-19 infection is associated with a wide range of symptoms which range from mild fever to life-threatening pneumonia.[7] Olfactory dysfunction is a common manifestation of viral infection in the upper airway.[8] Olfactory dysfunction is a characteristic feature of COVID-19 patients which may be the only symptom or associated with other symptoms, but its exact pathogenesis is not clear. The olfactory dysfunction in COVID-19 patients may result from viral-induced olfactory nerve damage, local inflammation in the nasal cavity, or both.[9] A previously published systematic review showed a prevalence of olfactory dysfunction found in 50% of COVID-19 patients.[10] Current data suggest a high rate of early recovery, however, approximately

Table 1: Clinical profile of patients with post-COVID olfactory dysfunction

Patient profile	Number of patients ($n=72$), *n* (%)
Sex	
Male	46 (63.88)
Female	26 (36.11)
Age (years)	
18–30	30 (41.66)
31–58	42 (58.33)
Home isolation	44 (61.11)
Hospital treatment	28 (38.88)
Diabetes mellitus	14 (19.44)
Hypertension	10 (13.88)
Received systemic steroid	12 (16.66)

Table 2: Treatment output of patients with post-COVID olfactory dysfunction

Time of treatment	Number of patients recovered (%)
First week	0
Second week	11 (15.27)
Third week	34 (47.22)
Fourth week	20 (27.77)
Sixth week	4 (5.55)
Lost follow-up	3 (4.16)

10% of COVID-19 patients have not shown any recovery and still present anosmia or hyposmia.[10] In this study, 72 (23.07%) patients presented with olfactory dysfunction out of the 312 COVID-19 patients. Olfactory dysfunction is classified into two types such as conductive type (physical blockage of the airflow into the olfactory mucosa) and sensorineural type (damage of the olfactory neural signaling pathway).[11] The exact etiopathogenesis for the sensorineural type of olfactory dysfunction is still known.[12] In our study, all cases underwent diagnostic nasal endoscopy and MRI to rule out the conductive type of the lesions in the COVID-19 pandemic. MRI is also useful to identify the lesion in the olfactory epithelium.

Viruses causing common colds such as influenza, parainfluenza, rhinovirus, and coronavirus are common pathogens responsible for the postviral olfactory loss.[13] COVID-19 infection has been associated with a high chance of olfactory dysfunction along with taste disturbances.[14] The SARS-CoV-2 might damage the olfactory epithelium and alter the number and functions of its receptors.[15] It is a hypothesis that the olfactory dysfunctions are not associated with viral damage to the neuronal cells. Nonneuronal cells which express ACE2 receptors such as olfactory epithelium sustentacular cells, Bowman's gland cells, microvillar cells, horizontal basal cells, and olfactory bulb pericytes may be the target cells for SARS-CoV-2.[16] In patients of prolonged anosmia and longstanding olfactory dysfunctions, the involvement of the stem cells which express lesser levels of ACE2 receptors could be considered as the cause.[17] However, the exact etiopathogenic mechanism for underlying chemosensitive dysfunctions in COVID-19 patients has not been elucidated. One study showed that diabetes mellitus, hypertension, and duration of steroid administration at the time of COVID-19 treatment have a significant relation with severity and duration of olfactory dysfunction.[18] In this study, 19.44% of patients were diabetic, 13.88% were hypertensive, and 16.66% were taking systemic steroids during their treatment period.

The clinical manifestations of COVID-19 infections include fever, dry cough, and dyspnea.[3] COVID-19 patients often present with acute onset of smell and/or taste disturbances with the presence or absence of other clinical manifestations of the COVID-19 infection. Several COVID-19 patients complain of impairment of smell and taste interchangeably. SARS-CoV-2 usually affects olfactory and gustatory systems, and in the majority of the cases, these clinical manifestations are not associated with retronasal olfaction (flavor) rather than gustatory dysfunction (sweet, sour, salty, and bitter).[19,20] For this cause, it is thought that chemosensory impairment is likely to olfactory in COVID-19 patients. In one study on COVID-19 patients, anosmia showed a high rate of recovery of olfactory dysfunction within 1–2 weeks after the onset of the dysfunction.[21] In this study, the majority of the patients (47.22%) got recovery from olfactory dysfunction by the 3rd week. One study in Italy showed that olfactory disturbance in COVID-19 patients is often seen in younger patients and women.[22] In this study, patients were in the age group of 18–58 years and more number of patients (58.33%) with olfactory dysfunction specifically in 31–58 years. Proper history taking, endoscopic examination of the nasal cavity, and imaging are important components for the diagnosis of the suspected olfactory dysfunction following COVID-19 infection. The requirement of imaging in COVID-19 patients has yet to be established, and so should be reserved for patients with persistent olfactory dysfunction. MRI is important imaging to find out the lesion on the olfactory epithelium.

The prognosis of sensorineural type of olfactory dysfunction is poor and also irreversible. Postviral olfactory dysfunction also shows a poor response to treatment. If the sensorineural type of olfactory dysfunction recovers, the majority of the cases show improvement within 6 months. One study shows that the sensorineural type of olfactory dysfunction may not show an effective outcome to the oral or topical steroids.[23] If olfactory dysfunction improves spontaneously in COVID-19 patients, specific treatment may not be needed. However, if the olfactory impairment persists for more than 2 weeks, it is reasonable to consider treatment. The effectiveness of the available treatment options for olfactory dysfunction in COVID-19 infection is not known, however, the treatments targeting COVID-19-related olfactory dysfunction may be potentially helpful. Oral corticosteroids are usually administered in different otorhinolaryngological conditions such as idiopathic sudden sensorineural hearing loss, sudden-onset facial nerve palsy, and acute postviral anosmia.[24] Steroid administration is often associated with hearing improvement in case of sudden-onset sensorineural hearing loss whereas an improvement in case olfactory recognition suggests that corticosteroids may be useful for acute, reversible stages of olfactory mucosal injury in case of acute postviral anosmia.[24] Exogenous steroids have been classically associated with the suppression of body immunity. Hence, during the COVID-19 pandemic, the corticosteroids should be judiciously used as it may harm innate immunity and affect the first line defense and increase the viral load. However, the adaptive immunity should also be taken into consideration concerning COVID-19 immunopathology and coincides with the appearance of a specific antibody against SARS-CoV-2.[25] However, steroid therapy in COVID-19 patients shows low mortality rates and increases survival.[26,27]

In the initial period of the pandemic, oral corticosteroids were strongly contraindicated by the World Health Organization; however, mounting evidence shows significant benefit on mortality in severe types of COVID-19 infection.[28] One study was showing the improvement of the olfaction with the use of systemic corticosteroids in some patients with postviral olfactory dysfunction.[29] Olfactory training is another important treatment option for olfactory dysfunction and is successful in patients with loss of smell sensation after upper respiratory tract infection.[30] Although the outcome of an olfactory training program is under investigation, the neuronal basis of this treatment remains poorly understood. Olfactory training is done with sniffing of rose, lemon, and clove for 20 s twice daily in each nostril.[31] In this study, all the participants underwent olfactory training along with intranasal corticosteroid spray.

In post-COVID olfactory dysfunction, other supportive medications include intranasal sodium citrate which seems to modulate the olfactory receptor transduction cascades, intranasal vitamin A which may act as a promotor for olfactory neurogenesis, and systemic omega-3 which usually act through neurodegenerative or anti-inflammatory means.[31] The latter two medications may act as adjuvant therapies in olfactory training. However, to date, there is no documentation regarding the effectiveness of therapies in olfactory training. However, currently, there is no evidence of these therapies that are effective in COVID-19 patients.

Conclusion

An intact smell is needed for the human being to identify the chemical signals from surroundings. Any defect in the sensation of smell affects the quality of life. Hyposmia and anosmia are common clinical manifestations found in COVID-19 patients. Early treatment of olfactory dysfunction in post-COVID patients helps to protect the quality of life. Intranasal corticosteroid is an important treatment option in the current scenario for preventing olfactory dysfunction. Olfactory training along with intranasal steroid spray increases the chance of recovery from olfactory impairment. However, more studies are required to know more treatment options for post-COVID olfactory dysfunction. There are also a greater number of studies that are required to validate our findings and find out other treatment options for avoiding the longstanding sensorineural type of olfactory dysfunctions.

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Conflicts of interest

There are no conflicts of interest.

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