Effect of nasal corticosteroid on cacosmia after COVID-19

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Abstract

Background: Olfactory disorders may be an isolated symptom of (COVID-19) infection. Multiple treatment modalities have been attempted to treat them.

Objectives: compare the effect of nasal corticosteroid on COVID-19 positive patients aiming to decrease the duration of olfactory qualitative, quantitative and residual abnormalities as cacosmia with those who hadn't taken nasal corticosteroid

Patient and methods: This study included 200 patients who presented to the Otorhinolaryngology Department, divided into equal two groups: Group1 (treated group) All patients were given two sprays (50 mcg of mometasone furoate in each spray) in each nostril twice daily (total daily dose of 400 mcg). Group 2 (untreated group) those who weren't administered nasal corticosteroid or systemic corticosteroid in anosmia treatment.

Result: Anosmia in group 1 improved by 61% in the first week,83% in the second week,100 % after one month, and regular follow-up was done for 6 months while in group 2 improvement was 42% in the first week,59% in the second week,73% after one month .In group 2 out of 100 patients 30 patients complained of cacosmia after initial anosmia 3 of them reported improving smell after 1 week then 2 weeks later cacosmia appeared and none of them were improved within the 6 months of follow up with significant p-value between 2 groups <0.001.

Conclusion: Cacosmia in the COVID-19 patient must be taken seriously with the trial of different lines of treatment. Nasal corticosteroid is highly recommended in treating anosmia in COVID-19 patients and preventing a high recurrence.

Keywords: COVID-19; Anosmia; Cacosmia; Steroids.

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Introduction

Olfactory disorders, both qualitative and quantitative often occur simultaneously.The qualitative type represents odor identification disorders (dysosmia), which include parosmia (odor perception alteration in the presence of odor) and phantasma (receiving smellswithout beingpresent). The unpleasant smell of all odours (cacosmia) is a special type of dysosmia. The quantitative type includes hyposmia (decrease in smell) and anosmia (lack of smell) compared with normosmia (normal smell perception) **(Seok Hyun 2014)**

the pathogenesis of parosmia is still unknown but some theories have been put forward; 1) olfactory receptor neurons partially lost, 2) intraneuronal loss of olfactory bulb, 3) pathology of the central nervous system, 4) abnormalities in axonal targeting from regenerating fibers after injury, and 5) altered olfactory map after olfactory injury **(Seok Hyun 2014)**.

Dysosmia may significantly decrease quality of life because of foul odor, altered taste, and weightloss. **(Frasnelli et al. 2004, Muller etal. 2006)**, and it may (especially cacosmia) develop late in COVID-19 **(Topal etal.2021)**.

In most patients, olfactory disorders regarding viral infection are hyposmia accompanied by dysosmia **(Seiden et al. 2001)**.Anosmia has been as an early isolated symptom of coronavirus disease 2019 (COVID-19) **(Gautier et al. 2020,Hjelmesæth etal. 2020)**

There are two theories to explain the olfactory disorders because by COVID-19-19 infection. The first; is the affection of the central nervous system by the virus penetrating the nasal epithelium, cribriform lamina, olfactory bulb, and the olfactory nerve pathway, to cause anosmia or hyposmia **(Netland et al. 2008)**. The second is peripheral viral involvement of the nasal epithelium which has greater expression of ACE-2 receptors. The virus bindto these receptors causing degeneration of the nasal mucosaepithelial cellsleading toinflammation and damage of the neural olfactory receptors **(Lao et al. 2020, Whitcroft et al. 2020,Ralli et al. 2020)**. Angiotensin-converting enzyme 2 receptors binding by COVID-19 19 virus is the responsible for COVID-19 19 human infection and these receptors' expression is different between organs **(Yan etal. 2020)**

Different mechanisms and pathogenesis make determining of treatment of olfactory function difficult **(Zhang et al. 2021)**.Multiple treatmentmodalities including olfactory training (OT), corticosteroid, theophylline, budesonide (nasal irrigation), intranasal calcium buffers, and antibiotics have been attempted to treat **(Daval et al. 2020, Harless et al. 2016, Kim et al. 2020)**

Corticosteroids as anti-inflammatory acting on the immune system by blocking the production of substances that trigger inflammation, such as prostaglandins, and this lead to relieving pain, swelling, and redness both systemically and locally, immunosuppressive; impairing the production of defensive white blood cells, called T-cells so suppress the action of the immune system and Vasoconstrictive; block the inflammatory compound called histidine and, by doing so, can reduce mucus secretions that can congest airways and other organs**(Becker. 2013)**.

Corticosteroids may also block the virus from infecting cells. Singanayagam's reported that steroid inhalers reduced the number of ACE2 receptors in animal

models and human cells. **(Finney et al. 2021)**

Using nasal steroids for olfactory disorder due to COVID-19 might disrupt the virus's ability to invasion and decrease the subsequent damage of both nasal epithelium and nerve fibers. In this study, we compare the effect of nasal corticosteroids on patients proven to be COVID-19 positive complaining from anosmia aiming to decrease the duration of olfactory qualitative, quantitative and residual abnormalities as cacosmia with those who hadn't taken nasal corticosteroid

Patients and Methods

This case-control study included 200 patients presented to the Otorhinolaryngology Department, South Valley University Hospital in the period from 10-2020 to 12-2021, they were divided into equal two groups with a follow-up period of 6 months.Their ages range from22 years to 63 years with a mean of 43 years,93were males while females were107. Group1(treated group) All patients were given two sprays (50 mcg of mometasone furoate in each spray) in each nostril twice per day (total daily dose of 400 mcg) for 7 days and reassessed after twoweeks, one month, and two months.Stopping of local corticosteroid nasal spray was indicated in those patients who regain smell. Group 2 (untreated group) who weren't administerednasal corticosteroid orsystemic corticosteroidin anosmia treatment

The study protocol was approved by the Ethics Committee of Qena Faculty Of Medicine South Valley University And written informed consent was obtained from all included subjects. Code number SVU-MED-ENT030-4-22-7- 419.

The inclusion criteria were PCR-confirmed SARS-CoV-2 infection, age ≥ 18 years, and recently developed anosmia. The exclusion criteria included pregnancy, the presence of psychological disorders, history of olfactory affection before the COVID-19-19 era, extensive sinonasal diseases, previous nasal and orsinonasal surgery, and olfactory affection for more than 15 days.

The smell test used here was described in 1990 by H. Kenneth Walker for olfactory nerve assessment [Walker 1990]. Two concealed vials of non-irritating common household substances were used: ground coffee (Nescafe Red Mug Instant Coffee, Nestle) and scented artificial strawberry flavor (Strawberry Culinary Essence 28 mL, Foster Clark's, Foster Clark Products Ltd.).The patient was instructed to closehis/her eyes and one nostril with the index finger. the concealed vial was brought within 30 cm of the nostril Patients were instructed to sniff repetitively and to tell when an odor was detected,for all patients, the duration of sniffing was standardized to within 60 seconds.Patients unable to identify both odors with both nostrils were recorded as "anosmia

Statistical analysis

Data entry and data analysis were done using SPSS version 22 (Statistical Package for Social Science). Data were presented as numbers, percentages, mean, median, and standard deviations. The Chi-square test and Fisher Exact test were used to compare qualitative variables. Independent samples t-test was used to compare quantitative variables between groups for parametric data. P-value considered statistically significant when $P < 0.05$.

Results

In this study, male patients represent 44% and 49% while female patients represent 56% and 51% in groups 1 and 2 respectively. The mean age is relatively equal in both groups (42.87 in group 1 and 43.74 in group 2).Thirty-eight (38%) were working in group 1 and 41% in group 2 while 62%werenon-workingin group 1 and 59% in group 2. Regarding smoking 10%,11%were smokers in groups 1 and 2 respectively, and 90%, and 89% were non-smokers in groups 1 and 2 respectively as shown in (**Table. 1**).

Table 1. Demographic data of the studied groups

Variables	Group I (n= 100)		Group II (n= 100)		P-value
	No.	%	No.	%	
Sex:					
• Male	44	44.0%	49	49.0%	0.478
• Female	56	56.0%	51	51.0%	
Age: (years)					
• Mean ± SD	42.87 ± 11.49		43.74 ± 12.69		0.612
• Range	22.0-62.0		22.0-63.0		
Occupation:					
• Working	38	38.0%	41	41.0%	0.664
• Not working	62	62.0%	59	59.0%	
Smoking:					
• Smoker	10	10.0%	11	11.0%	0.818
• Non-smoker	90	90.0%	89	89.0%	

In our study anosmia in group 1 improved by 61% in the first week,83% in the second week,100 % after one month, and regular follow-ups were done for6 months while in group 2improvement was 42%in the first week,59% in the second week,73% after one month. In group 2, 30 patientsout of 100 patients complainedof cacosmia after initial anosmia 3 of them reportedimproving smell after 1 week then 2 weeks later cacosmia appeared and none of them improved within the follow-upperiod with a p-value <0.001as shown in (**Table.2, Fig.1**).

Table 2. Smell test results among the study groups

Smell test	Group I (n= 100)		Group II (n= 100)		P-value
	No.	%	No.	%	
After 1 week:					
• Improved (Negative)	61	61.0%	42	42.0%	0.007*
• Not improved (Positive)	39	39.0%	58	58.0%	
After 2 weeks:					
• Improved (Negative)	83	83.0%	59	59.0%	<0.001*
• Not improved (Positive)	17	17.0%	41	41.0%	
After 1 month:					
• Improved (Negative)	100	100.0%	73	73.0%	<0.001*
• Not improved (Positive)	0	0.0%	27	27.0%	
After 2 months:					
• Improved (Negative)	100	100.0%	70	70.0%	<0.001*
• Not improved (Positive)	0	0.0%	30	30.0%	

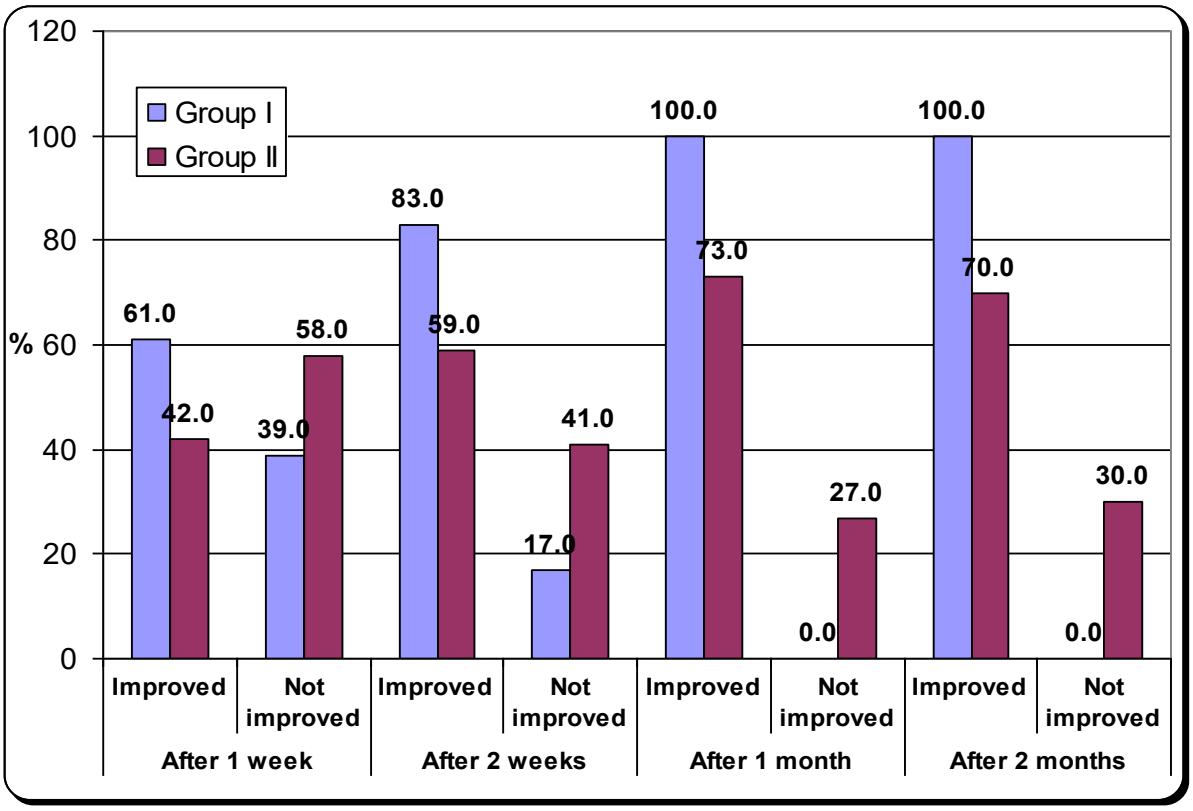

Fig.1. Percentage of improvement in the sense of smell among the study groups

In our study smoking hasno direct relation to improvement in both groups. Also, on considering the occupational factor in this study non-worker was more than a worker with no significant relationship between the two groups. (**Tables. 3 and 4**).

Table 3. Smell test after 1 week according to personal data (Group I)

Personal data	Improved (n= 61)		Not improved (n= 39)		P-value
	No.	%	No.	%	
Occupation:					
• Working	28	73.7%	10	26.3%	0.042*
• Not working	33	53.2%	29	46.8%	
Smoking:					
• Smoker	7	70.0%	3	30.0%	0.736
• Non-smoker	54	60.0%	36	40.0%	

Table 4. Smell test after 1 week according to personal data (Group II)

Personal data	Improved (n= 42)		Not improved (n= 58)		P-value
	No.	%	No.	%	
Occupation:					
• Working	17	41.5%	24	58.5%	0.928
• Not working	25	42.4%	34	57.6%	
Smoking:					
• Smoker	6	54.5%	5	45.5%	0.519
• Non-smoker	36	40.4%	53	59.6%	

Discussion

Fever, body pain, fatigue, and cough are the frequent symptoms of COVID-19 19. During the disease course gastrointestinal symptoms, neurological complications, and neuropsychiatric symptoms. Olfactoryand gustatory dysfunction is also frequently seen in COVID-19 infection **(Topalet al. 2021)**. Five studies from European countries, China, Italy, the USA, and Iran revealed dysgeusia and or anosmia in almost three-quarters of COVID-19 patients with a total of 10,847 COVID-19patients; 8,816 (81.27%), and 8,119 (74.85%) presented with/developed dysgeusia and/or anosmia, respectively **(Hosseini et al. 2020)**

Smell disorders have a strong impact on the quality of life, these impairments affect the ability to sense odors in foods and the environment, and they may lead to malnutrition, weight loss, food poisoning, depression, and exposure to dangerous chemicals. Smell disorders have been also associated with increased mortality. **(WHO. Coronavirus disease 2019)**

Assessment of olfactory function and diagnosis of olfactory dysfunction should include information on the triggering events and toxicants. Cigarette smoke impacts the respiratory tract, where inflammation and mutagenic and carcinogenic effects are the most common outcomes. Some of its ingredients are destructive to the sensory systems, others have toxic effects on the airway, possibly leading todamage or death of cells. The smoking components cause a decrease in the cleaning mechanism of the airways and hyperplasia of mucus cells, resulting in increased mucus production.**(Blancard et al. 2004)**

Physiologically, the changes caused in the olfactory neuroepithelium may be structural and/or functional. There is a decrease in sensory cell production capacity, causing a loss of sensibility to odors and olfactory recognition. Taste affection is a result of the change of type, numbers, and blood supply of the taste buds caused by tobacco consumption. **(Deems et al. 1991)**

Smoking as a potential cause of smell or taste impairment has rarely been studied. Two of the published reports included only small samples **(Fortier et al 1991, McLean et al. 2004)**,and the third one found smoking to be an important factor in the occurrence of smell dysfunction **(Frye et al. 1990)**. However, in our study smoking has no direct relation to improvement in both groups. also, on considering the occupational factor in this study non-workers were more than a worker with no significant relationship

between the two groups The proportion of olfactory dysfunction caused by occupational exposure remains unclear. **(Mott et al. 1991)**.

In our study 30 patients out of 100 untreated with corticosteroid nasally developed cacosmia within 2 months,three of them develop it after initial improvement of anosmia

In this study, corticosteroids were very effective in the treatment of anosmia in COVID-19 patients and in preventing the late presentation of cacosmia however **Topal et al. (2021)**revealed that 17 patients out of 120 develop late cacosmia on nasal corticosteroid and olfactory training in his study. **Hosseini et al 2020** studied the effect of coffee on anosmia and ageusia in COVID-19 patients. They reported that Coffee has a specific amount of consumption, which is 15–20 mg of coffee for patients with no underlying disease and 20–30 mg for underlying disease patients. All results showed that the recovery of non- underlying disease patients was higher than the underlying patients.

Conclusion

Cacosmia as alate annoying symptoms in the COVID-19 patient must be taken seriously with the trial of different lines of treatment.Nasal corticosteroid is highly recommended in treating anosmia in COVID-19 patients and preventing a high recurrence

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