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Research Article

Evaluation of Olfactory Dysfunction in Patients with COVID-19

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Abstract

In the present context of the COVID-19 pandemic, the olfactory dysfunctions (OD) in patients that are positive for SARS-CoV-2 have been more intense and of early emergence, which is the reason why it is important to study the olfactory function in these patients.

The purpose of this study was the evaluation of the olfactory dysfunction measured through threshold and olfactory discrimination tests (Connecticut). The research was carried out at the Respiratory Hospital of the Santa Casa de Belo Horizonte and included 99 patients infected with SARS-CoV-2, who were evaluated from July 2020 to February 2021. The olfactory test showed that 66% of the patients had some degree of hyposmia in the right nasal cavity and 69,1% in the left nasal cavity. The ages ranged from 19 to 86 years old and the average age was 58.7 years old (+-14.5). When comparing gender and age (< = 60 years old and > 60 years old) in relation to the highest degree of hyposmia, it was possible to verify that the gender variable (male VS. female) did not show a significative difference in hyposmia, p = 0.845. In relation to age, it was possible to see a statistically significant difference, p = 0.003. Patients under the age of 60 showed a higher proportion of normality, followed by mild and moderate hyposmia when compared to those aged 61 and over. The proportion of severe hyposmia/anosmia was higher in those aged 61 and over.

Keywords: Smell; Anosmia; Olfactory Dysfunction; COVID-19; Connecticut

Abbreviations

OD: Olfactory Dysfunction; O_2: Oxygen; NC: Nasal Cannula; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction; CCCRC: Connecticut Chemosensory Clinical Research Center

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, was initially identified by the end of December 2019 in Wuhan, a province in Hubei, China, and was disseminated quickly around the world [1,2].

Clinical Manifestations of COVID-19 vary from light symptoms like cough, fever, fatigue and headache to severe symptoms like dyspnea, severe pneumonia, and respiratory failure. Frequently, patients also present taste changes and olfactory dysfunction (OD), which consist mainly consist mainly of a decrease in the sense of smell (hyposmia) or its complete loss (anosmia) [1,3].

The OD have been increasingly reported in infected individuals, with recent studies showing a prevalence of up to 62% in individuals with positive Reverse Transcriptase Polymerase Chain Reaction (PCR) for SARS-CoV-2. They can appear in the beginning of the course of the disease and occur independently or with other symptoms, being useful to help identifying and isolating patients with the suspected disease [2,3,5,6]. Such disfunction has a strong impact in the quality of life, since it can lead to malnutrition, weight loss, food poisoning, depression and exposure to dangerous chemicals [7].

Its pathogenesis is still not well understood but some hypotheses suggest that the OD may result from inflammation and obstruction of the olfactory cleft, causing localized conductive loss, from damage to the supporting cells of the olfactory epithelium, or even the direct injury to the olfactory bulb. In patients with prolonged deficits, a central mechanism seems to be involved [1-3,14].

In view of the growing prominence that the OD have gained as a key symptom in the COVID-19 pandemic due to its high prevalence among infected patients and the important role of the population screening, the following study aimed to evaluate the olfactory function of patients in the acute phase of the infection through an objective olfactory test as well as the OD characteristics in patients admitted to the Santa Casa de Misericórdia Hospital, in Belo Horizonte, reference in the treatment of COVID-19 in the state of Minas Gerais, Brazil.

Materials and Methods

This is a cross-sectional study that analyzed data from 99 patients hospitalized in the wards of the Santa Casa de Misericórdia in Belo Horizonte, Minas Gerais.

The following criteria was used or the inclusion of participants in the study: patients that were hospitalized in wards and presenting acute COVID-19 confirmed by confirmed by positive RT-PCR result for SARS-CoV-2. All the patients that met these criteria and agreed to participate in the study were included. The study excluded patients hospitalized in Intensive Care Units and those who were disoriented in time and space.

Data collection was carried out from July 2020 to February 2021. The researchers collected information by using the Connecticut Chemosensory Clinical Research Center (CCCRC) survey and the olfactory test as a basis for the studied population. The olfactory function of eligible participants was measured only once.

The CCCRC is a valid test in medical literature, of easy application and widely used in researches. For the threshold test, 7 manipulated solutions of N-butanol with different standardized concentrations are presented. The highest concentration is 4% in 60 ml of water, the subsequent ones showing a 1:3 dilution of N-butanol. Two bottles are presented to the patient, one containing the dilution with N-butanol and the other with only water, always starting with the most diluted solution. The patient himself closes one of the nostrils and smells the odors with the contralateral one, being asked which of the two bottles has a stronger smell (water or N-butanol). It is important to emphasize that at no time does the patient hold or have contact with the vials. The threshold is assessed when the patient identifies four times the odor at the same dilution. In case of error, the next more concentrated vial is offered. The entire process is carried out first through one nostril and then through the other. At the end, the correct answers are calculated and an average is performed for the score.

Regarding discrimination, 7 known and common odors are offered to the patient (cinnamon, paçoca, coffee, chocolate milk, naphthalene, talc and soap), without the patient seeing the contents of the bottle. Patients are asked to identify each odor through a list containing the 7 real odors, plus 7 names of distracting odors. The grade is given according to the number of hits (ranging from 0 to 7). The score of odor and discrimination thresholds are evaluated separately and an arithmetic average is performed for the score in each nasal cavity. Thus, a classification is made between anosmia (0 - 1.75), severe hyposmia (2.0 - 3.75), moderate hyposmia (4.0 - 4.75, light hyposmia: 5.0 - 5.75) and normosmia (6.0 - 7.0).

The data obtained from the evaluated variables were compiled and expressed through descriptive statistical analysis. For continuous variables, measures of central tendency (mean and median) and dispersion (standard deviation) were obtained. For categorical variables, the absolute frequency and percentage for each category were calculated.

To compare proportions between the independent variables and the response variables, the chi-squared test, the Fisher's Exact Test or the Monte Carlo Method were used, each one meeting the necessary assumptions. Gender, age with the highest degree of hyposmia and supplemental use of O_2 were compared. Data analysis was performed using SPSS statistics version 23.0 and Microsoft Excel 2016.

The study was approved by the institution's Committee on Ethics in Research (protocol 35468820.6.0000.5138) and all participants signed an informed consent form.

Results and Discussion

This study evaluated olfactory dysfunctions using the Connecticut Objective Test in 99 patients infected by SARS-CoV-2 with positive RT-PCR, who were hospitalized at Santa Casa-BH between July 2020 and February 2021.

Table 1 summarizes the clinical-epidemiological characteristics and test results of the patients. The male gender was predominant,

63 cases (63.3%) and the ages ranged from 19 to 86 years and the mean age was 58.7 years (±14.5). The smell test showed that 66% of the patients had some degree of hyposmia in the right nasal cavity, and 10 (10.3%) were classified as having anosmia. In the left nasal cavity, 69.1% of the patients had some degree of hyposmia and amongst these, 6 (6.2%) were classified as anosmia. As for the supplementary use of O_2, the majority used NC (nasal catheter), 71.1%).

Variables	n	%
Gender (n = 99)		
Male	63	6.,6
Female	36	36.4
Age	58.7(±14.5)	19-86
Connecticut Right Nostril (n = 97)		
Normal	33	34.0
Light Hyposmia	21	21.6
Moderate Hyposmia	16	16.5
Severe Hyposmia	17	17.5
Anosmia	10	10.3
Connecticut Left Nostril (n = 97)		
Normal	30	30.9
Light Hyposmia	23	23.7
Moderate Hyposmia	16	16.5
Severe Hyposmia	22	22.7
Anosmia	6	6.2
Hyposmia (higher degree) (n = 97)		
Normal	22	22.7
Light Hyposmia	26	26.8
Moderate Hyposmia	15	15.5
Severe Hyposmia	22	22.7
Anosmia	12	12.4
Use of supplemental O2 (n = 90)		
No Use of supplemental O2	14	15.6
CN	64	71.1
Face mask	8	8.9
IOT + VM	4	4.4
Age (average ± standard deviation; Minimum and maximum)		

Table 1: Characterization of patients diagnosed with COVID-19 hospitalized at Santa Casa de BH - July/2020 - February/2021.

When comparing sex and age (< = 60 years old and > 60 years old) in relation to the highest degree of hyposmia, it was possible to verify that the gender variable (male x female) did not present a significant difference regarding hyposmia, p = 0.845), that is, the groups were similar in relation to the proportions of the categories evaluated. Regarding age, there was a statistically significant difference, p = 0.003. Patients younger than 60 years old had a higher proportion of normality, followed by mild and moderate hyposmia when compared to those aged 61 years or older, and the ratio of severe hyposmia/anosmia was higher in those aged 61 and over (Table 2).

Regarding the supplementary use of O_2, no statistically significant association could be observed regarding Gender and Age, p = 0.831 and p = 0.886, respectively. The proportions were similar (Table 3).

In May 2020, the World Health Organization recognized olfactory dysfunction (OD) as one of the symptoms caused by SARS-CoV-2 [9]. Despite being widely observed in clinical practice and published in international studies, it is a disorder related to COVID-19 that still needs to be evaluated by objective tests of smell and not just by anamnesis reports, in order to achieve greater accuracy [10,11].

In this study, the olfactory threshold and discrimination test was used objectively - Connecticut (Connecticut Chemosensory Clinical Research Center), which is validated in Brazil, and with feasibility characteristics for large-scale application, such as in a hospital environment. This method was used in order to avoid subjective responses of the olfactory function of the evaluated patients.

The olfactory dysfunction in individuals with COVID-19 can be caused by edema in the nasal mucosa (conductive) or by viral aggression directly on the olfactory system (involvement of the olfactory epithelium and supporting cells or neurons). Another proposed mechanism for the development of post-viral OD would be the increase in cytokine production. In the Henkin study, a limitation is related to the inaccurate reporting of anosmia/hyposmia in hospitalized patients. Patients who have been admitted to an intensive care unit or ward may have difficulty reporting the presence of an olfactory dysfunction during the acute setting of SARS-CoV-2 infection. Another limitation was the lack of quantification of olfactory loss. Therefore, the results obtained are restricted to patient reports only, differently from the present study, which evaluated only patients in the ward who were able to recognize olfactory al-

Variables Normal Light Hyposmia + Moderate			Hyposmia			Total	Value p*
			Severe Hyposmia + Anosmia				
Gender	Male	n	15	25	22	62	0,845
		%	68.2%	61.0%	64.7%	63.9%	
	Female	n	7	16	12	35	
		%	31.8%	39.0%	35.3%	36.1%	
Age	Up to 60 years old	n	15	24	9	48	0,003
		%	71.4%	58.5%	27.3%	50.5%	
	61 or more	n	6	17	24	47	
		%	28.6%	41.5%	72.7%	49.5%	
*Chi-squared test							

Table 2: Comparison of Gender and Age in relation to the degree of hyposmia in patients diagnosed with COVID-19 admitted to Hospital Santa Casa de BH.

Variables No use of supplemental O_2 NC			Use of supplemental O_2			Total	Value p*
			IOT + VM				
Gender	Male	n	8	47	3	58	0.831
		%	57.1%	65.3%	75.0%	64.4%	
	Female	n	6	25	1	32	
		%	42.9%	34.7%	25.0%	35.6%	
Age	Up to 60 years old	n	8	33	2	43	0.886
		%	57.1%	46.5%	50.0%	48.3%	
	61 or more	n	6	38	2	46	
		%	42.9%	53.5%	50.0%	51.7%	
*Chi-squared test via Monte Carlo Simulation							

Table 3: Comparison of Gender and Age in relation to Supplemental Use of O_2 in patients diagnosed with COVID-19 admitted to Hospital Santa Casa de BH.

terations, excluding patients in intensive care and applying an objective test of smell with an established score.

In another study carried out in Brazil through interviews and subjective assessment of smell, 79.2% of patients positive for COVID-19 had an olfactory dysfunction (hyposmia and/or anosmia). There was a significantly higher prevalence of OD in patients with mild clinical conditions compared with patients with severe acute respiratory syndrome and those with critical illness. In addition, there were more cases of OD among patients who were admitted to the ward, when compared to those who were admitted to the ICU. Likewise, Yan., *et al*. (2020) evaluated 196 patients and concluded that those with anosmia or hyposmia had a lower rate of hospitalization when compared to those with normal olfactory function [13]. Therefore, they suggest that patients with flu syndrome caused by SARS-CoV-2, in the absence of an olfactory dysfunction, should seek medical attention earlier, due to the greater likelihood of pulmonary involvement and greater chance of developing se-

vere acute respiratory syndrome. They also highlighted that the presence of OD could be used as a clinical marker related to the severity of the disease, as well as the APGAR score in the newborn [13].

In contrast to these findings, Moein., *et al.* (2020) and Vaira., *et al*. (2020) found no association between olfactory dysfunction and disease severity. Vaira stated that the smell changes reported by critically ill patients can be overlooked in the context of prolonged hospitalization and invasive ventilatory support [14-16].

Another study carried out with a Brazilian population that included patients admitted to the ICU, ward and participants with outpatient treatment suggests that patients with hyposmia/anosmia may present a state of better immunological competence, with a greater chance of having SARS-CoV-2 in the upper airways [17].

Moein., *et al*.. (2020) applied the UPSIT test (University of Pennsylvania Smell Identification Test) to 60 in-patients with COVID-19 to measure olfactory dysfunction. About 98% of those studied had olfactory alterations, of which 83% had anosmia or severe hyposmia. A relevant piece of information is that only 35% of this sample had a complaint of olfactory dysfunction before the examination. In general, changes in smell are more noticeable by the patient in cases of more significant losses, such as anosmia. Thus, although it has not yet been quantified, it can be inferred that the number of olfactory dysfunctions may be higher than that recorded in individuals infected with SARS-CoV-2.

In the present study, an objective test of smell was also used, being chosen the CCCRC due to its easy application and mainly low cost. Older patients (>61 years old) had more hyposmia compared to those younger than 60 years. This may be due to the greater aggressiveness of SARS-CoV 2 in the olfactory epithelium of the elderly or some degree of previous degeneration of olfactory fibers by senility.

Finally, despite the significant sample of patients, this present study was carried out in a single hospital, being, therefore, geographically limited. In addition, no olfactory threshold test was performed in critically ill patients who were in the intensive care unit, which means that an objective result could not be established between the loss of smell and the severity of the disease.

Conclusion

The olfactory dysfunction in patients infected with COVID-19 appears to be more than a symptom of this new infection. Hyposmia/anosmia in these patients may be a predictor of the disease and be useful in screening and early diagnosis. The application of the objective test of smell reveals the real involvement of the olfactory epithelium caused by SARS-CoV-2, in addition to differentiating the intensity of aggression in each nasal cavity separately. In this study, older individuals had a higher degree of hyposmia/anosmia, which has an important impact on quality of life.

Conflict of Interest

The authors have no conflicts of interest to this work.

Bibliography

1. Mutiawati Endang., *et al*. "Anosmia and dysgeusia in SARS-CoV-2 infection: incidence and effects on COVID-19 severity and mortality, and the possible pathobiology mechanisms-a systematic review and meta-analysis". *F1000Research* 10 (2021).

2. Meng Xiangming., *et al*. "COVID-19 and anosmia: A review based on up-to-date knowledge". *American Journal of Otolaryngology* 41.5 (2020): 102581.

3. Mastrangelo Andrea., *et al*. "Smell and taste disorders in COVID-19: from pathogenesis to clinical features and outcomes". *Neuroscience Letters* 748 (2021): 135694.

4. Rocke John., *et al*. "Is loss of sense of smell a diagnostic marker in COVID-19: a systematic review and meta-analysis". *Clinical Otolaryngology* 45.6 (2020): 914-922.

5. Borsetto Daniele., *et al*. "Self-reported alteration of sense of smell or taste in patients with COVID-19: a systematic review and meta-analysis on 3563 patients". *Rhinology* 58.5 (2020): 430-436.

6. Aziz Muhammad., *et al*. "The association of "loss of smell" to COVID-19: a systematic review and meta-analysis". *The American Journal of the Medical Sciences* 361.2 (2021): 216-225.

7. Glezer Isaias., *et al*. "Viral infection and smell loss: The case of COVID-19". *Journal of Neurochemistry* 157.4 (2021): 930-943.

8. Saussez Sven., *et al*. "Anosmia: an evolution of our understanding of its importance in COVID-19 and what questions remain to be answered". *European Archives of Oto-rhino-laryngology* 278.7 (2021): 2187-2191.

9. de Souza Ellen Lelis., *et al*. "A importância do plasma convalescente e/ou globulina hiperimune em pacientes com doença coronavírus 2019 (Covid-19)/The importance of convalescent plasma and/or hyperimmune globulin in patients with coronavirus disease 2019 (Covid-19)". *Brazilian Journal of Health Review* 4.5 (2021): 22506-22514.

10. Kosugi Eduardo Macoto., *et al*. "Recuperação incompleta e tardia da perda súbita do olfato na COVID-19". *Brazilian Journal of Otorhinolaryngology* 86 (2020): 490-496.

11. Romano Fabrizio Ricci., *et al*. "Olfato e Paladar: Da Anatomofisiologia ao Diagnóstico e Tratamento". Thieme Revinter, (2021).

12. Brandão Neto Deusdedit., *et al*. "Chemosensory dysfunction in COVID-19: prevalences, recovery rates, and clinical associations on a large Brazilian sample". *Otolaryngology–Head and Neck Surgery* 164.3 (2021): 512-518.

13. Yan CH., *et al*. "Self-reported olfactory loss associates with outpatient clinical course in COVID-19". *International Forum of Allergy and Rhinology* 10.7 (2020): 821-831.

14. Moein Shima T., *et al*. "Smell dysfunction: a biomarker for COVID-19". *International forum of allergy and Rhinology* 10.8 (2020).

15. Hopkins Claire., *et al*. "Self-reported olfactory loss in COVID-19: is it really a favorable prognostic factor?". *International Forum of Allergy and Rhinology*. Wiley-Blackwell, (2020).

16. Vaira Luigi Angelo., *et al*. "Objective evaluation of anosmia and ageusia in COVID-19 patients: single-center experience on 72 cases". *Head and Neck* 42.6 (2020): 1252-1258.

17. Brandão Neto Deusdedit., *et al*. "Chemosensory dysfunction in COVID-19: prevalences, recovery rates, and clinical associations on a large Brazilian sample". *Otolaryngology–Head and Neck Surgery* 164.3 (2021): 512-518.

18. Henkin Robert I., *et al*. "Interleukin 6 in hyposmia". *JAMA Otolaryngology–Head and Neck Surgery* 139.7 (2013): 728-734.