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Case Report

The Effect of Vagus Nerve Stimulation Applications on Taste and Smell Loss in COVID-19 Syndrome: Case Report

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Abstract

Loss of the sense of taste and smell is a common side effect of Covid 19. It is thought that transcutaneous ear vagus nerve stimulation may affect taste and smell as a result of neural connections. We present a 27-year-old female participant diagnosed with loss of taste and smell for more than 1 year. The Connecticut Chemosensory Clinical Research Center (CCCRC) olfactory test was used to test the sense of smell. To test the sense of taste, 3 drops of taste test were applied. It was found that during the application period of 1 session per day for 15 days, there was a progressive improvement in the sense of taste and smell. However, it was found that the effect was not significant in restoring the sense of smell and the ability to distinguish odors.

Keywords: COVID-19, vagus nerve stimulation, anosmia, ageusia

INTRODUCTION

Coronavirus has emerged as a global health threat due to its accelerating geographical spread in the last two decades. The virus is believed to be derived from a zoonotic source and is thought to be transmitted directly and by contact. The symptomatic phase is characterized by severe respiratory failure with fever, cough, and myalgia. Diagnosis is confirmed using reverse transcriptase PCR (1). Anosmia, loss or alteration of the sense of smell, is one of the most common symptoms of COVID-19, affecting around 53% of people (2). The acute loss of sense of taste and smell after COVID-19 is the hallmark symptom, affecting between 20 and 85 percent of patients. However, the pathophysiology and potential treatments for Covid-19-related taste and smell loss are not fully understood. Reviewing potential pathological pathways and treatment options for COVID-19 smell and taste loss may be an option in the treatment of persistent dysfunction (3).

CASE REPORT

In November 2020, a 27-year-old female patient who applied to the COVID-19 outpatient clinic as a contact with complaints of runny nose, fever, and headache, SarCovV2 nasopharyngeal swab test was positive and grounded glass image was found on CT examination. At the end of the 7th day, the patient's symptoms worsened and blood tests revealed CRP 14.55 (ref. 0-5), Ferritin 9 (ref. 13-150), Blood urea nitrogen (BUN) 25mg/dl (ref. 5-50), Creatinine 0.66mg/dl (ref. 0,3-1,4), Aspartate Transaminase 13U/l (ref. 5-50), Alanine Aminotransferase 13U/l (ref. 5-50), Troponin-T 3ng/l (ref. 0-14), lactic dehydrogenase 131U/l (ref. 50-480). During the treatment, the patient used Favicovir for 7 days and continued his treatment at home. The person started to experience loss of taste and smell from the 3rd day of the disease. At the end of the 14th day, the test was negative, but the sense of taste had been partially restored and the patient had completely lost his sense of smell. Afterward, the loss of taste and smell continued steadily for more than 1 year and transcutaneous auricular vagus nerve stimulation (taVSS) was initiated.

The study was designed in accordance with the Declaration of Helsinki and approval no. 2021/4 was received from Gümüşhane University Scientific Research and Publication Ethics on 09.06.2021.

taVSS is a stimulant application that can be easily applied

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to healthy individuals to provide autonomic nervous system regulation, and; is actively used to improve general health status including sportive performance. The application was performed as noninvasive transcutaneous auricular vagus nerve stimulation from both ears and the application parameters were; Frequency: 10 Hz, Transition time: 300 micro sec, and application time: 20 min. The applications were performed with Vagustim device (Figure 1).

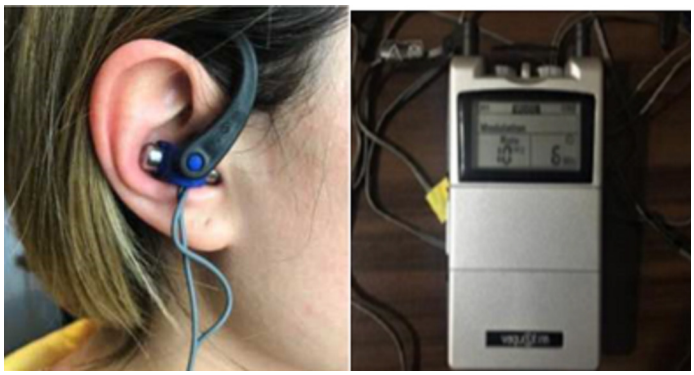

Figure 1. taVNS with Vagustim device

The application was performed in a total of 15 sessions, 5 days a week. Evaluation measurements were carried out before and after the application on each application day, and the evaluation methods were applied as follows;

To test the participants' sense of smell, the Connecticut Chemosensory Clinical Research Centre (CCCRC) Odor Test was used before and after application. The CCCRC test consists of the n-butanol odor threshold test and the odor identification test. For the n-butanol test, butanol solutions numbered from zero to seven were used and pure water was used as a control. The bottle containing 4% n-butanol was numbered zero. The other bottles contained 1/3 dilutions of the previous concentration prepared with distilled water. The threshold was defined as the correct preference for the butanol bottle on 4 consecutive trials and the N-butanol test was scored out of 7(4).

For the odor identification test, cinnamon, chocolate, coffee, soap, peanut, baby powder, naphthalene, and Viks odors were used to test olfactory nerve stimulation and trigeminal nerve stimulation as determined by Veyseller et al. The participant was asked to identify the correct odor from a list of odors that included a distractor response. After evaluation of the N-butanol and odor tests, the values for each nostril were divided by 4 to obtain the mean value, which was between 0 and 7, for each nostril (5).

A global test method, the "three drops" method, was used to assess the participant's 4 taste sensations: sweet (sucrose), salty (sodium chloride), sour (citric acid), and bitter (quinine sulfate). Three drops of liquid (two drops of pure water and one drop of sweetener) were pipetted onto the participant before and after each application. For each of the 4 taste qualities, the test was started with a dilution below the threshold of detection and was gradually increased. The flavor concentrations used were sweet: 0.4, 0.2, 0.1, 0.05 g/ml sucrose, salty: 0.25, 0.1, 0.04, 0.016 g/ml sodium chloride, sour: 0.075, 0.041, 0.0225, 0.0125 g/ml citric acid, bitter: 0.0015, 0.0006, 0.0002, 0.0001 quinine hydrochloride. The lowest-density solution is numbered 1 and the highest-density solution is numbered 4. The participant was asked to identify the flavored drop and rate the taste quality using a visual analog rating scale. The relative scaling for "very low density / very high density" was assessed in the range of 0 to +100, represented by a physical length of 200 mm at each scale (6).

IBM SPSS Statistics 22 was used for statistical analysis in the evaluation of the results obtained in the study. Shapiro-Wilks tests were used to assess the compatibility of the parameters with normal distribution, and it was found that the parameters did not have a normal distribution. Wilcoxon sign test was used for changes in parameters after taVSS compared to before taVSS.

There was no statistically significant change in the value of sweet 1 in the taste evaluation after the application compared to the period before the application ($p>0.05$). The increase in the taste score of the sweet 2 value after the application compared to the value before the taVSS application is statistically significant ($p:0.015$; $p<0.05$). The increase in post-application taste scores compared to pre-application taVSS is statistically significant for sweet 3 ($p:0.048$; $p<0.05$). The increase in taste scores after application compared to before the taVSS application is statistically significant for the sweet 4 score ($p:0.041$; $p<0.05$) (Table 1).

Table 1: Evaluation of taste changes before and after taVSS treatment

	Before taVSS	After taVSS	
	mean±SD (median)	mean±SD (median)	p
Sweet 1	14.7±6.4 (10)	18.7±5.2 (20)	0.058
Sweet 2	23.3±12.9 (20)	32±7.7 (30)	0.015*
Sweet 3	48.7±12.5 (50)	56.7±8.2 (60)	0.048*
Sweet 4	74.7±16 (80)	82.7±8.8 (80)	0.041*
Salty 1	23.3±11.8 (20)	22±6.8 (20)	0.705
Salty 2	44.7±16.8 (40)	47.3±8.8 (50)	0.150
Salty 3	70.7±12.2 (70)	75.3±9.9 (80)	0.124
Salty 4	96±8.3 (100)	98.7±3.5 (100)	0.102
Sour 1	25.3±9.2 (20)	26.7±6.2 (30)	0.608
Sour 2	44±13.5 (40)	49.3±8.8 (50)	0.085
Sour 3	66±11.2 (60)	70±9.3 (70)	0.207
Sour 4	92±7.7 (90)	92.7±7 (90)	0.763
Bitter 1	11.3±7.4 (10)	13.3±6.2 (10)	0.317
Bitter 2	32.7±13.3 (30)	34.7±10.6 (40)	0.438
Bitter 3	77.3±20.5 (80)	75.3±16 (80)	0.715
Bitter 4	96.7±7.2 (100)	90±12.5 (90)	0.026*

taVSS: transcutaneous auricular vagus nerve stimulation, SD: standard deviation, Wilcoxon sign test, *p<0.05

Salty 1, salty 2, salty 3, and salty 4 values did not show a statistically significant change in taste evaluation after the application compared to before the taVSS application (p>0.05) (Table 1).

Sour 1, sour 2, sour 3, and sour 4 values did not show a statistically significant change in the taste evaluation after the application compared to before the taVSS application (p>0.05) (Table 1).

There was no statistically significant change in the taste evaluation of bitter 1, bitter 2, and bitter 3 values after the application compared to before the taVSS application (p>0.05). The decrease in taste scoring in the bitter 4 value after application compared to before the taVSS application is statistically significant (p:0.026; p<0.05) (Table 1).

There was no statistically significant change in the score of the odor assessment in threshold test 1 after the application compared to before the taVSS application (p>0.05). There was no statistically significant change in threshold 2 score odor assessment after application compared to before taVSS application (p>0.05). There was no statistically significant change in the identification scores after the application compared to the pre-application (p>0.05). Compared to before the taVSS application, there was no statistically significant change in CCRC scores after application (p>0.05) (Table 2).

Table 2: Evaluation of odour changes before and after taVSS treatment

	Before taVSS	After taVSS	
	mean±SD (median)	mean±SD (median)	p
Threshold test 1 score	3.5±2 (3)	4.1±2 (4)	0.142
Threshold test 2 score	2.3±1.5 (2)	2±1.1 (2)	0.356
Identification	1.4±0.7 (1)	1.7±0.6 (2)	0.166
CCCRC score	2.5±1.3 (2)	2.9±1.1 (3)	0.094

taVSS: transcutaneous auricular vagus nerve stimulation, CCCRC: connecticut chemosensory clinical research centre, SD: standard deviation, Wilcoxon sign test,*p<0.05

DISCUSSION

COVID-19, which has become a global pandemic, is characterized by symptoms such as fever, cough, difficulty breathing, as well as loss of taste and smell (7). Loss of taste and smell occur together, more than 80% of COVID-19 patients with smell loss also experienced taste disturbance, but did not report taste loss alone. However, loss of taste may be attributable to retronasal olfactory impairment rather than impaired gustation (taste) (8). Research using taste tests is needed to determine conclusively whether SARS-CoV-2 can damage taste transmitters or brain regions related to the taste centers of the brain (9). This confusion of taste- and olfactory-mediated sensations often makes both smell and taste tests necessary to accurately diagnose chemosensory disorders (10).

A quarter of individuals with COVID-19 had some degree of loss of olfactory function by the end of the acute recovery period (9). As in the case in the literature, only sweet and bitter taste sensations were found to be impaired by the 3-drop taste test, and no impairment was observed in salty and sour tastes. Again, our patient was evaluated as anosmia as a result of the CCCRC odor test.

If the loss of odor lasts longer than 2 weeks, treatment should be considered. The effectiveness of current treatments for patients experiencing odor loss associated with COVID-19 is unknown (7). Vagus nerve electrical stimulation may be clinically effective for COVID-19 complications (11). Significant changes were observed in cerebral regions involved in odor and taste processing caused by VSS administration (12), failed to show significant changes in olfactory perception during stimulation in a study in depressed patients (6). Although it is known that the taste sensation of the back of the tongue is associated with the vagus nerve, there is insufficient data on the interaction between vagal nerve stimulation and the olfactory and gustatory systems. In our study, improvement was observed in sweet and bitter taste sensations after VSS application, while no change was observed in salty and sour taste sensations. There was no statistically significant difference in the sense of smell. However, the patient's sense of smell increased. In addition, auricular vagus nerve stimulation was well tolerated by the patient and no side effects were observed during the study period.

CONCLUSION

In this case report, we thought to reveal that taVSS applications are one of the possible methods to be used in the loss of taste and odor after COVID-19. Our study shows that taVSS is a promising application, especially for the improvement of taste parameters. In this direction, a pilot study should first be designed with more cases, and then a randomized controlled study should be carried out by increasing the number of cases further. This case report is not inclusive because it was performed on a single case, but the positive result is promising for further research.

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Conflict of Interest: *The authors have no conflicts of interest to declare.*

Ethical approval: The study was designed in accordance with the Declaration of Helsinki and approval no. 2021/4 was received from Gümüşhane University Scientific Research and Publication Ethics on 09.06.2021.

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