

ORIGINAL ARTICLE

Impact of Topical v/s Systemic Steroids on Regaining Olfaction in Post Covid-19 Patients; A Randomized Controlled TrailUSAMA NAVEED CHEEMA¹, SHAHI ZEB², LAIBA IRFAN³, MIRZA ZEESHAN SIKANDAR⁴, SYED ARSLAN ASHRAF⁵, KHALID MUNIR⁶¹Department of Pediatrics, Ferooq Hospital Lahore.²Department of Otorhinolaryngology, Central Park Medical College, Lahore.³Department of Otorhinolaryngology, Central Park Teaching Hospital, Lahore.⁴Department of Surgery, Central Park Medical College, Lahore.⁵Department of Medicine, Raza Medical Complex, Lahore.⁶Department of Otorhinolaryngology, Central Park Medical College, Lahore.Correspondence to: Dr. Mirza Zeeshan Sikandar, ORCID: 0000-0002-5499-7884, Email: m.zee.shan@hotmail.com, Cell: +92-336-8656736**ABSTRACT****Background:** Covid-19 is a spectrum of infection not only causing fever and respiratory changes but including alteration in chemosensory functions including; olfactory dysfunction and gustatory dysfunction. In covid-19, olfactory dysregulation could be treated with either systemic steroids or with topical steroids.**Objective:** To assess and compare role of systemic and topical steroids in regaining normal olfactory functions.**Materials & Methods:** A Randomized control trial was conducted at Central Park Teaching Hospital Lahore after getting ethical approval and prior written informed consent from participants. A total of 35 patients were recruited were segregated into two groups; Group 1 who were treated with topical steroids (n=17) and Group 2 who were given and treated with systemic steroids (n=18). Time frame of regain of olfaction was compared between the groups using Mann Whitney U test. A p value less than 0.05 was considered as significant.**Results:** A total of 35 participants participated in this randomized controlled trial who were segregated into two groups with the mean ages of 47.12 + 11.94 and 43.72 + 13.74 with no significant mean difference. On appliance of Mann-Whitney U test in Group 1 and group 2 (52 + 39 v/s 4 + 2) it was observed that systemic steroid patients regain olfaction earlier as compared to group 1 (topical steroids) with the p value of .0001.**Practical implication:** Systemic Steroids will help in prompt regaining of normal olfaction and should be part of COVID-19 infection management.**Conclusion:** Olfaction management till the regaining of normal olfactory functions should be part of covid-19 management and role of steroids in crucial yet unavoidable. Systemic steroids play a key role in early regain of normal olfactory response so should be encouraged under the physician observation.**MeSH Words:** Covid-19, olfaction, steroids, respiratory disorders, randomized controlled trial.**INTRODUCTION**

Covid-19 is a spectrum of infection caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) first reported in February 2020 in Pakistan¹. It's clinical signs not only include fever, cough, sore throat, fatigue² but pulmonary pneumonia and in a fraction of patients' pulmonary fibrosis leading to respiratory failure and multi-organ failure³. Covid-19 spectrum is not only limited to respiratory and inflammatory responses but it can also cause central neuropathy including alteration in chemosensory functions including; olfactory dysfunction and gustatory dysfunction⁴. As per WHO guidelines, changes in olfaction have been considered part of covid-19 infection and should be managed simultaneously⁵.

Olfactory changes and dysfunctions have also been reported in various infections including; rhinovirus, pseudomonas and also in covid due to inflammatory responses of nasal mucosa causing alterations in smell and taste, but in severe cases it can lead to olfactory dysfunction⁶. Olfactory dysfunction has been defined as the decreased or diminished functioning of olfactory receptors or system leading to the hyposmia or in some cases of absolute anosmia⁷. Such impairment and olfactory loss in patients with confirmed COVID-19, was reported in China, in hospitalized patients in Italy, in United States, and also in in Europe⁸. Olfactory changes are one of the most persistent symptoms of longstanding COVID-19 infection, impacting health and quality of life of patients.

Olfactory dysfunction in covid-19 patients could be most long-standing symptom and it can take up to year to regain normal olfaction, therefore role of steroids become crucial in treatment of these infections⁹. Steroids have always been a topic of debate in the treatment of long-standing infections as well as complications⁹. In covid-19 infections role and use of steroids have been a crucial decision. Systemic steroids act in multiple ways to ameliorate the symptoms but inhibiting various inflammatory pathways including

nonspecific Cox inhibition, Cox-2 inhabitation, negative feedback regulation of cytokines and overall suppression of immune response of the host for ongoing infection¹⁰. On the other hand, topical steroids have been considered as safe but slow route in the treatment of nasal and local dermal infections. In covid-19, olfactory dysregulation could be treated with either systemic steroids or with topical steroids¹¹.

Olfaction management and regaining of normal olfaction can take weeks to years based on the therapy¹². Olfaction correction is a part of managing covid-19 infection and steroids could be a potential resort in regaining olfaction, but data is lacking in our part of world. Therefore, we warrant to conduct this study to assess and compare the role of systemic and topical steroids in regaining normal olfactory functions in local populace.

MATERIALS & METHODS

A Randomized control trial was conducted at Central Park Teaching Hospital Lahore in collaboration with Al-Shafi Hospital Lahore after getting ethical approval from institutional review board of Central Park Teaching Hospital and Medical College as per guidelines of declaration of Halinski from June 2021 to October 2022. In this trial, a total of 35 patients were recruited with the age range of 28 to 68 years who had covid-19 infection causing anosmia or other olfaction disorders from 2021-2022 followed by confirmation of viral infection with Real Time Polymerase Chain Reaction (RT-PCR) or positive rapid antigen surface test (RAST). Prior written informed consent was obtained from all the study participants and were segregated into two groups; Group 1 who were treated with topical steroids (n=17) and Group 2 who were given and treated with systemic steroids (n=18). Steroid therapy was carried out until regain olfaction and double blinding of the participants was done to eliminate any bias in this study. Any patient having any history of turbinate hypertrophy, nasal fracture, nasal congestion and cranial fracture or facial fractures were excluded from this trial.

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A detailed demographic and personal history were obtained in which active symptoms including shortness of breath, fever, cough, body aches and sore throat were recorded. Active complaints were categorized based on the central neuropathy; loss of olfaction (CN1 neuropathy) and loss of olfaction and taste (CN1 and CN7 neuropathy). Follow up of the study participants were carried out not only till settlement of covid-19 symptoms including aforementioned signs & symptoms but till the regain of olfaction. Nasal disorders, nasal patency and other olfactory disorders were also recorded. The gain and impact of steroid was assessed and confirmed with use of several Oduors; mainly spirit, clove and rose were used. Time for regain of olfaction was recorded in terms of weeks and patients were followed until the regain of olfaction in both groups.

Statistical Analysis: Data was entered into Microsoft Excel and was duly checked and compared for errors. After crosschecking the data, it was exported into Statistical Package for the Social Sciences (SPSS) version 25. Qualitative data was assessed and represented in bar charts, pie charts and graphs after calculation of frequencies and percentages. Normality of the data was assessed by Shapiro wilk test (p=.000) and time frame of regain of olfaction was compared between the groups using Mann Whitney U test. A p value less than 0.05 was regarded as significant.

RESULTS

A total of 35 participants participated in this randomized controlled trial who were segregated into two groups; group 1 (using topical steroid, n=17) and group 2 (using systemic steroids, n=18) with the mean ages of 47.12 + 11.94 and 43.72 + 13.74 with no significant mean difference and p value of 0.442 on appliance of independent sample t test. All the study participants were from urban setting and gender distribution was Group 1 (3 females and 14 males) while in group 2 (7 females and 11 males). In group 1 only one subject was hypertensive and six were both hypertensive as well as diabetic while on the other hand in group 2; six subjects were hypertensive, three were diabetic and two were having psoriasis. In all the study participants in both groups, covid-19 was diagnosed with standard WHO criterion as explained in figure 1.

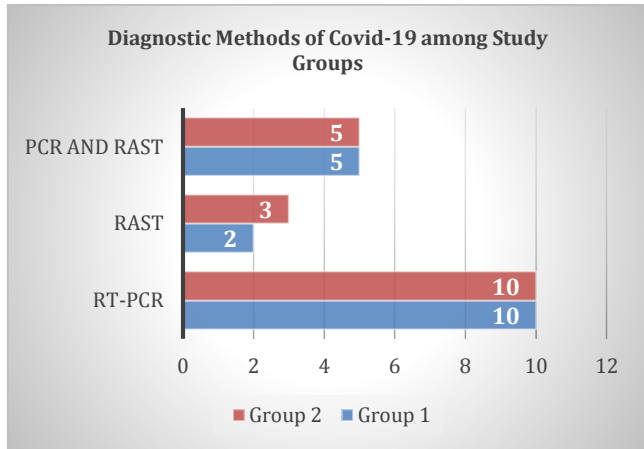


Figure 1: Confirmatory Diagnostics used in Study for Confirmation of Covid-19 Infection.

Table 2: Comparison of Regaining Period of Olfaction in Weeks in Study Groups based on Mann-Whitney U Test.

Groups	Median (weeks)	IQRs	Difference of medians	Mann-Whitney U	Wilcoxon W	Z	p-value (2-tailed)
Group 1 (Topical Steroids, n=17)	52.00	39	48	6.50	177.50	-5.053	.0001
Group 2 (Systemic Steroids, n=18)	4	2		Mann Whitney U test			Null hypothesis rejected at α 0.05

DISCUSSION

Our study appreciated that the use of systemic steroids could be advantageous in regaining the olfactory functions disturbed by the

Incidence of covid-19 symptoms before initiation of medical therapy was done as explained in table 1 and were compared in both groups. In our study sore throat affected all the study participants with an incidence of 100 percent, afterwards was fever with incidence of 88.57% overall. All the other signs and symptoms have been explained in table 1. Interestingly, symptoms of central neuropathy in terms of facial nerve were also recorded which was 11.42 percent in whole study population.

Table 1: Percentages of Incidence of Signs and Symptoms of Covid-19 in Study Participants and Study Groups

Parameters	Group 1 % (n=17)	Group 2 % (n=18)	Overall % (n=35)
Sore Throat	100%, (17)	100%, (18)	100%, (35)
Body Aches	52.94%, (9)	66.67%, (12)	60%, (21)
Shortness of Breath	29.41%, (5)	55.55%, (10)	42.85%, (15)
Fever	88.23%, (15)	88.88%, (16)	88.57%, (31)
Cough	35.29%, (6)	55.55%, (10)	45.71%, (16)
Anosmia	76.47%, (13)	61.11%, (11)	68.57%, (24)
Loss of Smell & Taste	5.88%, (1)	27.77%, (5)	17.14%, (6)
Odynophagia	29.41%, (5)	50.0%, (9)	40.0%, (14)
Effect on Facial Nerve	11.76%, (2)	11.11%, (2)	11.42%, (4)

Olfaction disorders were also recorded in study population as explained in figure 2. Absolute hyposmia was predominant in both groups, following these symptoms steroid therapy was initiated and doses were given, and responses were recorded in terms of weeks as explained in table 2. On the application of Mann-Whitney U test in Group 1 and group 2 (52 + 39 v/s 4 + 2) it was observed that systemic steroid patients regain olfaction earlier as compared to group 1 (topical steroids) with the p value of .0001. On regain of olfaction at 4th week in systemic steroid patients (group 2) and in the 52nd week in topical steroid patients (group 1) was confirmed with the use of odors including clove, spirit and rose.

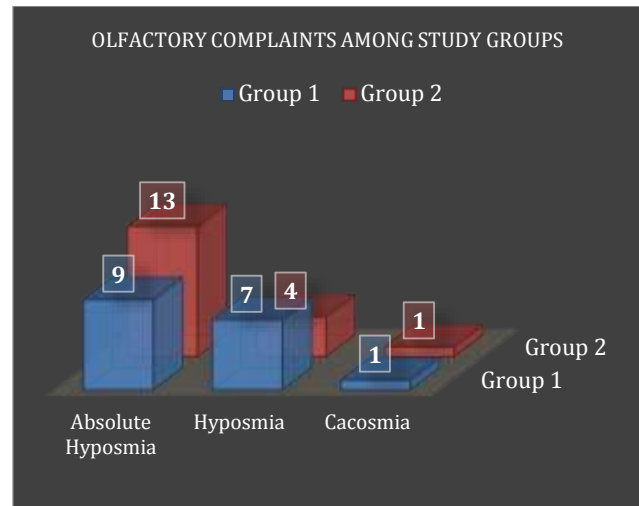


Figure 2: Incidence of Olfactory Signs in Study Population.

mechanisms that includes nasal obstruction and rhinorrhea, inflammatory neuropathy with high leukocyte infiltration in lamina propria, focal atrophy of the olfactory mucosa and extensive olfactory epithelial dysfunction in patients with longstanding hyposmia¹³. These evidence supports the possible effect of therapeutic corticosteroids in preventing and treating long standing olfactory dysfunction.

Study conducted by Stefen et.al showed the role of systemic and local steroids in the improvement of olfactory dysfunction and their assessment showed systemic administration of corticosteroids result in improvement of olfactory function earlier as compared to local application of corticosteroids which are coincident with our results that systemic steroids can get olfaction restored as early as two weeks due to similar study technique¹⁴. In study by Hossein et.al the mometasone furoate nasal spray was used and its role was evaluated for the recovery of patients that suffered from severe microsomnia or anosmia. The mometasone furoate nasal spray in addition to olfactory education showed great improvement in amelioration of symptoms by COVID-19 as compared to olfactory training alone¹⁵ which is in accordance with our results that use of topical nasal sprays help in regaining olfaction in due time.

Our results have shown systemic steroids help in early regain of olfaction when compared to topical steroids which is alike research work, the effect of oral methylprednisolone was evaluated in 27 patients with COVID-19¹⁶. After 10 weeks (about 2 and a half months), the patients who used oral corticosteroids had higher mean score as compared to control. In a study by Rashid et.al the effectiveness of topical betamethasone in COVID-19 patients was assessed and compared¹⁷. They concluded that the nasal drops had no notable effect on the anosmia recovery time, which is contrary to our results that use of topical steroids help in regaining olfaction. Our findings are limited and cannot be generalized due to smaller sample size, lack of previous olfactory status and limitation of resources.

CONCLUSION

Olfaction management till the regaining of normal olfactory functions should be part of covid-19 management and role of steroids in crucial yet unavoidable. Systemic steroids play a key role in early regain of normal olfactory response so should be encouraged under the physician observation. Therefore, use of systemic steroids in management of covid for regaining olfaction must be encouraged for prompt results.

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