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Olfactory dysfunction in COVID-19

Zaburzenia węchowe w zakażeniu COVID-19

Authors' Contribution:
A – Study Design
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C – Statistical Analysis
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E – Literature Search
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ABSTRACT: The COVID-19 pandemic is a result of increasing globalization. However, thanks to clinicians' efforts and the cooperation between research centers, the best methods for diagnosis and treatment of COVID-19 infection are constantly being developed. According to the most recent research, olfactory disorders have been included in the earliest symptoms. This article is a synthetic summary of current literature about the occurrence of olfactory disorders in patients with SARS-Cov-19. The article presents pathophysiological mechanisms, a typical clinical image and the available diagnostic tools for a better understanding of olfactory disorders in patients with SARS-Cov-19. The effectiveness of psychophysical olfactometry and accurate medical history was highlighted in the discussion. The authors suggest the possibility of effective diagnostics of olfactory disorders in the form of teleconsultation and emphasize the importance of the role of laryngologists in the diagnosis of COVID-19 and the need to disseminate knowledge about olfactory disorders to inhibit the SARS-CoV-19 pandemic. The authors postulate to create a simple model based on physical examination, which would recognize SARS-Cov-19 infection with high sensitivity. Appreciating the importance of olfactory disorders may allow for more effective isolation of asymptomatic carriers, which would clearly inhibit the development of COVID-19 pandemic. In addition, the paper presents therapeutic management of olfactory dysfunction lasting for more than two weeks.

KEY WORDS: anosmia, coronavirus, COVID-19, olfactory disorders, pandemic, psychophysical olfactometry, SARS-CoV-2

STRESZCZENIE: Pandemia COVID-19 jest wynikiem postępującej globalizacji. Jednak właśnie dzięki wysiłkom klinicystów i umiędzynarodowieniu współpracy ośrodków badawczych nieustannie opracowywane są najlepsze metody diagnostyki oraz leczenia zakażenia COVID-19. Zgodnie z najaktualniejszymi badaniami, do najwcześniej występujących objawów zostały zaliczone zaburzenia węchu. Niniejsza praca poglądowa stanowi syntetyczny zbiór i podsumowanie aktualnego piśmiennictwa na temat występowania zaburzeń węchu u chorych na SARS-Cov-19. W artykule prezentowane są: mechanizmy patofizjologiczne, typowy obraz kliniczny oraz dostępne narzędzia diagnostyczne dla prawidłowego rozpoznawania zaburzeń węchu u chorych na SARS-Cov-19. W dyskusji wyróżniona została skuteczność olfaktometrii psychofizycznej i dokładnego wywiadu lekarskiego. Autorzy pracy sugerują możliwość skutecznego prowadzenia diagnostyki zaburzeń węchu w formie telekonsultacji oraz podkreślają, jak istotna jest rola laryngologów w diagnostyce COVID-19 i konieczność rozpowszechniania wiedzy na temat zaburzeń węchu w kontekście ograniczenia pandemii. Postulują również utworzenie prostego modelu opartego o badanie przedmiotowe i podmiotowe, który z wysoką czułością rozpoznawałby zakażenia SARS-CoV-2. Docenienie wagi zaburzeń węchu może pozwolić na skuteczniejsze izolowanie bezobjawowych nosicieli, co wyraźnie zahamowałoby rozwój pandemii. Ponadto w pracy zaprezentowane zostało postępowanie terapeutyczne w przypadku zaburzeń węchu utrzymujących się dłużej niż dwa tygodnie.

SŁOWA KLUCZOWE: anosmia, COVID-19, koronawirus, olfaktometria psychofizyczna, pandemia, SARS-CoV-2, zaburzenia węchowe

ABBREVIATIONS

ACE2 – Angiotensin-converting enzyme 2
ARDS – acute respiratory disease syndrome
COVID-19 – acute respiratory disease caused by SARS-CoV-2 virus
RT-PCR – real-time reverse transcription PCR
SARS-CoV-2 – virus causing acute respiratory disease 2
SNOT-22 – Sino-nasal Outcome Test
TMPRSS2 – TMPRSS2 protease

INTRODUCTION

The SARS-CoV-2 virus is an etiological agent responsible for the COVID-19 pandemic. The described disease entity is an acute respiratory infection transmitted by airborne droplet nuclei first diagnosed in December 2019 in central China (Wuhan city – primary outbreak). As of the date of this publication (07/06/2020), a total of 6,799,713 cases of COVID-19 have been confirmed worldwide, of which 397,388 (5.8%) people have died. This is a proof of the huge scale of this phenomenon. In Poland, the outbreak made

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25,986 people ill and caused 1,153 deaths (4.4%) [1]. According to the data of the Chief Sanitary Inspectorate (GIS), 17% of infected people in Poland are healthcare professionals. In addition to anesthesiologists and dentists, otolaryngologists are the highest risk group of infection with SARS-CoV-2 virus [2]. The course of the disease may present variable course. Most patients have mild symptoms and a good prognosis. However, it is to be remembered that a developing coronavirus infection could lead to pneumonia, acute respiratory distress syndrome (ARDS), thromboembolic complications, sepsis, septic shock, multi-organ failure and death. This aggressive and severe disease affects approximately 10–20% of patients. One of the first symptoms which often anticipates the leading symptoms by several days (such as cough, fever and dyspnea) are disturbances of smell and taste.

Olfactory dysfunction can be qualitative and quantitative, and the reasons may be attributed to damage to the peripheral portion (the olfactory epithelium inside the nasal cavity) or the central portion (the olfactory pathway, olfactory neurons) of the olfactory system. The group of quantitative smelling disorders includes: hyposmia (loss of sense of smell), anosmia (complete lack of the sense of smell), hypersomnia (hypersensitivity to the sense of smell), and qualitative parosmia (a "wrong" perception of odors), pseudosmia (misperception of smell), phantosmia (olfactory hallucinations), cacosmia (unpleasant olfactory hallucinations), agnosmia (loss of the ability to detect familiar smells) [3].

ANOSMIA IN COVID-19 INFECTION

The most recent publications of international research teams from Germany, Great Britain, Italy, Iran and the United States indicate anosmia as one of the significant symptoms of COVID-19 infection [4–9]. The incidence of olfactory and taste dysfunction ranges from 34% to 68% depending on the studied group. It is of serious clinical value that in a large number of patients isolated anosmia was the only symptom of COVID-19 infection [10, 11]. An Iranian study found that 59 out of 60 patients hospitalized due to COVID-19 have an olfactory dysfunction according to the psychophysical UPSIT olfactory tests [12]. They were defined as a reduced or distorted ability to detect odors when sniffing, which has often been perceived in mild or even asymptomatic cases of COVID-19. In an Italian study carried out on 202 patients with mild symptoms, 64% reported a loss of smell in the SNOT-22 test [13]. After the emergence of an array of evidence suggesting that the sense of smell is impaired in COVID-19 infection, it was recognized that the sudden onset of smell and taste dysfunctions is one of the key symptoms of coronavirus infection – AAO – H&NS (USA) and BRS-ENT studies (Great Britain) [11, 14]. For the above reasons, the appearance of those symptoms is a sufficient reason for healthcare professionals to use elevated PPE (including FFP2 or FFP3 masks) and to isolate patients. In Italy, among patients hospitalized for COVID-19, olfactory or taste dysfunction were more frequently observed in younger patients and in women [8]. Most of the unpublished, unconfirmed reports from hospitals treating patients infected with SARS-CoV-19 report that the resolution of olfactory symptoms occurs in about two weeks. The percentage of patients developing persistent infectious olfactory dysfunction remains unknown due to the lack of long-term follow-up and research. According to research conducted in a mice model by Bilińska et al., infection with the SARS-CoV-2 coronavirus causes damage to the supporting cells that are part of the olfactory epithelium. The olfactory neurons are indirectly made dysfunctional, indicating that the mechanism of olfactory dysfunction is linked with infection of the nervous system, or at least its peripheral portion. The target proteins for the coronavirus are ACE2 and TMPRSS2 present in the supporting cells. Moreover, it was observed that older mice have an elevated amount of those proteins, which can explain their greater susceptibility to infection [15].

DIAGNOSIS AND TREATMENT OF ANOSMIA IN COVID-19

Symptoms of sudden loss of smell in view of the pandemic should be taken extremely seriously, and patients who have experienced those should be quarantined and undergo a SARS-CoV-2 RT-PCR test during isolation. The assessment of the olfactory organ may be performed in patients with confirmed COVID-19 if their clinical condition allows it [16]. Overall, a poor correlation has been observed between the results of objective tests and the subjective assessment of olfactory dysfunction. The majority of studies conducted to date suggest that, as a rule, a considerable percentage of people with loss of smell are unaware of the existing deficit until they are assessed using professional techniques [17, 18]. Modern methods of olfactory testing, both objective – olfactory potentials (OERPs), electro-olfactogram (EEAs) and subjective – olfactory screening tests, qualitative and quantitative, which are based on psychophysical olfactometry [3], can be very helpful. Some can be performed remotely, which allows for safe collection of data and is acceptable in some COVID-19 positive patients, for whom it is not possible to perform psychophysical tests. The role of imaging methods of the paranasal sinuses and the brain in patients infected with COVID-19 has not yet been precisely defined. Imaging (MRI and CT) can be used to exclude intracranial abnormalities and/or the structure of the sinuses and the ostiomeatal complex. It also allows evaluating the morphology of the olfactory bulb and groove, which may be helpful in obtaining diagnostic and prognostic information related to the presence of olfactory dysfunction. Imaging can play a key role in identifying other causes and finding possible alternatives in patients with persistent olfactory impairment. As one of the few areas of the nervous system, the olfactory organ retains the lifelong ability to regenerate. The olfactory cells located in the nasal cavity are constantly replaced by new ones arising from stem cells. Two weeks after the onset of infection is a period during which the olfactory disorder should subside. If the clinical condition does not improve, it is justified to enter treatment for this dysfunction. The effectiveness of existing methods of treating olfactory dysfunction in patients infected with Covid-19 is unknown, but it can be assumed that they are helpful as in the case of post-infectious episodes of loss of smell. It should be remembered that the treatment of an olfactory dysfunction depends on the damaged area. Studies have shown the high effectiveness of olfactory training in patients suffering from post-infectious olfactory dysfunction, which consists of alternating and deliberate smelling of a specially produced set of

fragrances for 20 seconds at least twice a day for a minimum of 3 months. This therapy is associated with low costs and is free from any adverse side effects. The positive effects of oral and nasal corticosteroids in post-infectious olfactory dysfunction have not been proven, and a potential risk of their use has even been suggested [16]. To ensure safety, systemic corticosteroids should not be used in COVID-19, especially if no symptoms of inflammatory disease have been demonstrated in imaging and/or endoscopy. Persons who used nasal steroids chronically before COVID-19 infection are recommended to continue them [20]. Medicines for which there are positive reports regarding their effectiveness in the treatment of post-infectious olfactory dysfunction are: intranasal sodium citrate modulating the cascade of transduction of olfactory signals and intranasal vitamin A promoting olfactory neurogenesis which, together with high doses of omega-3 acids having anti-inflammatory and stimulating neuroregeneration effects, support olfactory training [16, 19]. To date, the effectiveness of these treatments in COVID-19 infected patients has not been proven.

CONCLUSIONS

The olfactory epithelium is the gateway to infection. Suddenly emerging olfactory dysfunction in a patient is in itself sufficient for the isolation of the individual and diagnosis for SARS-Cov-19. For reasons of high infectivity, the best methods for assessing disorders are psychophysical olfactometry and a thorough interview. The therapeutic approach to olfactory dysfunction that lasts longer than two weeks should be based on olfactory training and the use of intranasal vitamin A and omega-3 acids.

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