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Effect of Nasal and Systemic Corticosteroids on Persistent Post-COVID-19 Olfactory Dysfunction

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ORIGINAL ARTICLE

Effect of Nasal and Systemic Corticosteroids on Persistent Post- COVID-19 Olfactory Dysfunction

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Abstract

Background: ***Several investigations have demonstrated that Nasal and systemic corticosteroids may enhance the olfactory function of certain individuals, while others have found no significant effect.***

Aim: ***To examine the effectiveness and safety of nasal and systemic corticosteroids in the therapy of chronic olfactory dysfunction following COVID-19.***

Patient and methods: ***This randomized controlled clinical study was conducted on fifty non-hospitalized confirmed COVID-19 patients after recovery with persistent smell disorder. They were classified into two equal groups: Group A involved twenty-five cases who received 2 weeks of OC (methylprednisolone 0.5 mg/kg/day) and OT, and Group B involved twenty-five cases who received 2 weeks of NC (mometasone furoate spray 2 sprays inside every nostril once daily) and OT. This study was carried out in the Otorhinolaryngology Surgery Department at Al-Hussien University Hospital.***

Results: ***In Group A, pre-treatment data related to smell disorders Normosmia, Hyposmia, Anosmia, and Cacosmia were (0%, 20%, 72%, and 8%), respectively, while post-treatment data were (0%, 8%, 20%, and 12%), respectively. In Group B, Pre-treatment data related to smell disorders Normosmia, hyposmia, anosmia, and cacosmia were 0%, 8%, 80%, and 12%, respectively, while post-treatment data were 56%, 20%, 24%, and 0%, respectively. Group A and Group B showed complete improvement, with percentages of 20% and 56%, respectively.***

Conclusion: ***Nasal corticosteroids demonstrated further progress in the treatment of cases after COVID-19 infection than systemic corticosteroids. They may improve olfactory function in some cases. More investigation is required to confirm these findings.***

Keywords: Nasal and Systemic Corticosteroids; Olfactory Dysfunction; COVID-19

1. Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory ailment that is attributed to the SARS-CoV-2 novel coronavirus. Since its December 2019 discovery in Wuhan, China, it has quickly increased throughout the world, evolving into a pandemic. Pneumonia is predominantly transmitted via respiratory aerosols generated during pharyngitis, sneezing, or coughing by an infected individual.[1]

Loss of taste and smell (olfactory impairment) is a prevalent symptom of COVID-19 infections. According to studies, up to 80% of people who carry COVID-19 have reported experiencing an absence of taste and smell. This olfactory dysfunction can occur before or together with other symptoms and can persist even after the resolution of other symptoms.[2]

Corticosteroids are a type of medication that can reduce inflammation and are commonly used to treat various medical conditions. In the context of persistent post-COVID-19 symptoms, corticosteroids have been studied for their potential to improve olfactory dysfunction and other symptoms.[3] Both oral and nasal corticosteroids have been studied for their potential to improve olfactory dysfunction in individuals who have persistent post-COVID-19 symptoms.[4]

This study aimed to examine the effectiveness and safety of nasal and systemic corticosteroids in treating chronic olfactory dysfunction following COVID-19.

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2. Patients and methods

This randomized controlled clinical study was conducted on fifty non-hospitalized confirmed COVID-19 patients after recovery with persistent smell disorder. They were classified into two equal groups: Group A involved twenty-five cases who received two weeks of OC (methylprednisolone 0.5 mg/kg/day) and OT, and Group B involved twenty-five cases who received two weeks of NC (mometasone furoate spray two sprays inside every nostril once daily) and OT. This study was carried out in the Otorhinolaryngology Surgery Department at Al-Hussien University Hospital.

Inclusion criteria: Post-COVID patients with persistent smell disorder lasting for more than 2 weeks and exhibited positive PCR results for SARS-CoV-2 RNA on nasopharyngeal as well as the throat samples, healing of all signs associated with COVID-19 excluding olfactory disorders including hyposmia, anosmia, parosmia, cacosmia, phantosmia, or heterosmia, age ≥ 18 years and developed smell abnormalities with sniffin' sticks test score below 11 (normosmia, anosmia, or hyposmia).

Exclusion criteria: Any disease that impairs the sense of smell, such as fungal rhinosinusitis, nasal polyposis, or nasal tumours; background of anosmia prior to the COVID-19 era; history of having undergone sinonasal surgery in the past; conditions that impair the immune system (including AIDS or chemotherapy); current infection; a peptic ulcer; diabetes; glaucoma; a mental illness; or a recent attenuated vaccination are all contraindications to the use of OC.

Method: All cases were subjected to detailed history taking, including the onset and duration of disease, general examination, local ENT examination, and detailed nasal examination. Investigations included CBC, which was associated with significant neutrophilia and lymphopenia in severe cases; CRP, which indicated the presence of inflammation in the body, which can be a sign of an active COVID-19 infection; serum ferritin, used as a supplementary test in some cases in combination with other diagnostic methods to help monitor the severity of COVID-19 and track the patient's response to treatment; D dimer, which indicated the presence of clotting or inflammation in the body; computed tomography (CT) and magnetic resonance imaging (MRI) of the olfactory bulbs;

CT: CT of the chest was the gold standard for suspected COVID-19 cases. It showed characteristic signs of COVID-19 infection such as ground-glass opacities (increased lung attenuation that commonly occurs bilaterally and peripherally), air space consolidations (dense areas), crazy paving appearance (relating to geographic areas of ground glass and interlobular septal thickening), bronchovascular thickening in the lesion, and traction bronchiectasis. The CT scan of the paranasal sinuses was utilised to determine whether or not COVID-19 was present in the upper respiratory tract, including nasal cavities and sinuses. While COVID-19 primarily affects the lower respiratory tract, it can also involve the upper respiratory tract in some cases. The findings on a CT scan of the paranasal sinuses in COVID-19 varied, ranging from normal to mild changes to more severe findings such as sinusitis or mucosal thickening.

Olfactory assessment: (trigeminal assessment). A threshold test and an identification of aromas were conducted utilizing the Connecticut Chemosensory Clinical Research Center (CCCRC) olfactory test.

Olfactory Training: The OT apparatus comprised four sniff bottles or jars, with an approximate volume of fifty ml per bottle or jar. Cotton pads saturated with 1 ml of an odorant were placed inside each vial or container. For conventional OT, cases smell each of the four odours separately for at least twenty to thirty seconds twice per day (ideally prior to meals in the morning and before sleep in the evening). Olfactory training lasted until the end of the study or until there was a full improvement in olfactory sensation.

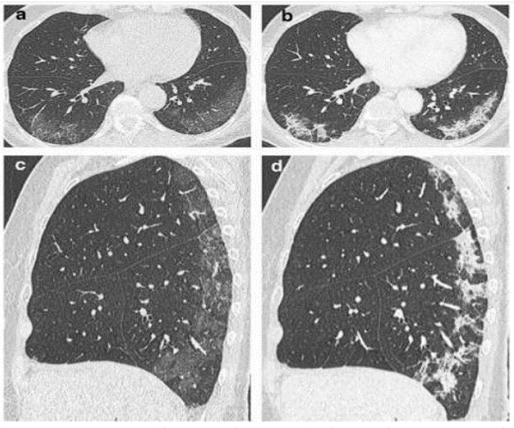

Figure 1. Bilateral peripheral ground-glass opacities are observed on CT axial as well as sagittal scans through the beginning stage of the COVID-19 infection (A&C). As the disease advances, proceed to consolidation (B & D).

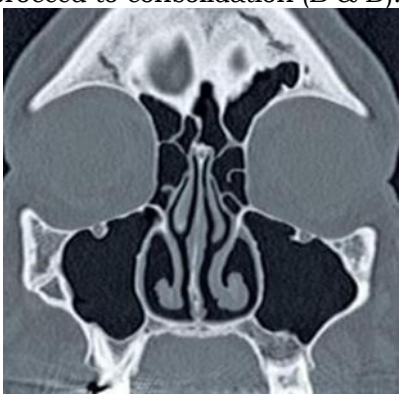

Figure 2. Coronal CT demonstrate well aerated

paranasal sinuses to exclude obstruction problems

Statistical Analysis: The computation was performed utilizing the IBM SPSS software program version 20.0 on the inputted data. (IBM Corp., Armonk, New York). The Kolmogorov-Smirnov test was employed to assess the normality of variable distributions. Paired t-tests were utilized to compare two periods of normally distributed quantitative variables. Analysis of Variance with Repeated Measures (ANOVA) was used to contrast the various periods of study for normally distributed quantitative variables. For pairwise comparisons, post-hoc tests (adjusted Bonferroni) were implemented. Utilizing the Pearson connection coefficient, two normally distributed quantitative variables are correlated. At the five per cent significance level, the derived results were deemed significant. [5]

3. Results

There was a statistically significant difference between the two studied groups as regards age: chronic rhino sinusitis, chronic rhinitis, asthma, and chronic obstructive pulmonary disease. There was no statistically significant difference between the two studied groups with regard to sex, smoking and allergy. (Table 1)

There was no statistically significant difference between the two studied groups as regards CT findings (round glass opacities, consolidation, vascular enlargement, interlobular septal thickening, air, bronchogram sign, subpleural bands, crazy paving, air trapping, reversed halo sign, and pleural effusion). (Table 2)

The CT paranasal sinuses score pre- and post-treatment for both groups is shown in Table 3 (full obstruction two, partial obstruction one, and no obstruction zero). There was a statistically significant difference regarding the Lund-Mackay CT total score in group A (p = 0.0371) and group B (p = 0.01361) between pre- and post-treatment. (Table 3)

In Group A, pre-treatment data related to smell disorders Normosmia, Hyposmia, Anosmia, and Cacosmia were (0%, 20%, 72%, and 8%), respectively, while post-treatment data were (0%, 8%, 20%, and 12%), respectively, in the same group. In Group B, pre-treatment data related to smell disorders Normosmia, Hyposmia, Anosmia, and Cacosmia were (0%, 8%, 80%, and 12%), respectively, compared to post-treatment data (56%, 20%, 24%, and 0%), respectively, in the same group. (Table 4)

Group A and Group B showed complete improvement with percentages of 20% and 56%, respectively, while partial improvement was 44% and 20% for Group A and Group B, respectively. Some patients showed no improvement, with 36% in Group A and 24% in Group B. (Table 5)

Table 1. Relation between tested groups regarding demographic data and history of chronic diseases (n = 50).

	GROUP A N= 25	GROUP B N= 25	P VALUE	STATISTICALLY SIGNIFICANT
AGE				
MEAN ± SD	33.36±6.58	24.92±4.19 SIG.		<0.0001
RANGE (MIN-MAX)	25-45	19-34		
SEX				
MALE	12 (48%)	10(40%)	0.7771	N.S
FEMALE	13 (52%)	15(60%)		
SMOKING				
NEGATIVE	15 (60%)	17(68%)	0.7683	N.S
POSITIVE	10 (40%)	8(32%)		
HISTORY DATA				
HISTORY OF ALLERGY NEGATIVE	11(44%)	18(72%)	0.0856	N.S
POSITIVE	14(56%)	7(28%)		
CHRONIC RHINOSINUSITIS: NEGATIVE	8(32%)	23(92%)	<0.0001	SIG.
POSITIVE	17(68%)	2(8%)		
CHRONIC RHINITIS: NEGATIVE	14(56%)	22(88%)	0.0275	SIG.
POSITIVE	11(44%)	3(12%)		
ASTHMATIC PATIENT:				
NEGATIVE	14(56%)	23(92%)	0.0128	SIG.
POSITIVE	11(44%)	2(8%)		
CHRONIC OBSTRUCTIVE PULMONARY PATIENT	:			
NEGATIVE	8(32%)	21(84%)	<0.0001	SIG.
POSITIVE	17(68%)	4(16%)		

Statistical test used: Chi-square test p-valueless than or equal to 0.05 considered statistically significant (ninety-five percent confidence interval).

Table 2. Relation between tested groups regarding CT findings (n = 50)

	GROUP A N= 25	GROUP B N= 25	P VALUE	STATISTICALLY SIGNIFICANT
CT FINDING				
GROUND-GLASS OPACITIES N (%)	23(92%)	21(84%)	0.221	N.S
CONSOLIDATION N (%)	12(48%)	15(60%)	0.714	N.S
VASCULAR ENLARGEMENT N (%)	9(36%)	7(28%)	0.532	N.S
INTERLOBULAR SEPTAL THICKENING N (%)	14(56%)	13(52%)	0.643	N.S
AIR BRONCHOGRAM SIGN N (%)	7(28%)	8(32%)	0.822	N.S
SUBPLEURAL BANDS N (%)	6(24%)	8(32%)	0.741	N.S
CRAZY PAVING N (%)	3(12%)	4(16%)	0.321	N.S
AIR TRAPPING N (%)	0(0%)	1(4%)	0.952	N.S
REVERSED HALO SIGN N (%)	3(12%)	2(8%)	0.852	N.S
PLEURAL EFFUSION N (%)	3(12%)	2(8%)	0.852	N.S

Table 3: Relation between tested groups regarding Lund-Mackay CT Score Data Pre and

	Pre-Treatment N=25	*Post- Treatment N=25*	*p value*	*significant*
RIGHT				
FRONTAL	1.12±0.78	1.01±0.76	0.8551	N.S
ANTERIOR ETHMOIDS	1.2±0.76	0.91±0.78	0.0159	SIG.
POSTERIOR ETHMOIDS	1.08±0.86	0.98±0.86	0.624	N.S
MAXILLARY	1.16±0.8	0.86±0.8	0.039	SIG.
SPHENOID	1.12±0.83	1.08±0.86	0.8682	N.S
OSTIOMEATAL COMPLEX	1.62±1.02	0.88±1.01	0.0163	SIG.
LEFT				
FRONTAL	1.11±0.91	1±0.91	0.7576	N.S
ANTERIOR ETHMOIDS	1.16±0.8	1.08±0.76	0.7185	N.S
POSTERIOR ETHMOIDS	1.08±0.81	0.88±0.73	0.3633	N.S
MAXILLARY	1.28±0.94	1.12±0.93	0.5467	N.S
SPHENOID	0.64±0.49	1.24±0.83	0.0035	SIG.
OSTIOMEATAL COMPLEX	1.92±0.4	0.96±1.02	0.0001	SIG.
LUND-MACKAY CT TOTAL SCORE	13.8±6.63	10.68±7.1	0.0371	SIG.
LUND-MACKAY CT SCORE GROUP B:				
RIGHT				
FRONTAL	1±0.76	0.76±0.44	0.1804	N.S
ANTERIOR ETHMOIDS	1.12±0.73	0.88±0.33	0.1419	N.S
POSTERIOR ETHMOIDS	1.24±0.78	0.88±0.33	0.0412	SIG.
MAXILLARY	1.28±0.68	0.96±0.2	0.0316	SIG.
SPHENOID	1.24±0.72	1±0	0.0531	N.S
OSTIOMEATAL COMPLEX	1.2±1	0.84±0.37	0.102	N.S
LEFT				
FRONTAL	1.44±0.72	0.96±0.2	0.003	SIG.
ANTERIOR ETHMOIDS	1.32±0.63	0.92±0.28	0.0017	SIG.
POSTERIOR ETHMOIDS	1.17±0.74	0.92±0.28	0.1419	N.S
MAXILLARY	1.30±0.7	0.92±0.28	0.0114	SIG.
SPHENOID	1.31±0.79	0.8±0.41	0.0065	SIG.
OSTIOMEATAL COMPLEX	1.11±1.01	0.08±0.28	<0.0001	SIG.
LUND-MACKAY CT TOTAL SCORE	13.92±5.79	9.51±1.71	0.0136	SIG.

Statistical test utelized: 2 sample T-test
N.S= Not Significant Sig.= Significant

Table 4. Relation between olfactory assessments data pre and post treatment.

	PRE-TREATMENT	*POST-TREATMENT*	*P VALUE*	*STATISTICALLY SIGNIFICANT*
	N= 25	*N= 25*		
OLFACTORY ASSESSMENTS				
GROUP A				
NORMOSMIA N (%)	*0(0%)*	*7(28%)*		
HYPOSMIA N (%)	*5(20%)*	*10(40%)*		
			*001**	*<0.0 SIG.*
ANOSMIA N (%)	*18(72%)*	*8(32%)*		
CACOSMIA N (%)	*2(8%)*	*0(0%)*		
GROUP B				
NORMOSMIA N (%)	*0(0%)*	*18(72%)*		
HYPOSMIA N (%)	*2(8%)*	*4(16%)*		
			*001**	*<0.0 SIG.*
ANOSMIA N (%)	*20(80%)*	*3(12%)*		
CACOSMIA N (%)	*3(12%)*	*0(0%)*		

Statistical test used: Chi-square test
N.S= Not Significant Sig.= Significant

Table 5. Relation between patient's improvement data regarding tested groups

	Group A N= 25	*Group B* N= 25	P VALUE	*statistical* SIGNIFICANT
COMPLETE IMPROVEMENT	5(20%)	14(56%)		
PARTIAL IMPROVEMENT	11(44%)	5(20%)	0.0285	SIG.
NO IMPROVEMENT	9(36%)	6(24%)		

4. Discussion

Contrary to other regions of the CNS, the olfactory system demonstrates neural plasticity that persists throughout an individual's lifetime, as evidenced by neurogenesis in the neuroepithelium and portions of the olfactory tract.[3]

In our study, the patients treated with NC (mometasone furoate spray, 2 sprays into every nostril once per day) and OT showed higher improvement (56% of complete improvement) than patients treated with oral corticosteroids (OC) (methylprednisolone 0.5 mg/kg/day) and olfactory training, with only 20% of complete improvement.

Due to the fact that olfactory dysfunction associated with COVID-19 has been recognized as a potentially beneficial treatment, corticosteroids have been the subject of a number of investigations examining the efficacy of various formulations, dosing, and routes of steroid administration. The positive impact of corticosteroids on olfactory dysfunction caused by COVID-19 could be attributed to their anti-inflammatory properties, which could alleviate inflammation of the olfactory neuroepithelium. Since topical and oral corticosteroids are readily available and inexpensive, their use is feasible in the majority of situations.[6]

Systemic corticosteroids have a more pronounced profile of adverse effects than nasal steroids, which may render them safer in comparison to oral corticosteroids. While topical steroids are presently employed to treat a wide range of conditions, they are not without the potential for adverse effects, including nasal irritation, epistaxis, and more severe local complications like ischaemia. Therefore, it is essential to evaluate the potential benefits and hazards of this treatment.[4]

As indicated previously, there has yet to be a consensus among the findings of various studies. Abdelalim et al.[7] examined the efficacy of topical corticosteroid (mometasone furoate) in treating anosmia and hyposmia in cases who had recovered from infection with COVID-19 in prospective, randomized, controlled research. The findings of this research indicated that intranasal corticosteroid therapy did not yield any discernible benefit over placebo in terms of anosmia duration, odour scores, or recovery

rates.

Rashid et al.[8] reached the same conclusion regarding the efficacy of intranasal betamethasone in placebo-controlled, randomized, double-blind clinical research involving 276 cases who had recuperated from infection with COVID-19 and experienced anosmia for a duration exceeding fifteen days.

Participants who used fluticasone nasal spray noted a considerable improvement in anosmia in additional research, including the one by Singh et al.[5] A multicenter randomized case-control study was conducted by Vaira et al.[6] to evaluate the performance of corticosteroid therapy for COVID-19 cases who presented with severe hyposmia or anosmia for a duration exceeding thirty days. In contrast to the control group, which did not undergo therapy, the treatment group experienced a distinct and more rapid enhancement in olfactory scores following administration of systemic prednisone, betamethasone nasal irrigation, and ambroxol (a decongestant and mucolytic).

Even though there are different opinions on this topic, the British Rhinological Society Consensus (BRS) says that people with nasal symptoms and loss of smell that last longer than two weeks shouldn't have to use topical steroids.[9]

The BRS consensus states that oral corticosteroids should not be prescribed to patients with persistent COVID-19 symptoms and olfactory dysfunction lasting more than two weeks. However, they are recommended as an optional treatment for individuals with olfactory dysfunction lasting over 2 weeks as an isolated symptom.[10]

In prospective observational controlled research involving 152 individuals across four institutions, Saussez et al.[11] compared various interventions for olfactory dysfunction following COVID-19: nasal corticoids in conjunction with olfactory training, olfactory training alone, or oral corticosteroids as well as olfactory training. The researchers concluded that patients who received oral corticosteroids in conjunction with olfactory training exhibited considerably higher rates of improvement (normosmics) after one month. However, after two months of assessment, no significant distinctions were observed between the groups, suggesting that corticosteroids merely expedite the recuperation process.

Strength of recommendation class C was assigned to six of the 36 studies on post-viral olfactory dysfunction that were analyzed in a May 2020 systematic review. These studies utilized systemic steroids as the treatment approach. Therefore, healthcare providers ought to weigh the advantages and disadvantages of corticosteroids in light of the medical comorbidities of their patients. [12]

4. Conclusion

In conclusion, the impact of systemic and NC treatments on chronic olfactory dysfunction following COVID-19 is still being studied, and more evidence is needed to determine their effectiveness. NC demonstrated further improvement in the treatment of cases after COVID-19 infection than systemic corticosteroids. Currently, there is some evidence suggesting that they may improve olfactory function in some cases; however, more investigation is required to confirm these findings.

Disclosure

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Authorship

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Conflicts of interest

There are no conflicts of interest.

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