

Characterization, treatment modalities, and self-perceived improvement of post-COVID-19 phantosmia: a case series of eleven patients*

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Rhinology Online, Vol 5: 44 - 48, 2022

<http://doi.org/10.4193/RHINOL/22.003>

***Received for publication:**

February 15, 2022

Accepted: March 22, 2022

Published: March 31, 2022

Abstract

Background: Loss of smell & taste is one of the early and sensitive symptoms of COVID-19 that usually improves over time. Post-COVID-19 phantosmia, a smell distorted sensation without the presence of odorants, has deleterious and long-lasting effects on the patient's quality of life. We aimed to present our experience with phantosmia.

Case presentations: We report a description of a series of eleven cases (age of 29 ± 9 years, and 54.5% females) of post-COVID-19 phantosmia without any other comorbidity, and the effects of combined treatment modalities (olfactory training, nasal irrigation with budesonide and oral prednisolone) on self-perceived improvement in phantosmia.

Conclusions: We postulate that the combined 10 days oral prednisolone, smell training, and nasal irrigation for three months improved post-COVID-19 phantosmia assessed as post vs. pre self-perceived improvement, although this was not aimed at as a treatment since it was not compared to untreated controls.

Key words: phantosmia, olfactory dysfunction, olfactory training, post-COVID-19 olfactory dysfunction, steroid therapy, self-perceived improvement

Introduction

Olfactory dysfunction (OD) is not only the most common neurological symptoms of patients with COVID-19, but it comes as the earliest and may be the only clinical manifestation⁽¹⁾. Management-wise, the post-COVID-19 olfactory dysfunction lacks proper guidance. Empirically, the persisting post-viral anosmia was managed by medication and/or olfactory training. Phantosmia, presence of smell in absence of stimulus, is one of the qualitative smells changes that depend on patient's history for diagnosis, and there are no tests to verify for it. It occurs mostly as a post-traumatic comorbidity. While topical and/or systemic corticosteroids along with olfactory training were used to manage post-COVID-19 olfactory dysfunction, investigations on persisting (after symptoms resolution and PCR-negative infection) post-COVID-19 phantosmia and its treatment are rare⁽¹⁻

⁶⁾. While olfactory training is an effective treatment for olfactory dysfunction, the antiinflammatory topical or systemic steroid treatments, by modulating the function of olfactory receptor neurons, are required to be initiated in the acute phase of the infection to be effective⁽⁷⁾.

Phantosmia commonly happens after head trauma and viral infections. Olfactory dysfunction, mainly loss of smell, is one of the crucial symptoms of COVID-19. Phantosmia, as a subtype of olfactory dysfunction, is rarely reported as a symptom of COVID-19. While anosmia was tackled in a good number of previous reports, characterization and management of phantosmia was reported in a limited number of studies^(6,8-10). However, loss of smell & taste is a more frequent early symptom of COVID-19, ranging from 75 - 88% of cases. They tend to recover within a few months, where the taste loss recovers faster than smell

Table 1. Description of demographics, clinical characteristics, and treatment modalities of patients with post-COVID-19 phantosmia (n = 11).

Age in years	Median ± IQR	28 ± 8
Gender (Male)	n (%)	5 (45.5%)
Loss of taste	n (%)	5 (45.5%)
Anosmia	n (%)	10 (90.9%)
Start of phantosmia after start of infection	Median ± IQR	90 ± 90
Duration of follow up in days till the start of combined treatment	Median ± IQR	392 ± 244
Self-perception of improvement on a scale of one to ten before combined treatment	Median ± IQR	0 ± 5
Self-perception of improvement on a scale of one to ten after combined treatment	Median ± IQR	5 ± 3

Data shown are frequencies; n (%), and median ± interquartile range (IQR).

loss^(6,7,11-17). However, some individuals reported other olfactory dysfunction (namely phantosmia) later after 2-4 months at a rate of 20-40% cases^(12,16,17).

The present case series describes post-COVID-19 phantosmia, and effectiveness of a combined treatment modality among patients with PCR-confirmed COVID-19 infection. We evaluated the effect of oral and nasal steroid, and olfactory training on olfactory dysfunction, using self-perceived improvement score. Among patients, we narrated two impressive stories about how post-COVID-19 phantosmia has affected the patients' quality of life. The first is for a young couple who visited the ENT clinic with a matrimonial problem due to post-COVID-19 phantosmia of the wife that almost resulted in their separation. The second was for a twelve-years-old boy with post-COVID-19 phantosmia. It resulted in significant weight loss, as he could not tolerate eating except a few unhealthy and innutritious fast-foods, while all home cooking smells were unbearably repugnant for him and induce retching and vomiting.

Case presentations

We present eleven cases of post-COVID-19 phantosmia. Phantosmia was defined as a hallucination of smell. Olfactory dysfunction in terms of anosmia was the presenting complaint among ten patients. The patient population belonged to Northern Saudi Arabia, where they were consecutively admitted and followed up at the ENT Clinic, Prince Moteb General Hospital, Sakaka, Saudi Arabia during the period from March 2020 to June 2021. Only patients with PCR-conformed COVID-19 were enrolled after signing a written informed consent. All the included patients were not vaccinated against COVID-19 at the time of infection. The patients with history of any comorbidity like head trauma, diabetes, COVID-related hospitalization, chronic nasal polyposis, history of cacosmia and chronic steroid use were excluded. The patients were examined, and different treatment modalities were initiated and evaluated for improvement over time, and were followed up for different duration; an appointment every four

weeks on average. Local nasal examination was carried out to rule out any coexisting chronic sinusitis, chronic nasal polyposis or superadded local infection. Self-perceived improvement was assessed by using visual analogue scale that rates the improvement on a scale from 0 to 10. The improvement, after three months, was presented as percentage improvement of the score compared with baseline score.

Intervention

Although was not aimed at as a treatment, the cohort of 11 cases were prescribed oral prednisolone burst (1 mg/kg twice daily for ten days) followed by nasal irrigation with budesonide in normal saline, and smell training for three consecutive months. The patients were instructed to add two mL vial of liquid Budesonide in 240 mL of normal saline (0.9%) in the sinus rinse bottle. They must tilt their head forward, put the bottle in a nostril aiming towards the top of head and squeeze the bottle slowly. They were instructed using a video to flush out the nose. The patient must repeat the process twice daily for three months (90 days). A synchronized smell training regimen was used for three months. Daily zinc supplementation (20 mg PO daily) was also prescribed. After three months of the combined regimen, self-perception of improvement score was compared with baseline score. They were provided with the facility of electronic video calling, if unable to reach the clinic. We presented the data as frequencies (n and %), and median interquartile range (IQR).

Results

The age range of the patients was 12 to 47 years (29 ± 9 years) and 54.5% were females (n = 6). Five patients had presented with taste loss (45.5%), while ten patients had anosmia as a presenting complaint (90.9%). Phantosmia among our patients started after a median duration of 90 days from infection. Median ± IQR for self-perceived improvement in olfactory dysfunction at the start of the combined treatment was 0 ± 5. After the combined administration for 100 days (10 days of oral steroids

Table 2. Detailed characteristics of each patient (n = 11).

Item	1	2	3	4	5	6	7	8	9	10	11
Age in years	47	22	27	26	29	27	40	12	28	28	34
Gender	F	F	F	F	M	M	M	M	M	F	F
Loss of taste	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes
Loss of taste after the first symptom in days	NA	NA	NA	NA	NA	0	3	14	14	NA	14
Development of anosmia after first symptom in days	3	2	3	4	10	3	3	0	14	8	2
Recovery from anosmia in days	120	300	90	21	7	42	14	NA	90	8	14
Start of phantosmia after start of infection	120	300	90	90	180	90	30	10	120	42	14
Duration of follow up in days till the start of combined treatment	485	471	446	403	403	392	338	273	202	134	69
Self-perception of improvement on a scale of one to ten before combined treatment	0	0	0	0	5	5	8	2	5	0	0
Self-perception of improvement on a scale of one to ten after combined treatment	5	6	4	2	5	5	8	8	5	3	7

F = female, M = male.

and 90 days of nasal irrigation, smell training, and zinc supplementation), median \pm IQR of the self-perceived improvement after the intervention was 5 ± 3 (Tables 1 and 2).

Discussion

The persistent olfactory dysfunction is caused by direct damage to the olfactory epithelium sensory neurons, and abnormal signal intensity of the olfactory bulb, along with neuro-inflammation by the retrograde persistent neuro-invasion of SARS-CoV-2 - that involves proinflammatory cytokines, e.g., TNF- α (7,18-21). Phantosmia is one of the rare phenomena among olfactory dysfunctions. The causes and prevalence of phantosmia are still not fully understood (6,15). Classified as central or peripheral phantosmia, peripheral phantosmia is primarily due to damage to olfactory receptors or neurons, usually occurring after a viral infection, while central phantosmia is due to damage to olfactory pathway (13,22,23). Available treatments include pharmacological treatment and surgical resection, depending on the cause of phantosmia. Endoscopic surgical resection of the olfactory cleft is the mainstay of treatment in trauma cases to the olfactory pathway (11). Chemosensory dysfunctions in women were less frequent, but longer lasting (24). Such a notion was not observed in the present small cohort of patients.

Post-viral phantosmia may resolve with time as nature takes its course to regenerate the neuronal endings and pathways. Oral and nasal corticosteroids with and without olfactory training has shown promising results (25,26). Oral and nasal corticosteroids significantly improved post-viral olfactory dysfunction (PVOD) particularly in combination with classic olfactory training. Mixing budesonide with normal saline irrigation and olfactory training was more effective than olfactory training alone; with

a significant improvement of PVOD in 42.6% of the patients (2,5,19,26-28). However, others did not detect superiority for steroid intranasal spray over olfactory training (3). Intranasal application of vitamin A, and systemic supplementation with omega-3 and zinc showed some promise (29).

For patients in the present case series, on a median follow up time of 392 days, the median of the self-perceived improvement before treatment was only 0.0 ± 5.0 on the visual analogue scale. After the combined treatment for 100 days (10 days of oral steroids and 90 days of nasal irrigation, smell training and zinc supplementation), the self-perceived improvement showed improvement. Reportedly, the quality of life has changed dramatically in patients with phantosmia that involves safety issues, like smelling gas leaks and fire, to personal hygiene like bathing for body odor changes, and eating issues that become less pleasant and disgusting, leading to weight loss, and all the related socio-psychiatric issues (11,13,30). Aberrant regeneration of the olfactory nerves, due to unresolved neuroinflammation may negatively impact olfactory recovery, inducing distorted olfactory signals and possible contribution of central misperception (31). The paucity of existing studies on the treatment of post-COVID-19 phantosmia is a challenge, which needs collaborative robust studies to dissect the underlying causes, pathogenesis of phantosmia, and to establish a unifying guideline for its treatment.

Conclusion

In conclusion, post-COVID-19 phantosmia hampers the daily life activities of patients for long durations. The effects are physical, psychological, and social, including matrimonial. The suggested modality containing oral steroid burst treatment, nasal steroid irrigation in saline, and smell training was effective in improving

post-COVID-19 phantosmia, although was not aimed at as a treatment since it was not compared to an untreated control group. Moreover, prednisolone was not previously characterized as a treatment. There is a need for research to determine the pathogenesis of phantosmia and a more efficient treatment for it.

Acknowledgments

No acknowledgements to be mentioned.

Funding

The reporting of this case series was not funded and was conducted as a part of my employment duties at Jouf University.

Ethics approval and consent to participate

Informed consents were collected from all participants.

Consent for publication

Written informed consents were collected from all participants, and the study and reporting details were explained to participants before they consented to join the study. All participants were informed of their right to withdraw at any time during the study's duration with no consequences, as participation was entirely voluntary.

Availability of data and materials

All data and study protocol are already included.

Conflict of interest

None declared.

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