CLINICAL STUDY

INVESTIGATION OF THE EFFECT OF VACCINATION STATUS ON TASTE AND SMELL IN INDIVIDUALS WITH CORONAVIRUS DISEASE 2019 (COVID-19)

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SUMMARY

Objective: Changes in smell and taste are one of the most common symptoms of COVID-19. It is aimed at determining the frequency of taste and smell changes in individuals with COVID-19 and examining the effect of different doses of the vaccine on these changes.

Material and Methods: A 20-question Google Survey, in which only individuals who have had COVID-19 can participate, was created. The study was conducted with a total of 350 people (307 females and 43 males), with a mean age of 30.126± 8.534 years.

Results: The most common symptoms were headache in 70% of cases (n = 254) and change in taste or smell in 69.4% (n= 243). 35.8% (n=87) of the participants did not recover their taste and smell changes. There was no statistically significant relationship discovered between the number of vaccine doses and the presence or severity of taste or smell changes (p>0.05).

Conclusion: In this study, patients with a high prevalence of COVID-19 experienced taste and/or smell changes. It was observed that the dosage amount of the vaccine did not prevent taste and smell changes, nor did it reduce their severity. Changes in taste and smell may impair the quality of life and thus negatively affect individuals socially and psychologically. Therefore, there is a need to develop effective treatments other than vaccination to prevent taste and smell changes in COVID-19 patients, reduce their severity if they occur, treat them, and increase the rate of recovery.

Keywords: Smell, taste, vaccination, coronavirus, olfaction

KORONAVİRÜS HASTALIĞI 2019 (COVID-19) GEÇİREN BİREYLERDE AŞILANMA DURUMUNUN TAT VE KOKU ÜZERİNDEKİ ETKİSİNİN İNCELENMESİ

ÖZET

Amaç: Koku ve tat değişiklikleri COVID-19'un en yaygın semptomlarından biridir. COVID-19'lu bireylerde tat ve koku değişikliklerinin sıklığının belirlenmesi ve aşının farklı dozlarının bu değişiklikler üzerindeki etkisinin incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: Sadece COVID-19 geçirmiş bireylerin katılabileceği 20 soruluk bir Google Anketi oluşturulmuştur. Çalışma, yaş ortalaması 30,126± 8,534 yıl olan toplam 350 kişi (307 kadın ve 43 erkek) ile yürütülmüştür.

Bulgular: En sık görülen semptomlar vakaların %70'inde (n=254) baş ağrısı ve %69,4'ünde (n= 243) tat veya koku değişikliğiydi. Katılımcıların %35,8'inin (n=87) tat ve koku değişiklikleri eski haline dönmemiştir. Aşı dozu sayısı ile tat veya koku değişikliklerinin varlığı veya şiddeti arasında istatistiksel olarak anlamlı bir ilişki bulunmamıştır (p>0.05).

Sonuç: Bu çalışmada, COVID-19 geçiren kişilerde yüksek oranda tat ve/veya koku değişiklikleri görülmüştür. Aşının dozaj miktarının tat ve koku değişikliklerini önlemediği gibi şiddetini de azaltmadığı belirlenmiştir. Tat ve koku değişiklikleri yaşam kalitesini bozabilir ve dolayısıyla bireyleri sosyal ve psikolojik olarak olumsuz etkileyebilir. Bu nedenle, COVID-19 hastalarında tat ve koku değişikliklerini önlemek, ortaya çıkarsa şiddetini azaltmak, tedavi etmek ve iyileşme oranını artırmak için aşı dışında etkili tedavilerin geliştirilmesine ihtiyaç vardır.

Anahtar Sözcükler: Koku, tat, aşılama, koronavirüs, olfaksiyon

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INTRODUCTION

In Coronavirus Disease 2019 (COVID-19) patients, although the classic signs and symptoms such as cough, fever, and respiratory distress are the most well-known ones, taste and smell disorders are also important symptoms reported[1,2]. Studies have revealed that changes in smell and taste are one of the most common symptoms of COVID-19[3], and it is stated that loss of smell and taste can be used to predict COVID-19 status[4]. It is seen that the prevalence of taste and smell disorders due to COVID-19 reported in the literature varies due to differences such as the type of study and the country where the study was conducted. While subjective studies have reported that taste and smell

disorders can vary between 33.9 to 85.6%[5-7], Moein et al. reported objective olfactory impairment at a high rate of 98%[8].

Taste and smell changes reported after COVID-19: hyposmia (decreased sense of smell), parosmia (distorted smell in the presence of a familiar smell source), anosmia (loss of smell), and phantosmia (olfactory experience in the absence of an smell source), as well as tageusia (loss of taste), dysgeusia (impairment of basic tastes such as salt, sour, sweet, bitter) and decreased chemesthesia (chemical sensitivity experienced as sensations such as the burning of hot pepper, the cooling of mint or the warmth of ginger)[9-11]. It is accepted that smell and taste disorders affect individuals' mood, enjoyment of food, ability to detect hazards, social life, and health status[12,13]. Burges et al. reported that people experience anxiety, disgust, confusion, frustration, depression, worry, and hopelessness as a result of the loss or impairment of smell and taste caused by COVID-19, and that the impact of the smell and taste change is far-reaching and alarming[11].

Studies are still being conducted on the effect and nature of COVID-19 on taste and smell changes, which are important for the quality of life of individuals, but whose importance is not recognized until the deterioration is seen[3,14,15]. In some patients with COVID-19, taste and smell changes may be long-lasting and even permanent[16,17]. It is important to detect taste and smell changes early and prevent them from lasting for a long time, which negatively affect the quality of life by depriving people of various daily pleasures and social ties[16] and may cause conditions such as anorexia, food avoidance, malnutrition, depression, and anxiety[18]. In the literature, few studies have examined the effect of vaccination status on taste and smell changes. However, in these studies, taste and smell changes were compared by grouping them as "no vaccination" or "partial vaccination"[14]. There were no studies that looked at the effect of vaccine dosages on taste and smell changes. It is not known whether the vaccine dosage reduces the occurrence or severity of taste and smell changes. Therefore, in this study, it is aimed to determine the frequency of taste and smell changes in individuals with COVID-19 and examine the effect of different doses of the vaccine on smell and taste changes.

MATERIAL AND METHODS

Ethics committee approval for this study was received from Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee decision number 139/09. This study was conducted according to the guidelines in the Helsinki Declaration.

Participants and Procedure

The inclusion criteria were to have previously undergone COVID-19 and to be over 18 years of age. Being under 18 years of age and entering incorrect data that cannot be analyzed (for example, the person asked about symptoms wrote "Q" as an answer) were determined to be exclusion criteria. According to the inclusion and exclusion criteria, the study was conducted with a total of 350 people, 87.7% of whom were female (n=307) and 12.3% (n=43) were male, with a mean age of 30.126 ± 8.534 years (Table 1).

The researchers used Google Forms to create a questionnaire for the study that only included mixed qualitative and quantitative questions for those who had undergone COVID-19. In the questionnaire, multiple-choice, open-ended, short-answer, and Likert-type questions were used in a mixed method. The questionnaire was designed in 4 sections: a consent question, general information, information about vaccination, and information about taste and smell. The questionnaire had 20 questions in total, including one about consent, five about demographic information, seven about the vaccine and COVID-19 symptoms, and seven about taste and smell changes.

People were asked to help with the research by filling out the questionnaire and sharing it with their social contacts. The questionnaire was sent out anonymously through different social media sites like Instagram, Facebook, WhatsApp, etc.

Data Analysis

The SPSS 26 program was used to analyze the research data. In descriptive characteristics, those showing normal distribution were shown with the mean (mean) and standard deviation (SD). The Kolmogorov Smirnov test was used to evaluate whether the data related to the variables were normally

distributed. Relationships between categorical variables were analyzed with Chi-Square tests. The Kruskal-Wallis test was used to compare more than two independent groups. In the analyses, $p<0.05$ was considered statistically significant.

RESULTS

It was determined that 72.3% (n=253) of the participants were university graduates; 17.7% (62) were master's or doctoral graduates; 18% (n=63) were academicians; 19.1% (n=67) were health workers and 15.1% (n=53) were teachers. There were respondents from 57 out of 81 provinces of Turkey (Table 1).

Among the participants, 88.9% (n=311) had received at least one dose of vaccine before. It was determined that 71.4% (n=222) of the first dose was BioNTech vaccine and 28.6% (n=89) was Sinovac vaccine, 72.8% (n=220) of the second dose vaccine was BioNTech and 27.2% (n=82) was Sinovac, while 89.7% (n=148) of the third dose vaccine was BioNTech and 10.3% (n=17) was Sinovac (Table 2).

The COVID-19 symptoms of the participants lasted a mean of 9.293±4.687 days, and 92.6% (n=324) did not have any hospitalization. Only 2.6% of the participants survived COVID-19 without symptoms. The most common symptoms were reported to be headache in 70% (n=254), change in taste and/or smell in 69.4%, sore throat in 52.9%, and fever in 52.3% (Table 3). During COVID-19, 68% of the patients stated that they used at least one medication.

Regarding taste and smell changes after COVID-19, 49.7% (n=174) stated that they experienced taste and smell together, while 30.6% (n=107) stated that they experienced neither. 14.9% (n=52) stated that they only experienced a decrease in smell, 4.9% (n=17) only experienced a change in taste. 35.8% (n=87) of the participants did not recover their taste and smell changes. Taste and smell changes of those who were restored were restored after 32.927±62.376 days and 31.183±61.392 days, respectively (Table 4).

Among those who did not experience taste and/or odor changes, 8.4% had never been vaccinated, 22.2% had received 1 dose, 40.2% received 2 doses, 35.5% received 3 doses, 11.2% received 4 doses, and 2.8% received 5 doses. Among those who experienced taste and/or odor changes, 14.3% had never been vaccinated, 2.9% had received 1 dose, 38.7% had received 2 doses, 35.4% had received 3 doses, 9.1% had received 4 doses, and 1.6% had received 5 doses. In addition, 79.9% of those who had never been vaccinated, 77.8% of those who received a single dose, 68.6% of those who received 2 doses, 69.4% of those who received 3 doses, 64.7% of those who received 4 doses, and 57.1% of those who received 5 doses experienced taste and/or odor changes.There was no statistically significant relationship found between the status of experiencing taste or smell changes and the number of vaccine doses (Table 5).

The severity of smell (Table 6) and taste changes (Table 7) did not differ significantly between vaccine groups ($p> 0.05$).

Table 1: Sociodemographic characteristics of the participants.

Age (mean±SD) years	30.126 ±8.534
Gender % (n)	
Female	87.7 (307)
Male	12.3 (43)
Education % (n)	
Primary School	0.9 (3)
Middle School	0.9 (3)
High School	8.3 (29)
University	72.3 (253)
Master's degree or doctorate	17.7 (62)
Occupation % (n)	
Health worker	19.14 (67)
Academician	18.00 (63)
Teacher	15.14 (53)
Student	14.86 (52)
Retiree	5.71 (20)
Officer	6.00 (21)
Engineer	5.43 (19)
Other	15.71 (55)
Number of different provinces lived in	57

Table 2: Vaccination status of participants.

Have you been vaccinated? % (n)	
Yes	88.9 (311)
No	11.1 (39)
How many doses of vaccine have you received? % (n)	
1 dose	2.6 (9)
2 dose	39.2 (137)
3 dose	35.4 (124)
4 dose	9.7 (34)
5 dose	2.0 (7)
When did you pass COVID-19? % (n)	
Before vaccination	35.1% (123)
After the 1st dose of vaccine	7.1% (25)
After the 2nd dose of vaccine	27.7% (97)
After the 3rd dose of vaccine	24.0% (84)
After the 4th dose of vaccine	4.9% (17)
After the 5th dose of vaccine	1.1% (4)
Which dose and which vaccine did you receive? (n)	
1 dose	222 BioNTech 89 Sinovac
2 dose	220 BioNTech 82 Sinovac
3 dose	148 BioNTech 17 Sinovac
4 dose	34 BioNTech 7 Sinovac
5 dose	4 BioNTech 3 Sinovac

Table 3: Participants' characteristics of COVID-19 symptoms.

Have you been hospitalised? % (n)	
Yes	7.4 (26)
No	92.6 (324)
What were your symptoms? % (n)	
Asymptomatic	2.6 (9)
Nausea and vomiting	14 (49)
Diarrhoea	13.4 (47)
Runny nose	40.3 (141)
Sore throat	52.9 (185)
Fire	52.3 (183)
Cough	54.6 (191)
Taste and/or smell changes	69.4 (243)
Headache	70.0 (245)
On average, how many days did your symptoms, except taste and smell, last? (mean±SD)	9.293±4.687

Table 4: Participants' characteristics related to smell and taste change.

If you have experienced a change in taste and odour. Select one of the following. %(n)	
Only taste change	4.9 (17)
Only smell change	14.9 (52)
Taste and smell change together	49.7 (174)
If there was a change in your taste and smell; Did it return to what it was before COVID-19? % (n)	
Yes	64.2 (156)
No	35.8 (87)
If there was a change in your taste. In how many days did it start to recover? (mean±SD)	32.927 ± 62.376
If there was a change in your smell. In how many days did it start to recover? (mean±SD)	31.183 ± 61.392

Table 5: Chi-square analysis results regarding the number of doses of vaccine and taste/smell changes.

			Taste and Smell Changes		
			No taste and/or smell changes	I experienced taste and/or smell changes	
Number of Vaccine Doses	Not vaccinated	Number	9	30	X^2= 2.226 p= 0.824
		Line %	23.1	76.9	
		Column %	8.4	12.3	
	1 Dose	Number	2	7	
		Line %	22.2	77.8	
		Column %	1.9	2.9	
	2 Dose	Number	43	94	
		Line %	31.4	68.6	
		Column %	40.2	38.7	
	3 Dose	Number	38	86	
		Line %	30.6	69.4	
		Column %	35.5	35.4	
	4 Dose	Number	12	22	
		Line %	35.3	64.7	
		Column %	11.2	9.1	
	5 Dose	Number	3	4	
		Line %	42.9	57.1	
		Column %	2.8	1.6	

Table 6: Difference analysis results regarding the severity of smell changes in vaccine groups according to 5-point likert scale (0= same as before, 5= very bad).

	Group	**n**	**Mean**	**Standard Deviation**	**Rank Average**	**X^2**	**p**
Experiencing Smell Change After First Experiencing COVID-19	Not vaccinated	35	2.4571	2.06288	151.61	0.867	0.973
	1 Dose	8	2.5000	1.85164	160.13		
	2 Dose	119	2.5462	2.10628	154.13		
	3 Dose	108	2.4352	2.16287	149.28		
	4 Dose	26	2.6154	2.13686	157.60		
	5 Dose	7	2.0000	2.00000	129.64		
Experiencing Smell Change After Second Experiencing COVID-19	Not vaccinated	13	1.0769	1.93484	80.73	1.306	0.934
	1 Dose	4	0.5000	1.00000	74.25		
	2 Dose	66	0.8485	1.72976	74.90		
	3 Dose	44	0.7273	1.56061	74.27		
	4 Dose	19	0.3684	0.83070	71.21		
	5 Dose	2	0.0000	0.00000	57.50		
Experiencing Smell Change After Third Experiencing COVID-19	Not vaccinated	10	0.0000	0.00000	60.00	1.831	0.872
	1 Dose	4	0.0000	0.00000	60.00		
	2 Dose	54	0.0926	0.68041	61.15		
	3 Dose	37	0.2703	1.14622	63.35		
	4 Dose	16	0.0625	0.25000	63.75		
	5 Dose	2	0.0000	0.00000	60.00		

Table 7: Difference analysis results regarding the severity of taste changes in vaccine groups according to 5-point likert scale (0= same as before, 5= very bad).

	Group	n	Mean	Standard Deviation	Rank Average	X^2	p
	Not vaccinated	34	2.1176	2.11438	145.51		
Experiencing Taste	1 Dose	8	1.2500	2.31455	108.50		
Change After First	2 Dose	113	2.4336	2.09539	157.04	5.656	0.341
Experiencing COVID-	3 Dose	107	1.9346	2.12918	138.77		
19	4 Dose	25	2.4800	2.23830	161.32		
	5 Dose	7	1.7143	1.97605	131.93		
	Not vaccinated	13	1.5385	2.02548	98.15		
Experiencing Taste	1 Dose	5	0.0000	0.00000	61.50		
Change After Second	2 Dose	72	0.7778	1.58534	79.36	5.975	0.309
Experiencing COVID-	3 Dose	48	0.8125	1.65871	80.10		
19	4 Dose	19	0.4737	1.12390	76.55		
	5 Dose	2	0.0000	0.00000	61.50		
	Not vaccinated	9	0.0000	0.00000	63.00		
Experiencing Taste	1 Dose	5	0.0000	0.00000	63.00		
Change After Third	2 Dose	58	0.1207	0.59464	66.43	3.243	0.663
Experiencing COVID-	3 Dose	45	0.4667	1.37510	70.73		
19	4 Dose	16	0.1250	0.34157	71.00		
	5 Dose	2	0.0000	0.00000	63.00		

DISCUSSION

Taste and olfaction are important to the quality of life of individuals due to their effects on feeding, swallowing, and food intake. Olfaction is also important for social communication life[12,13]. In this study, the presence, duration, and severity of taste and smell changes in individuals who had COVID-19 were determined based on the subjective declarations of the individuals. The effect of vaccination status on the presence and severity of taste and smell changes in individuals who have never been vaccinated, who have received 1, 2, 3, 4, and 5 doses of vaccine, and the effect of different doses of vaccination on taste and smell changes in individuals who have had more than one COVID-19 were examined.

In our study, it was found that 88.9% of the participants were vaccinated, and most of the participants received 2 or 3 doses of vaccine. This may be due to the fact that most of the participants were health workers, academicians, and teachers. In Turkey, the inclusion of non-vaccinated people in public institutions on the condition that they provide weekly Polymerase Chain Reaction (PCR)[19] has forced people to be vaccinated. For this reason, many people had to be vaccinated or receive the second dose in order not to give PCR every week.

Headache was the most prevalent symptom among the participants in our study (70%), then taste and smell changes (69.4%). These results showed that the prevalence of taste and smell changes after COVID-19 is high in Turkey and supported some studies on the symptoms of COVID-19 in other countries[15]. New-onset loss of smell and/or taste was used in the differential diagnosis of COVID-19 when it first started[20], and the fact that it was the second highest symptom according to our findings confirms this decision. The causes of taste and smell dysfunction in COVID-19 are currently unclear[21]. The reason why the loss of taste and smell is so intense may be due to some mechanisms underlying COVID-19. The

COVID-19 pandemic is the SARS-CoV-2 virus, which is genetically related to SARS-CoV-1. Both share the angiotensin-converting enzyme 2 receptor (ACE2), which appears to be used by the virus to enter the cell[6]. These receptors are found in nasal epithelial cells such as goblet and ciliated cells and in the epithelium on the dorsal surface of the tongue. Since the virus damages taste and olfactory cells by binding to the ACE2 receptor, it is likely that patients with taste and smell disorders are frequently encountered in COVID-19 infections[22-25]. In addition, some studies and animal models support the hypothesis that the main target of SARS-CoV-2 in the olfactory epithelium is Bowman's gland cells and sustantecular cells, and that the main cause of olfactory loss is the infection of these cells. The inflammatory process around the olfactory nerve may indirectly affect olfactory fibres and develop olfactory disorders[26,27]. For taste changes, it is thought that, following infection of epithelial cells in the tongue, inflammatory cytokines inhibit the regeneration of taste buds. IFN receptors and toll-like receptors are abundant in taste buds and have been shown to inhibit regeneration[28,29]. It is also thought that the cytokine storm occurring in other cells may cause an increase in ACE2 secretion in the taste buds themselves, and SARS-CoV-2 may enter and infect the cell[30].

In our study, 49.7% (n=174) of the participants reported that they experienced taste and smell together, 14.9% (n=52) reported only a decrease in smell, and 4.9% (n=17) reported only a change in taste. In a meta-analysis study, it was found that the prevalence of taste disturbance varied between 5.6% and 62.7% and the combined prevalence was 38.2%[31]. Tong et al. reported the pooled prevalence of smell and taste dysfunction as 52.73% and 43.93%, respectively[32]. In general, the percentage of taste alteration is lower than smell alteration, as in our study[21]. In another study, taste disorders were observed in 60.7%[33]. In our study, considering those who experienced taste and smell together and those who experienced only smell, 64.6% experienced smell change and 54.6% experienced taste change. Numerous studies have observed that subjective assessment tends to underestimate the true prevalence of olfactory dysfunctions compared to psychophysical testing[17,34]. It has also been reported that taste and smell changes increase with increasing age[14,15]. In our study, a high percentage of taste and smell changes were obtained despite the subjective declaration and a young age range of 30 years on average. This showed that COVID-19 is a remarkable problem for the sense of taste and smell.

Rizzo et al. found that 30.5% of the patients continued to have taste and smell disturbances 1 year after COVID-19 and did not recover[35]. In our study, it was determined that 35.8% of the patients who experienced taste and smell changes did not recover. The findings of our study are compatible with those reported by other authors. In the studies conducted, the duration of recovery for individuals with taste and smell changes was more than one month on average[36]. Rizzo et al. also found that 88.2% recovered after 4 weeks in their study[35]. Similar to other studies, the participants in our study who reported that their taste and smell changes had improved returned to their previous taste and smell in an average of 1 month. These results show that the spontaneous recovery period is long. This may be due to a variety of reasons, ranging from complete destruction of the olfactory epithelium to personal immune factors and persistence of the virus in olfactory and gustatory structures after initial recovery[37-39].

In our study, it was observed that vaccination status had no effect on taste and smell changes. This is an important finding in the literature. Even after receiving five doses of the vaccine, some people reported taste and smell changes after COVID-19. Although the number of vaccines received as a percentage decreased as the number of vaccinations increased, there was no statistically significant difference. This showed that, in general, vaccines do not have a protective effect on the olfactory-chemosensory system, and that COVID-19 has an effect on taste and smell changes in all cases, even if different types and dosages of vaccines are administered. Rizzo et al. (2022) discovered no difference in taste and smell changes between fully and partially vaccinated patients[14]. The findings of our study support the results of Rizzo et al. Furthermore,

when we examined the mean severity of taste and smell changes on a 5-point Likert scale in unvaccinated and different doses of vaccinees in our study, we discovered that vaccination status had no effect on the severity of taste and smell changes. These results showed that vaccination had no effect on the absence of taste and smell changes, nor did it have any effect on the severity of taste and smell changes. The lack of effect of vaccination status or dosage on taste and odor changes and severity could be attributed to the fact that current vaccines rely on systemic injection, which stimulates the production of circulating potentially cytotoxic T cells and immunoglobulin G (IgG) against SARS-CoV-2. This is because these cells are poorly effective at generating mucosal immune responses, i.e., secretory IgA. As a result, the taste and smell neuroepithelium appears to be vulnerable to SARS-CoV-2 even in vaccinated patients[40]. In addition, although the Omigron variant has been reported to cause less taste and smell alteration compared to the delta[14], taste and smell alteration did not differ in the 1st, 2nd, and 3rd time COVID-19 patients in our study. This showed that it should be taken into consideration that COVID-19 still continues to cause chemosensory impairment.

Even though 57 provinces took part, this study is limited because it is based on data from small samples. This may affect the generalizability of the findings. Although the education level of the participants was high, it was based on self-report, and some answers may be incomplete or biased. But it's important to remember that even though objective tests are important, people's own subjective feelings are likely to have a bigger effect on their quality of life. In addition, another limitation of the study is that the effects of taste and smell changes according to different vaccine types could not be compared since there were individuals with different vaccine types at each dose.

CONCLUSION

In conclusion, in this study, a high prevalence of approximately 70% of individuals with COVID-19 experienced taste and/or smell changes, and this was the 2nd most common symptom reported by patients. The majority of people reported changes in taste and smell at the same time. It was determined that it took an average of one month for the taste and smell changes to return, and there were also individuals who did not return at all. It was observed that the dosage amount of the vaccine did not prevent taste and smell changes, nor did it reduce their severity. Taste and smell are important for people's quality of life. Changes in taste and smell may impair the quality of life and thus negatively affect induviduals socially and psychologically. Therefore, there is a need to develop effective treatments other than vaccination to prevent taste and smell changes in COVID-19 patients, reduce their severity if they occur, treat them, and increase the rate of recovery.

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