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Olfactory Training Outcomes in Post COVID-19 Olfactory Dysfunction

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Abstract
Objectives: The aim of study is to evaluate the olfaction recovery of patients who performed OT (olfactory training) in a post-COVID-19 PPVOD.
Methods: Study included 50 patients with a sudden loss of smell and a confirmed COVID-19 diagnosis from January 2020 to January 2021 in Kirkuk General Hospital. These participants were submitted to The Sniffin' Sticks test in order to identify those with persistent olfactory dysfunction who were treated either by olfactory training combined with a 10-day course of oral corticosteroids, or by olfactory training alone.
Results: Cross sectional comparative study for 50 patients have history of COVID-19 infection, mean age of patients [47 ± 10] years. [56%] of patients at age group ≥45 years, [44%] of patients are females and [56%] are males. The mean of TDI score increase after OT than before OT with significant difference.
Conclusion: Olfactory function appeared to improve only in peripheral aspects of post COVID-19 PPVOD after OT. patients <45 years have high mean of TDI score than patients ≥45 years old.
Keywords: Olfactory training, outcomes, COVID-19, olfactory dysfunction

Introduction

Olfactory complaint for long time is a broadly reported after an acute, mild or moderate, COVID-19 infection. Olfaction recovery is on reported in 40% to 63% and 70% of patients, respectively, 6 and 12 months after COVID-19.[1-4] Psychophysical olfactory assessments more efficient than subjective smell valuations, 70-95% of patients return to normal smell after 6 months.[5,6] Parosmia is the a chief qualitative dysosmia related with COVID-19 olfactory rescue and happens in 18% to 49%[3,7,8] of patients after 2 months after the acute phase of infection. Parosmia occur in 20% of normosmic patients[3] and gives to the difference between personal weakening and olfactory psychophysical assessments. Quality of life affected by long-lasting olfactory loss[8] also lead to bad diet lifestyles, alterations in social and individual relationships, depression, anxiety, nutritionals problems, cognitive damage.[9,10] Olfactory assessment involves presentation of odorants & tastants, with test results that depend on the patient's response. Such tests are more reliable than a subjective assessment alone and should be performed in patients with COVID-19 when possible.[11] Olfactory psychophysical assessment tools usually test one or a combination of odor threshold (minimum strength of an odor that can be perceived), odor discrimination (differentiation between different odors), and odor identification (identification of odors).[12] Ideally, tools targeting odor threshold, discrimination, and identification using a standard multicomponent olfactory testing device should be employed. However, when fast assessment or self-administration is necessary, such as in the assessment of patients with COVID-19, commercially available tools with fewer testing components, self-administered devices, or both may be considered.[13] The Sniffin' Sticks test is a psychophysical test that allows semi-objective assessment of the patient's olfactory performance by means of 3 subtests: threshold test T, discrimination test D and identification test I. So that the TDI score is a global olfactory score that is the sum of the previous three scores. The initial classification of TDI scores defined functional anosmia as a TDI score ≤16.5, normosmia as a TDI score >30.5 and hyposmia as a score between these two values.[14] When COVID-19–related olfactory dysfunction improves spontaneously, specific treatment may not be required. However, when impairment persists beyond 2 weeks, it may be reasonable for treatment to be considered.[15] Olfactory training should be initiated as soon as possible for patients with post COVID-19 olfactory dysfunction. Patients may benefit from a limited intranasal or oral corticosteroid course.[16] Olfactory Training is a non-pharmacologic treatment option involving repeated odor exposure, with promising outcomes for treatment of post COVID-19 olfactory dysfunction. The mechanism of action for this therapy is thought to be related to regeneration of olfactory receptor neurons and/or improved higher order processing of olfactory information. Olfactory Training involves repeated and deliberate sniffing of a set of odorants (commonly 4 intense odors lemon, rose, cloves, and eucalyptus) for 20 seconds each at least twice a day for at least 3 months (or longer if possible). This therapy has low cost and negligible adverse effects.[17] The aim of study is to evaluate the olfaction recovery of patients who performed OT in a post-COVID-19 PPVOD.

Methods

Study included 50 patients with a sudden loss of smell and a confirmed COVID-19 diagnosis from January 2020 to January 2021 in Kirkuk General Hospital. These participants were submitted to The Sniffin' Sticks test in order to identify those with persistent olfactory dysfunction who were treated either by olfactory training combined with a 10-day course of oral corticosteroids, or by olfactory training alone. All participants were subject to a second Sniffin' Sticks test after a mean of 12 weeks. The results of the tests were documented by individual TDI scores (threshold test T, discrimination test D and identification test I), below table shows TDI scores before and after olfactory training. Take the age and gender of patients. Statistical analysis done by SPSS 22, frequency and percentage used for categorical data, mean, median and SD for continuous data. T test used for evaluation differences between mean and

median of continues variables. *P*-value less or equal to 0.05 is consider significant.

Results

Cross sectional comparative study for 50 patients have history of COVID-19 infection, mean age of patients [47 ± 10] years. [56%] of patients at age group ≥45 years, [44%] of patients are females and [56%] are males, as show in Table 1.

The mean of TDI score increase after OT than before OT with significant difference, as show in Table 2 and Figure 1.

In Table 3, there is significant difference between the mean TDI score according to age groups, patients <45 years have high mean of TDI score than patients ≥45 years old. There is no significant difference between the mean TDI score according to gender.

Table 1. **Distribution of patients according to age group and gender**

Variables		Frequency	Percentage
Age (years)	<45	22	44.0
	45 and more	28	56.0
Gender	Females	22	44.0
	Males	28	56.0

Table 2. **Difference between the mean TDI score before and after**

TDI score	No.	Mean	Std. deviation	*P*-value
Before OT	50	22.9	5.4	0.0001
After OT	50	29.7	8.1	

P-value ≤0.05 (significant).

Discussion

Post-COVID olfactory loss persistent is considered common clinical problem affected patients after COVID-19 infection. OT is only therapeutic hope for post-COVID-19 olfactory weakened patients who are complaining numerous months' post infection, spontaneous olfactory recovery occurring in 40–70% of cases from 6 to 12 months.[2-4] Current study stated that an olfactory recovery in post-COVID-19 PPVOD patients who performed ~3.5 months of OT. That olfactory recovery was significant as the SST MCID increased by more than 6 points[18] on average. Interestingly, we observed more than a doubled normosmic patients' ratio after OT, going from 11 (25.6%) to 27 (62.6%). We reported only a T significant improvement and normalization after OT, followed by non-significant I improvement and D worsening. This is the exact opposite of spontaneous post-COVID-19 olfactory recovery study results[19,20] who reported an I improvement followed by a D and, finally, a slight T improvement. A small or non-significant increasing of T was underlined by Niklassen,[20] Bordin[19] and colleagues, respectively, after 4 and 6 months of spontaneous recovery. We previously confirmed these results[8] reporting that T was the most decreased olfaction subdimension as measured in a cohort of patients around 6 months after a post-COVID-19 PPVOD. As suggested by Iannuzzi et al.,[21] spontaneous recovery in the first two months[22] could be dedicated to a significant T progression, which may correspond to early olfactory neurons and sustentacular regeneration occurring around 2 to 4 weeks in an inflammatory

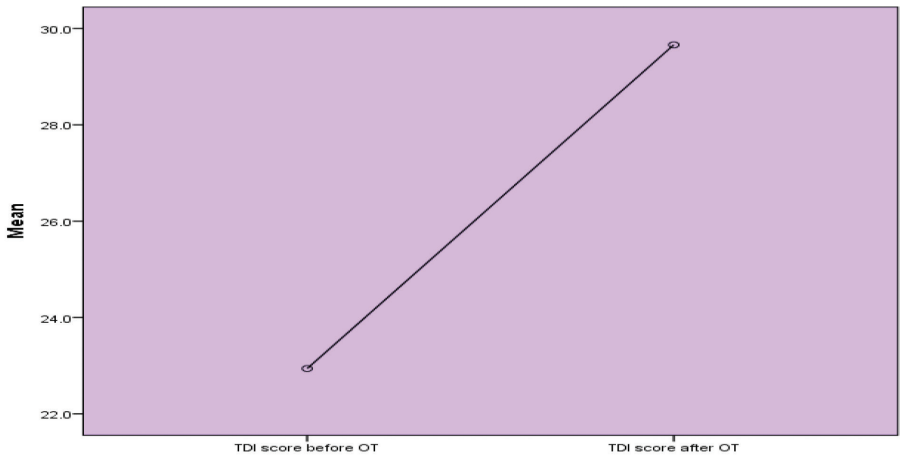

Fig. 1 **Mean of TDI score before and after OT.**

Table 3. **Difference between the mean TDI score according to age groups and gender**

TDI score after OT		*N*	Mean	Std. deviation	*P*-value
Age group (years)	<45	22	33.3	8.2	0.005
	45 and more	28	26.8	6.9	
Gender	Females	22	29.4	8.5	0.85
	Males	28	29.8	7.9	

P-value ≤0.05 (significant).

environment.[23] Moreover, TDI scores seemed to better improve in patients that performed the training for more than 2 months, compared to patients with lower adherence. The T subdimension appeared to improve the most in compliant patients, supporting the previous discussion. Thus, there is no other potential explanation to date that could validate a spontaneous T increase after 6 months on average with persistent post-COVID-19 olfactory loss, based on complete psychophysical evaluation, our normosmic population recovery proportions share some similarities to previously published cohorts who reported spontaneous recovery in 63%[7] to 73.5%[24] on average one year after the infection. Arnaud et al.[7] reported a spontaneous olfactory recovery TDI score of ~30 (as our post OT mean TDI) 18 months after COVID-19 infection but was not peer-reviewed. Specific to COVID-19, in COVID-19 PPVOD, OT alone was reported as significantly improving olfaction recovery only in other steroids efficiency evaluations studies but never again with a complete SST evaluation.[25] However, it is recommended[26] to integrate T, D and I study in olfactory evaluation. Indeed, OT effect on T, D and I in case of PPVOD is still unclear. Hummel firstly described a clear T increasing effect[17] of OT. So, according to our results, Oleszkiewicz et al.[27] reported a significant increasing effect on T and I in OT efficiency on post-infectious ($n = 57$) and idiopathic ($n = 51$) olfactory long-lasting dysfunctions. T-recovery could be explained by a peripheral regenerative[28] effect of OT with a regrowth of olfactory neurons, increase in olfactory receptor expression or a higher specific affinity for those existing as Hummel et al.[29] explained observing an improvement of electro-olfactogram after OT; and I-recovery (with D-recovery) by a more central processing allowing an olfaction dedicated area connectivity reorganization[30] and increase in olfactory bulbs.[31]

Conclusion

Olfactory function appeared to improve only in peripheral aspects of post COVID-19 PPVOD after OT. Patients <45 years have high mean of TDI score than patients ≥45 years old.

Conflicts of Interest

None.

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