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REVISION ARTICLE

Oral manifestations of COVID-19

Manifestaciones bucales de la COVID-19

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ABSTRACT

Introduction: at the beginning of the year 2020, the World Health Organization declared SARS-CoV-2 infection as an international emergency situation. The disease produced by this virus progressed rapidly and caused a high number of deaths. The main clinical manifestations produced by the new coronavirus are widely described in the literature; however, information about the alterations appearing at oral level is scarce.
Objective: to describe the main oral manifestations of SARS-CoV-2.
Methods: a bibliographic review was carried out, using articles retrieved from SciELO, PubMed, Ebsco and Springer. Thirty references were used.
Development: it has been suggested that the oral cavity is a perfect habitat for invasion by SARS-CoV-2 due to the special affinity that the virus has for cells with receptors for angiotensin-converting enzyme (ACE2) such as those of the respiratory tract, oral mucosa, tongue and salivary glands, thus affecting the functioning of the salivary glands, taste sensations, smell and the integrity of the oral mucosa. The new coronavirus would have the capacity to alter the balance of the oral microbiota, which added to a depressed immune system would allow colonization by opportunistic infections.
Conclusions: the main oral manifestations of COVID-19 reported in the literature are: hyposalivation, xerostomia, ageusia, hypogeusia, dysgeusia, herpetic lesions and candidiasis.

Keywords: Covid-19; Sars-Cov-2; Oral Manifestations.

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RESUMEN

Introducción: iniciándose el año 2020, la Organización Mundial de la Salud declaró a la infección por SARS-CoV-2 como una situación de emergencia internacional. La enfermedad producida por este virus progresó rápidamente y ocasionó un elevado número de fallecidos. Las principales manifestaciones clínicas producidas por el nuevo coronavirus se encuentran ampliamente descritas en la literatura, sin embargo, la información acerca de las alteraciones que aparecen a nivel oral, es escasa.
Objetivo: describir las principales manifestaciones orales del SARS-CoV-2.
Métodos: se realizó una revisión bibliográfica, mediante artículos recuperados en SciELO, PubMed, Ebsco y Springer. Se emplearon 30 referencias.
Desarrollo: se ha sugerido que la cavidad oral es un perfecto hábitat para la invasión por SARS-CoV-2 debido a la especial afinidad que tiene el virus por células con los receptores para la enzima convertidora de angiotensina (ECA2) como son las del tracto respiratorio, mucosa oral, lengua y glándulas salivales, pudiendo afectar, de este modo, el funcionamiento de las glándulas salivales, las sensaciones del gusto, olfato y la integridad de la mucosa oral. El nuevo coronavirus tendría la capacidad de alterar el equilibrio de la microbiota oral, lo que sumado a un sistema inmune deprimido permitiría la colonización por infecciones oportunistas.
Conclusiones: las principales manifestaciones orales por COVID-19 reportadas en la literatura son: hiposalivación, xerostomía, ageusia, hipogeusia, disgeusia, lesiones herpéticas y candidiasis.

Palabras clave: Covid-19; Sars-Cov-2; Manifestaciones Orales.

INTRODUCTION

A new variant of coronavirus was first seen at the end of 2019 in China, in Hubei province, especially in Wuhan city. It massively affected the population and caused in a short time an epidemic that went out of control and spread rapidly to the rest of the world, causing a pandemic. This outbreak began in a local seafood market.

The first cases occurred at the beginning of December 2019, on the 8th, in the city of Wuhan. On December 26, a few cases of an unknown pneumonia (four cases) were observed and within a month there were cases all over the country. On January 7, Chinese scientists identified the causative agent, a new coronavirus, which was subsequently named SARS-CoV-2, and the new disease caused by the virus was named COVID-19. By January 30, 7736 cases and 170 deaths had been confirmed in China, and 82 cases were confirmed outside China. On February 20, the epidemiological situation was alarming: 74 675 confirmed cases in the Asian country and 2121 deaths, and in the rest of the world there were 1073 cases and eight deaths.[1]

The virus is generally transmitted from person to person through small droplets of saliva, known as Flügge microdroplets, which are emitted when talking, sneezing, coughing or exhaling.[2]

The clinical symptoms presented by the patients were fever, dry cough, respiratory distress (dyspnea), headache and pneumonia, and eventually developing progressive respiratory failure caused by lung tissue damage and leading to death. The disease was determined to be caused by virus-induced pneumonia according to clinical symptoms and other criteria, such as a decrease in the number of lymphocytes and white blood cells - although the latter could sometimes be normal - new infiltrates on chest X-ray and no obvious improvement. The virus was successfully isolated in these patients.[3]

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On January 30, the World Health Organization declared the coronavirus epidemic an international emergency.(4)

The disease progressed rapidly and caused a high number of deaths. In Cuba, the first case of COVID-19 was reported on March 11, 2020.

At that time, in the rest of the world there were 125 048 confirmed cases (6 729 new cases that day) and 4613 deaths (321 new cases); of these, in China, there were 80 981 confirmed cases and 3173 deaths and in the rest of the world 44 067 confirmed cases, accumulating 1440 deaths, covering a zone of 118 countries, territories or areas. What the world would experience afterwards is already known to all.(5)

The information available on the main clinical manifestations produced by SARS-CoV-2 such as fever, dry cough, diarrhea and respiratory distress is ample and detailed, however, that on the more recently reported symptoms, mostly present at an earlier stage of infection, such as skin lesions, smell alterations and oral repercussions, is scarce.(6)

The impact of COVID-19 on oral health is mainly determined by the patient's immune system, the pharmacotherapy received and by the pathogenesis of the virus. It has been suggested that the oral cavity is a perfect habitat for SARS-CoV-2 invasion due to the special affinity of the virus for cells with receptors for angiotensin-converting enzyme (ACE2) such as those of the respiratory tract, oral mucosa, tongue and salivary glands.(7)

It has been demonstrated that SARS-CoV-2 is a neurotropic and mucotropic virus, being able to affect the functioning of the salivary glands, the sensations of taste, smell and the integrity of the oral mucosa. Studies indicate that this new coronavirus has the ability to alter the balance of the oral microbiota, which combined with a depressed immune system would allow colonization by opportunistic infections.(8)

Currently, there are doubts as to whether the origin of these oral manifestations is the result of direct viral infection, whether they are the product of the patient's systemic involvement or whether they occur as adverse reactions to the treatments received to treat COVID-19.(9)

There are multiple scientific articles that have investigated the oral cavity as the main route of SARS-CoV-2 infection, the consequences of the high risk of infection in dental practice and the possible use of saliva for diagnosis. However, there are few studies that relate COVID-19 with salivary gland disorders, taste and smell alterations, intraoral lesions, information that could be very useful for the prevention, diagnosis and treatment of the pathology.(10)

This review shows the current available evidence on oral mucosal manifestations, salivary gland disorders, and alterations in the olfactory and gustatory systems in the context of SARS-CoV-2 infection.

METHODS

A literature search was performed using national and international literature, in electronic and printed format, in the open access search engine SciELO, PubMed, Ebsco and Springer with the use of the following search terms: Covid-19; oral manifestations, oral mucosa.

The search for information sources was carried out between May and August 2022. A total of 30 bibliographic references were used. As a criterion for the selection of the literature, 99 % of the references used corresponded to the last five years since it is a very recent topic.

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DEVELOPMENT

The emergence of the new infectious disease COVID-19 has had a massive impact worldwide. The mode of spread of the infection, the resulting severe respiratory dysfunctions and the number of deaths globally, significantly compromising people's quality of life, has marked a before and after in the history of mankind. Salivary gland disorders.

Saliva has a vital function in maintaining the integrity of the tissues of the oral cavity since it allows its lubrication, cushions pH changes and has an antibacterial, antiviral and antifungal action. The volume of salivary secretion, under normal conditions, depends on multiple factors such as temperature, circadian rhythm, type of taste and chemosensory, masticatory or tactile stimulation.(11)

Sometimes, associated mainly to the patient's systemic condition and the consumption of certain drugs, hyposalivation develops. This is related to the presence of ulcerative lesions of the intraoral mucosa, dysgeusia, dysphagia and increased susceptibility to infections.(12)

The presence of hyposalivation and xerostomia has been reported in patients infected with SARS-CoV-2. Studies indicate that patients with hyposalivation have a higher risk of developing a severe respiratory infection, since lower salivary secretion may alter the barrier function of the airway mucosa, favoring viral adhesion and colonization. In turn, hyposalivation is related to a decrease in salivary proteins such as mucins, lysozyme, cathelicidin, lactoferrin, peroxidase, salivary agglutinin, alpha-defensins, beta-defensins and cystatins, which could potentially impede virus replication, especially of SARS-CoV-2. 17 Because of this, hyposalivation can be considered as a risk factor for the development of respiratory infections such as COVID-19.(13)

Olfactory and taste alterationsOlfactory and taste alterations

The olfactory system detects volatile chemicals through olfactory sensory neurons in the nasal cavity and food odors through the nasopharynx (retronasal olfaction).

The gustatory system responds to compounds in the mouth that elicit sensations of sweet, salty, bitter, sour and umami. Chemostasis detects other chemicals, found in herbs or spices, that evoke sensations such as burning, cooling or tingling. Often, these modalities combine and transfer a unique taste experience during a meal, so it is common that when there is a loss of retronasal olfaction and alteration in the somatosensory system, which transmits chemostasis, it is reported as a loss of taste.(14)

Chemosensory alterations of these systems can result in quantitative (anosmia, hyposmia; ageusia, hypogeusia) and qualitative (dysgeusia, parosmia) changes in taste and smell, respectively.(15)

The association of viral infections with alterations of smell and taste is frequent since viruses can cause inflammation of the nasal mucosa and rhinorrhea. However, the case of COVID-19 seems to be somewhat particular, as it is not associated with these features. Although it is known that SARS-CoV-2, due to its affinity for ECA2 receptors, can infect tongue keratinocytes, the mechanism by which it affects the senses is not entirely clear and although an alteration of smell can lead to an alteration of taste, it is possible that they do not occur together since they have different peripheral and central neural mechanisms.(16)

It is thought that the virus may have the ability to infect taste receptor cells, cranial nerves that carry taste and chemoesthetic information, or may even infect surrounding blood vessels and cells of the central nervous system.(17)

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Research shows that the prevalence of smell and taste disturbances in patients with COVID-19 varies between 58-86 % and 54-88 %, respectively.[18]

Of these manifestations the most frequent would be the qualitative ones, mainly anosmia and ageusia. It has been pointed out that smell and taste alterations would follow in prevalence with fever, dry cough and fatigue.[19]

Other authors state that these would be the most prevalent manifestations of COVID-19, especially in patients with mild to moderate severity of infection and who are female.[20]

Therefore, they are considered excellent predictors of infection and in case of presenting them, it is recommended that the patient be isolated until the results of the laboratory test are available.

Intraoral findings

In the oral cavity there may be manifestations of underlying diseases of bacterial or viral origin. Among these are: oral ulcers, gingivorrhage, glossitis, halitosis and orofacial pain. The most prevalent oral lesions of viral etiology are ulcers and blistering lesions of the tissues. Several case reports have confirmed the presence of oral manifestations in patients with COVID-19.[21]

These are considered to be mainly due to the patient's immunocompromised state, poor oral hygiene and co-infection with other viral or bacterial infections.[22]

The most reported intraoral findings in patients with COVID-19 correspond to candidiasis and herpetic lesions. It has been suggested that recurrent oral ulcers may be an inaugural symptom of COVID-19. However, as these findings are still recent in the literature, it is unclear whether they are due to coronavirus infection per se or whether they are secondary manifestations to the patient's systemic condition.[23]

Herpetic lesions

Ulcers or blisters may appear at the oral level, corresponding to elementary lesions, commonly observed in other viral processes such as foot and mouth disease, herpetic gingivostomatitis and oral cytomegalovirus infection.[24]

Also macular lesions and oral petechiae on the palate in patients hospitalized with COVID-19 infection.[25]

Of the cases reported in the literature, lesions have been found to be quite heterogeneous among patients, and even in the same patient.[26]

Different presentations, locations and sizes are described.[27] Oral manifestations have occurred in COVID-19 patients with no relevant medical history, being described in healthy patients and also in patients with underlying diseases.[28]

Although oral mucosal lesions have been reported in patients infected with SARS-COV-2 virus, it is believed that the cause would not be the virus itself, but that the lesions would be secondary to drugs administered for treatment, or due to compromise and deterioration of the immune system, which also brings with it opportunistic infections.

The most reported are co-infections of Candida albicans and/or other viruses.

Despite these assumptions, some of the studies reviewed point to the theory of a vascular and thrombotic effect on the oral mucosa generated by the SARS-CoV-2 virus. Similarly, oral mucosal lesions could be triggered by factors such as stress.[29]

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t is essential to emphasize the importance of the ACE2 receptor (Angiotensin Converting Enzyme 2), which is distributed in the cell membrane of various organs and tissues, such as the respiratory tract, nervous system, digestive system and skeletal muscle. Within the oral cavity it is present in epithelial cells of the oral and gingival mucosa, its presence in epithelial cells of the tongue and salivary glands stands out, due to the high expression at the lingual level, the tongue is described as a susceptible organ. Some authors point out that salivary glands and periodontal sacs could act as a reservoir of the virus.

This would be the main receptor of the SARS-CoV-2 virus, causing cells with distribution of this receptor to trigger inflammatory reactions in the associated organs and tissues, which is why at the lingual level, several authors point out that this interaction could be responsible for the development of taste disorders in patients with COVID-19 disease. It has also been described that the interaction between the virus and this receptor alters the function of oral keratinocytes and the epithelial lining of the salivary gland ducts after infection. Additionally, saliva and nasal secretion could be fluids with high viral load being involved in the development of these oral alterations described.[30]

Something on which multiple authors agree is the need for further studies and exhaustive research to know the pathogenic mechanisms of SARS-CoV-2 on oral tissues, and thus determine whether oral mucosal lesions are directly or indirectly related to the progression of COVID-19.

CONCLUSIONS

The main oral manifestations of COVID-19 reported in the literature are hyposalivation, xerostomia, ageusia, hypogeusia, dysgeusia, herpetic lesions and candidiasis. It has been proven that the oral cavity is the perfect portal of entry for SARS-CoV-2 infection due to the special affinity of the virus for the ECA2 receptors present in the cells of the oral mucosa, tongue and salivary glands. Once the disease is established, the virus would have the capacity to alter the balance of the oral microbiota and immunosuppress the patient, allowing the possible appearance of opportunistic infections. The above, together with pharmacological therapy and salivary gland disorders, whose etiology is still not entirely clear, would contribute to the development of oral manifestations and sensory disorders, which could occur at an early stage and be very useful for the timely diagnosis of the disease.

Conflict of interest:
The authors declare that there is no conflict of interest.

Authors' Contribution:
AEGC: was responsible for conceptualization, formal analysis, project administration, writing - original draft, writing - review and editing.
YHR: responsible for conceptualization, formal analysis, project management, writing - original draft, writing - revision and editing.

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