



Pediatric COVID-19: Prolonged Olfactory and Gustatory Disorders

Pediyatrik COVID-19: Uzun Süreli Koku ve Tat Bozuklukları

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Abstract

Objective: Qualitative and quantitative disorders of the sense of taste and smell associated with coronavirus disease-2019 (COVID-19) are reported as being relatively rare in pediatric patients than in adults. Our aim is to support the literature by evaluating pediatric cases with taste and smell disorders related to COVID-19.

Method: The patients admitted between November 2020-November 2021 due to quantitative and/or qualitative disorders of sense of smell and taste were included in the study. The course of sensory disorders of study patients were gathered from the medical records and evaluated retrospectively.

Results: Fifteen patients were admitted for taste and/or smell disorders with or without a history of symptomatic COVID-19 infection. All of the cases (100%) had anosmia and 14 (93.3%) had ageusia. Parosmia and phantosmia were present in all and 13 children (86.6%), respectively. Eight cases (53.3%) had both phantogeusia and parageusia. Complete resolution of anosmia and ageusia took 24.7 ± 14.5 and 19.6 ± 8.4 days, respectively. Parosmia and phantosmia were resolved in 9.5 ± 2.8 and 10.1 ± 2.5 months. The recovery of parageusia and phantogeusia was shorter than that of qualitative disorders of smell sensation (8.7 ± 2.4 and 8.7 ± 2.5 months, respectively). Cranial magnetic resonance imaging and electroencephalogram examinations were normal in 9 of the cases (60%).

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19) ile ilişkili tat ve koku alma duyusunun nitel ve nicel bozukluklarının pediyatrik hastalarda yetişkinlere göre nispeten nadir olduğu bildirilmektedir. Amacımız, COVID-19 ile ilişkili tat ve koku alma bozukluğu olan pediyatrik olguları değerlendirerek literatürü desteklemektir.

Yöntem: Kasım 2020-Kasım 2021 tarihleri arasında koku ve tat alma duyusunda nicel ve/veya nitel bozukluk nedeniyle başvuran hastalar çalışmaya dahil edildi. Çalışmaya alınan hastaların duyu bozukluklarının seyri tıbbi kayıtlardan elde edilerek retrospektif olarak değerlendirildi.

Bulgular: On beş hasta semptomatik COVID-19 enfeksiyonu öyküsü olsun veya olmasın tat ve/veya koku bozuklukları nedeniyle yatırıldı. Tüm olgularda (%100) anosmi ve 14'ünde (%93,3) ageuzi vardı. Parosmi ve fantosmi, sırasıyla tüm çocuklarda ve 13 çocukta (%86,6) mevcuttu. Sekiz olguda (%53,3) hem fantogeuzi hem de parageuzi vardı. Anosmi ve ageuzinin tamamen iyileşmesi sırasıyla $24,7 \pm 14,5$ ve $19,6 \pm 8,4$ gün sürdü. Parosmi ve fantosmi $9,5 \pm 2,8$ ve $10,1 \pm 2,5$ ayda çözüldü. Parageuzis ve fantogeuzis'in iyileşmesi, nitel koku duyusu bozukluklarından daha kısa sürdü (sırasıyla $8,7 \pm 2,4$ ve $8,7 \pm 2,5$ ay). Kraniyal manyetik rezonans görüntüleme ve elektroensefalogram incelemeleri olguların 9'unda (%60) normaldi.

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Abstract

Conclusion: There is not enough data in the literature about the sensory disorders related to childhood COVID-19 infection. It is the first study recording the longest follow-up periods of sensory disorders in pediatric patients among the literature.

Keywords: COVID-19, gustatory dysfunction, olfactory dysfunction, smell, taste

Öz

Sonuç: Çocukluk çağı COVID-19 enfeksiyonuna bağlı duyuşal bozukluklar hakkında literatürde yeterli veri bulunmamaktadır. Çalışmamız, literatürde pediyatrik hastalarda duyuşal bozuklukların en uzun takip sürelerini kaydeden ilk çalışmadır.

Anahtar kelimeler: COVID-19, koku, koku alma bozukluğu, tat alma, tat alma bozukluğu

Introduction

The expanding list of clinical manifestations of coronavirus disease-2019 (COVID-19) includes various neurological manifestations (1-3). Disorders of taste and smell are among the most common neurological presentations of COVID-19. Both a reduction in the quantity of smell (hyposmia and anosmia) and taste (hypogeusia and ageusia), as well as changes in the quality of chemosensory perception (phantosmia, phantogeusia, and parosmia), are sensory disorders associated with COVID-19 (4,5). High prevalence rates of these symptoms have been reported in European studies, particularly in adult patients with COVID-19. In a multicenter study, smell and taste disorders were reported in 85.6% and 88% of cases, respectively, while in another study, severe loss of smell and taste was reported in as many as 53.7% and 52.2% of patients (6). Both quantitative and qualitative forms of taste and smell disorders are observed less frequently in pediatric patients (7). Therefore, data in the literature on the frequency, severity, duration, relationship with other symptoms of COVID-19, and prognosis of these sensory disorders in childhood COVID-19 infection remain limited. Here, we aimed to address these questions by evaluating pediatric patients with taste and smell disorders related to COVID-19.

Materials and Methods

Study Group

This retrospective case series included patients admitted to University of Health Sciences Turkey, Ankara City Hospital, Pediatric Neurology Department between November 2020 and November 2021 due to quantitative and/or qualitative disorders of the sense of smell and taste. Participants included in the study had positive serum severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) immunoglobulin (Ig)G antibodies; among these, polymerase chain reaction (PCR)-confirmed infection, a history of household contact, or neither was further documented for each patient, as detailed in the results section. A history of COVID-19 vaccination and a

history of similar sensory impairment or acute/chronic rhinosinusitis before the pandemic were accepted as exclusion criteria. Data regarding age, sex, COVID-19 serology, electroencephalogram (EEG), and brain magnetic resonance imaging (MRI) were collected from the medical records of the patients and evaluated retrospectively. Ethical committee approval for this study was obtained from the University of Health Sciences Turkey, Ankara City Hospital Ethics Committee (approval number: E2-22-1276, date: 16.02.2022). Written informed consent was obtained from the parents/legal guardians of the patients. Descriptive analyses were performed due to the small sample size. Categorical variables were presented as number (n) and/or percentage (%).

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Due to the small sample size (n=15), all analyses were descriptive in nature. Continuous variables, such as the duration of anosmia, ageusia, parosmia, and phantosmia, were expressed as mean $\pm$ standard deviation. Categorical variables, including sex distribution, presence of parosmia, phantosmia, and history of COVID-19 infection or contact, were presented as frequencies and percentages. No inferential statistical tests were applied.

Results

Fifteen patients, 80% of whom were girls (n=12), presented with taste and/or smell disorders, with or without a history of symptomatic COVID-19 infection, and were enrolled in the study. The mean age of the patients was 14.2 years (range, 12-17 years). At presentation to the outpatient clinic, upper respiratory tract examinations were normal in all patients. There was no evidence of active COVID-19 infection in any of the cases, and COVID-19 IgM was negative in all patients. Four of our cases (26.6%) had a history of COVID-19 infection confirmed by PCR. Additionally, three cases (20%) had a history of suspicious contact based on a positive family history. The remaining eight patients (53.3%) had no

history of suspected contact, family history of COVID-19 PCR positivity, and/or PCR-proven infection. All cases had anosmia, and 14 (93.3%) had ageusia at symptom onset. Parosmia was present in all 15 cases, whereas phantosmia was identified in 13 cases (86.6%). Eight cases (53.3%) had both phantogeusia and parageusia. Additionally, isolated parageusia as a qualitative taste disorder was present in one case (6.6%). Sensory disorders preceded other symptoms of COVID-19 in one of the four patients with a history of COVID-19 infection and occurred simultaneously with other symptoms in the remaining three patients. Complete resolution of anosmia and ageusia took 24.7 ± 14.5 and 19.6 ± 8.4 days, respectively. Parosmia and phantosmia resolved in 9.5 ± 2.8 and 10.1 ± 2.5 months, respectively. In our case series, recovery from parageusia and phantogeusia was shorter than recovery from qualitative disorders of smell (8.7 ± 2.4 and 8.7 ± 2.5 months, respectively) (Table 1). Cranial MRI and EEG examinations, performed in 9 of the 15 cases (60%) to exclude central causes, were normal.

Discussion

Qualitative and quantitative disorders of the sense of taste and smell associated with COVID-19 are reported less frequently in pediatric patients than in adults. Bernaola Abaira et al. (8) reported different degrees of taste and/or smell impairment in 8 (26.6%) of 30 symptomatic pediatric patients. Qiu et al. (9) and Somekh et al. (10) reported dysfunction of the sense of taste and smell in 10 (37%) of 27 and 28.8% of COVID-19-positive pediatric patients,

respectively. However, there are also studies reporting very low rates, such as 3.7% and 4.4% (11,12). The variability in reported prevalence may be related to the fact that COVID-19 infection is frequently asymptomatic in children and that subjective qualitative sensory disturbances are more difficult to recognize in younger age groups. Taste and/or smell disorders can be seen together with other symptoms of COVID-19, or they can occur as isolated clinical findings, particularly in pediatric patients (8,13-15). Only four cases (26.6%) in our series had a history of COVID-19 infection confirmed by PCR. In addition, three patients had a positive family history of COVID-19, but none of them had other clinical symptoms of COVID-19. Similar to our findings, Erdede et al. (13) reported a case with loss of taste sensation detected during investigation prompted solely by a positive family history.

Qualitative and quantitative olfactory disorders may occur simultaneously, or qualitative disorders may appear later than quantitative ones. Qualitative disorders of the sense of smell and taste often occur during long-term follow-up after infection (16,17). The likelihood of qualitative sensory disorders increases as the follow-up period in adult patients is prolonged, particularly after infection (17,18). However, qualitative impairments such as phantosmia have rarely been reported even in the absence of quantitative olfactory impairments (17,19). Recent studies suggest that persistent inflammation of the olfactory epithelium and neuronal injury caused by SARS-CoV-2 infection may contribute to prolonged qualitative sensory disturbances (20). In our

Table 1. Specific findings and duration of symptoms in patients

Patients	Age (year)	Gender (F/M)	Anosmia duration (day)	Ageusia duration (day)	Parageusia duration (mo)	Parosmia duration (mo) and type	Phantosmia (+/-, type)	Phantogeusia (+/-, type)
P1	13	F	15	15	10	13 rotten smell	+	+ metallic taste
P2	13	F	30	30	-	9 rotten smell	+ sewer smell	-
P3	12	M	30	15	7	7 food-related smell only	+	-
P4	15	F	30	30	14	14 rotten smell	+	+ metallic taste
P5	12	F	15	15	9	10 rotten cabbage	+ sewer smell	+ metallic taste
P6	17	F	10	10	-	12 rotten smell	+	-
P7	16	F	10	10	7	6 rotten smell	+ sewer smell	+ metallic taste
P8	13	F	60	30	-	7 various/mixed smells	+	-
P9	13	F	45	30	-	12 rotten smell	+	-
P10	15	F	15	-	-	12 rotten smell	+	-
P11	16	F	30	30	-	11 rotten smell	+ sewer smell	-
P12	16	F	20	10	7	6 rotten smell	-	+ metallic taste
P13	14	M	10	15	6	5 rotten smell	-	+ metallic taste
P14	14	F	35	20	10	9 rotten smell	+	+ metallic taste
P15	15	M	15	15	9	9 rotten smell	+ sewer smell	+ metallic taste

series, qualitative impairments of taste and smell appeared shortly after the quantitative impairments improved.

An association has been observed between taste and smell sensory disorders in childhood COVID-19 infection and patient age. As age increases in pediatric cases, the probability of experiencing taste and smell sensory disorders also increases. Taste and smell sensory disorders were reported only in children over the age of 10 years in the study by Somekh et al. (10). Gaborieau et al. (21) detected taste and smell sensory disorders only in children older than 6 years among 192 pediatric patients with a definite diagnosis or suspicion of COVID-19. Older children may also be more capable of recognizing and reporting subjective sensory changes compared with younger children. In two different studies, the age range of children with sensory disorders was reported as 15-17 and 10-18 years, respectively (9,15). The age range in our series was consistent with the literature at 12-17 years. In particular, qualitative taste and smell dysfunctions are subjective symptoms and cannot be evaluated using the objective tests applied for quantitative sensory disorders. Therefore, diagnosis of qualitative dysfunction may be difficult, especially in younger children, and such symptoms may be overlooked.

Dysfunction of the sense of taste and smell in pediatric cases is mostly seen in children with mild to moderate COVID-19 (8,9). Qiu et al. (9) reported that 6 and 4 out of 10 children with taste and smell loss had mild and moderate COVID-19, respectively. On the other hand, the authors emphasized the relationship between fever and taste-smell sensory disorders and found that sensory disorders were more common in patients with fever (14). The relatively low rate of severe disease in pediatric COVID-19 cases may partly explain why chemosensory disturbances are more commonly reported in mild or moderate clinical presentations. However, a clear relationship between the degree of taste and smell sensory impairment and the clinical severity of COVID-19 could not be demonstrated. Although different results regarding the severity of taste and smell sensory disorders have been reported, these sensory disorders are generally severe in COVID-19 infection, as observed in our study (8,10,14).

In adults, improvement in taste and smell sensory disorders is often observed within one month after diagnosis or after resolution of other symptoms (18,22-24). Delayed recovery over several months has also been reported, particularly in cases with quantitative disorders of smell (24,25). Recent longitudinal studies have shown that qualitative olfactory

disorders such as parosmia and phantosmia may persist for several months after the acute phase of COVID-19 infection (26). Although fewer studies are available in pediatric cases, similar results have been obtained. In the series by Bernaola Abaira et al. (8), quantitative disorders of taste and smell persisted for up to 120 days. In the study by Klopfenstein et al. (27), the mean duration of anosmia was reported as 8.9 days, with 98% of patients recovering within 28 days. In another study, complete recovery of the sense of taste and smell was observed within 2-15 days, with a mean of 5.7 days (14). Although it was stated in a multicenter study that most cases showed no clinical improvement in taste and smell during follow-up, no information was provided about the duration of follow-up (9). In our cases, complete recovery occurred after a mean of 25 days (range, 10-60 days) for anosmia and 20 days (range, 10-30 days) for ageusia. Although this was an adult study, the rate of complete recovery of smell has been reported to be low, particularly when olfactory dysfunction is the first presenting symptom of COVID-19. A similar pattern was not found for taste disturbance; however, qualitative olfactory disorders generally take longer to resolve (25). In another study, both patients whose phantosmia improved simultaneously with COVID-19 symptoms and cases with persistent phantosmia for up to 3 months were reported (19). In our series, parosmia and phantosmia improved between 5 and 14 months, while parageusia and phantogeusia improved between 6 and 14 months. These findings indicate that qualitative sensory disturbances may represent a long-term sequela of COVID-19 infection and may require prolonged follow-up in pediatric patients (2). Therefore, our case series reported one of the longest recovery periods described in the literature for qualitative impairment of the senses of smell and taste.

Study Limitations

This study has several limitations that should be considered when interpreting the results. First, the number of patients included in the study was relatively small, which may limit the generalizability of the findings. Second, the retrospective design of the study may have resulted in incomplete clinical data regarding the onset and progression of sensory symptoms. Third, objective smell and taste tests were not performed in all patients, and the evaluation of sensory dysfunction was largely based on subjective patient reports. This may have led to underrecognition of qualitative sensory disturbances, particularly in younger children who may have difficulty describing such symptoms. Fourth, only 4 of the 15 patients (26.6%) had PCR-confirmed

COVID-19 infection; the remaining patients were included on the basis of positive SARS-CoV-2 IgG serology and/or a history of household contact, in the absence of a positive PCR test. This heterogeneity in diagnostic certainty means that a definitive causal relationship between COVID-19 infection and the reported sensory disorders cannot be firmly established for all cases, and the possibility of referral bias toward patients with sensory complaints cannot be excluded.

Conclusion

In conclusion, taste and/or smell disorders can occur together with other symptoms of COVID-19, or they can occur as isolated clinical findings, particularly in pediatric patients. Since the cases in our study were mostly asymptomatic, we could not comment on the incidence of sensory disorders in COVID-19 infection. Impairment of the sense of taste and smell is a subjective complaint, which may make it difficult to detect in younger age groups. Therefore, a detailed past clinical history and family history of COVID-19 infection should be obtained in pediatric patients with isolated taste and/or olfactory sensory impairment. Pediatricians should keep COVID-19 infection in mind when a child presents with isolated quantitative and/or qualitative impairments of the senses of smell and taste.

Ethics

Ethics Committee Approval: Ethical committee approval for this study was obtained from the University of Health Sciences Turkey, Ankara City Hospital Ethics Committee (approval number: E2-22-1276, date: 16.02.2022).

Informed Consent: Written informed consent was obtained from the parents/legal guardians of the patients.

Footnotes

Authorship Contributions

Concept: H.Ö., Design: Ö.D., M.G., A.N.Ç.K., Data Collection or Processing: R.Ö., H.Ö., Ö.D., Ö.Y.K., M.G., A.N.Ç.K., Analysis or Interpretation: R.Ö., Ö.D., Ö.Y.K., M.G., A.N.Ç.K., Literature Search: R.Ö., H.Ö., Ö.Y.K., Writing: R.Ö.

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