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ETIOPATHOGENETIC ASPECTS AND FEATURES OF DAMAGE TO THE STRUCTURES OF THE ORAL CAVITY IN CORONAVIRUS INFECTION (REVIEW)

Giyazova Malika Mukhamadovna
Bukhara State Medical Institute
malikagiyazova85gmail.com

ANNOTATION

This review article combines studies on the main pathogenetic mechanisms of the development of lesions of the oral mucosa, the main signs of its pathology in COVID-19, common neurological symptoms. A comparative analysis of scientific achievements in the field of dental covitology is carried out. The peculiarity of coronavirus infection and the ways of its spread during infection with SARS-CoV-2 is characterized. The stages of development of oral cavity lesions in coronavirus infection are demonstrated and possible ways of their drug correction are shown. Such work will make it possible to develop diagnostic algorithms for early detection, prevention, treatment and rehabilitation of oral cavity injuries, horrific consequences of coronavirus infection, ways of optimal drug therapy can be chosen.

Keywords: COVID-19, oral pathology, SARS-CoV-2, saliva changes, coronavirus infection, neurostomatological syndromes, therapy of coronavirus-related oral pathology.

Coronavirus infection is a disease that for the first time has been identified as severe acute coronavirus 2 respiratory syndrome (SARS-CoV-2). Coronavirus characterized by the presence of an RNA protein with beta bonds, including SARS-CoV and SARS-CoV-2, which the pandemic has shown are deadly viruses that cause respiratory distress syndrome (RDS) [5, 9, 41]. By literature data and according to practical medicine in In 1960, six types of coronavirus were identified,causing disease in humans (SARS-CoV; MERS-CoV; SARS-CoV-2; Bat-CoV; Bat-CoV and RaTG13) [3, 12, 39]. In 2002, there was a major outbreak of SARS-CoV, known as severe acute respiratory syndrome (SARS), resulting in the death of about 10,000 people worldwide. Total only ten years later, another pathogenic coronavirus known as the Middle East respiratory coronavirus syndrome (MERS-CoV) has spread in the countries of the Middle East [12, 33]. SARS-CoV-2 is the seventh member of the family coronaviruses infecting humanity. Interestingly, the genome SARS-CoV-2 is aligned with the genomes of bat viruses (Bat- CoV and Bat-CoV RaTG13) in Rhinolophus

affinis species from the province Yunnan with 96% similarity. Structural analysis reveals mutation in the envelope protein (Spike protein) and the nucleocapsid protein. The coronavirus (SARS-CoV-2) has a simple structure with a small amount of proteins (4 in total): shell protein (E), spike protein (S), transmembrane protein (M), and nucleoprotein (N). Proteins E, S and M contribute to the penetration of the virus into cells host, virion entry and viral spread. The viral genome is closely related to the N protein, and helps protein E into the penetration of the virion [6, 11, 23]. As practice has shown, there are currently two ways transmission of SARS-CoV-2: direct and indirect. direct transmission involves contact with body fluids of an infected person human (airborne, respiratory route, i.e. through saliva), as well as through other biological fluids (faeces, urine, semen and tears). Signs and symptoms of COVID-19 can be divided into respiratory and extrarespiratory [13, 18, 34]. The most common respiratory symptoms are cough, fever and shortness of breath. There is a wide range extrarespiratory signs and symptoms, including lesions oral mucosa, neurological dysfunctions - loss of smell, loss of taste, headache associated with it myofascial pain, which can be considered diagnostic criteria for this disease. List of symptoms of coronavirus annually or, one might say confidently, at the time of each outbreak is updated, infection oral cavity, neurological symptoms, tissue damage salivary glands, severe forms of complications are not including an exception. To date, many scientific studies, where a wide range of non-specific lesions of the oral mucosa and subsequent neurological complications, mucosal degeneration of the oral cavity, of various etiologies, however, are not well understood formation, diagnosis, prevention, treatment of such diseases against the background of the SARS-CoV-2 virus. However, despite significant advances in covitology, pathogenetic aspects, ways of invasion, principle biological attack, issues of diagnosing lesions of the oral cavity, pathogenesis of possible neurological complications, prognosis of neurostomatological manifestations, dental assistance and preventive measures to prevent aggression of the SARS-CoV-2 virus in the mouth area, still remain open. According to WHO, there is a rather large list of symptoms coronavirus, which appear on the 2nd-14th day of infection (cough, aches and pains, fever, loss of taste and smell) [14, 19, 42]. Despite the short time the existence of a coronavirus infection, and exploring ways the spread of its pathogen, there are still no unambiguous evidence of preventing COVID-19 through compliance rules of personal hygiene and oral hygiene [16, 22, 27]. However, maintaining proper hygiene can reduce the frequency damage to the structures of the oral cavity, the development of neurological complications and neurostomatological syndromes. Does not exist certain characteristics of symptoms that occur in the mouth cavity, due to the continued evolution of the virus [19, 21, 38]. In addition, due to the

weakening of the protective functions body dental problems on their own can serve as a risk factor for infection, and a dental examination when it would be correct to include COVID-19 in the list of necessary research. Physicians from Brazil described the occurrence of ulcers and plaques, and also cracks in the tongue in an elderly patient, hospitalized with COVID-19 (2020) [32]. In addition, at infected may develop a taste disorder, fungus, candidiasis and other pathological conditions in the mouth. Russian experts believe that such symptoms can be observed in as secondary manifestations of infection, as well as side effects effects of medications, particularly antibiotics(2021) [1, 37]. Scientists from the Laboratory of Oral Histopathology of the Faculty health care of the University of Brazil revealed lesions oral mucosa in an elderly man admitted to hospital with COVID-19, in addition to loss of taste on the 24th day hospitalization developed yellow mouth ulcers similar to herpetic, as well as deep fissures and specific white plaque on the back of the tongue (2021) [33]. Often infected develop secondary conditions caused by the general effect of infection on the body, according to the type of dryness during mouth. According to Irina Makeeva, head of the department Therapeutic dentistry of the First Moscow State Medical University. THEM. Sechenov, secondary lesions of the oral cavity with coronavirus infection is often observed in diabetes, due to the action of drugs used to treat this disease (diuretic, lowering blood pressure, antiallergic, antibiotics) (2020) [27]. There are cases persistent lymphadenitis for no apparent reason (2021), on the body and on oral mucosa may develop ulcers that were previously never happened, loss of taste sensitivity (reception food is felt like “chewing soap, cotton wool” (2019) [7, 40]. CEO of the German Dental Implantology whom Maret Khashieva (2020) claims that against the background of this infection, herpes and stomatitis can appear, the balance of microflora is disturbed, candidiasis develops (thrush) of the oral cavity, gingivitis and periodontitis, which associated with reduced immunity [8, 11]. It should be noted, that caries in itself is not a "gateway" for infection, but immunity in any case will be "distracted" by such defeat. And this significantly weakens the protective body strength. Irina Makeeva's observations showed that SARS-CoV-2 is able to bind to the ACE-2 molecule (angiotensin converting enzyme 2), which is membrane protein, the entry gate for the virus into cells, and expresses (multiplies) on mucosal epithelial cells shells of the mouth (2020) [9, 24, 30]. According to Khurshid Z., Asiri F.Y., Al Wadaani H. mouth damage due to COVID-19 in the form of loss of taste and smell are common clinical complaints in dentists (2020) 16]. It is emphasized that the SARS-CoV-2 virus causes a wide range of nonspecific lesions of the oral mucosa mouth, however, a specific diagnosis of mucocutaneous lesions with COVID-19 will contribute to the prevention of diffuse spread of SARS-CoV-2, proper case management and their

dental care [20, 33, 41]. Neurological manifestations of COVID-19 in the form of loss of taste and smell requires further study at the receptor level, as this will allow a fresh look at the pathogenicity of SARS-CoV-2. Detection of the virus in salivary secretions is common phenomenon in this infection, and ongoing research should be focused on biochemical quality research saliva for rapid diagnosis of COVID-19, and in some cases, predictive criteria can be created specific pathological conditions depending on individual changes in the biological substrate, the value conditions of the oral mucosa, saliva. Thus, most oral tissues contain target cells for the Wuhan pathogen. However, while a clear parallel between the manifestations of dental diseases and the severity of coronavirus infection is impossible, because too few statistics are available and clinical observations that require careful analysis, long-term follow-up and dental inspections. The purpose of our further actions to study the main ways of infection and features of damage to the main structures oral cavity is the definition of significant neurostomatological syndromes and some biochemical saliva indicators in coronavirus infection. Coronavirus infections in the oral mucosa destroy epithelial cells and cause local inflammatory reactions that have a sudden onset and manifested by the association of single or multiple blisters or sores. Vesicles in the oral cavity, blisters, populous, macular rashes and ulcers are common clinical signs of viral infections [11, 29, 35]. With SARS-CoV-2 damage to the epithelium causes similar pathogenic signs in oral tissues such as ulcers, erosions, blisters, vesicles, pustules, fissured or depapillated tongue, spot, papule, plaque, pigmentation, bad breath, whitish areas, hemorrhagic crust, necrosis, petechiae, edema, erythema, Kawasaki-type angular cheilitis, atypical syndrome Suite and Melkerson-Rosenthal syndrome [9, 21, 31]. Most common sites of injury are the tongue (38%), mucosa the membrane of the lips (26%) and the palate (22%). Oral cavity lesions European literature data were almost the same for both sexes (49% women and 51% men). In patients over older age and severe COVID-19 disease more widespread and severe lesions oral cavity [3, 36]. Histological analysis of SARS-CoV-2 oral lesions shows vascular defects associated with capillaries oral mucosa [1, 38]. The pathogenesis of COVID-19 oral mucosal lesions is mainly associated with accumulation of lymphocytes and Langerhans cells in the subcutaneous vascular walls, and the virus itself causes destruction keratinocytes by cytotoxic lymphocytes (i.e. occurs local autoimmunization). Histological examination biopsies from patients with COVID-19 who also had cutaneous manifestations, confirms vascular ectasia with extended capillaries, blood-filled spaces and perivascular lymphocytic infiltrate with eosinophilia [28, 39]. It was found that the lack of oral hygiene, opportunistic infections, stress, immunosuppression, vasculitis and hyperinflammatory response

caused by COVID-19, are predisposing factors for the occurrence oral lesions in patients with COVID-19 [10, 25]. At patients also experienced discomfort on the tongue, plaque lesions, swelling of the palate, tongue and gums [19, 39]. Immune suppression can lead to conditioned aggression pathogens such as Candida albicans and development of the above changes in the language [18]. eight]. Medical correction and prevention of lesions oral mucosa COVID-19 can be carried out mouth rinses with antiseptic liquids (chlorhexidine, sodium hypochlorite, povidone-iodine), using topical or systemic corticosteroids, systemic antibiotics and antiviral drugs according to individual the needs of the patient's condition [23]. As mentioned above, SARS-CoV-2 infection accompanied by a sudden loss of taste and smell, which may be sporadic. According to researchers similar phenomena were more often detected among medical workers, severe and sometimes isolated loss of smell and/or taste [2, 38]. Nasal congestion has been proven to be the driving factor loss of smell caused by injury olfactory neuroepithelium. Loss of smell in most cases is associated with loss of taste [40]. In an online survey, 52% of people found changes in taste sensations. 21.9% of them reported change in the perception of spicy taste, 23.6% - salty, 29.2% - sour and 25.3% - sweet. Possible cause of taste loss COVID-19 may be associated with an increase in the number ACE-2 receptors on tongue keratinocytes, and cell death keratinocytes and mucus production can block taste receptors, which can negatively affect taste perception [32,40]. However, the presence of ACE-2 receptor activity on cells taste buds are currently not fully understood, therefore, the specific role of SARS-CoV-2 in pathology and damage to certain taste receptor cells (receptor cells and supporting cells) requires further developments and studies [29, 31]. Was shown, that GPCR can be found in a wide variety of body tissues, not only in the oral cavity, but also in the epithelial cells of the lungs, blood-brain barrier and blood vessels [38].

It will be interesting to study the specific role of SARSCoV- 2 and GPCRs (G protein-coupled receptors) in terms of pathogenesis of COVID-19. On the other hand, COVID-19 causes salivary gland dysfunction leading to dry mouth and can lead to impaired taste perception [33]. The treatment proposed by some authors with artificial saliva may improve the loss of taste caused by xerostomia [21]. Quantitative olfactory testing demonstrates that a decrease in the function of smell is major marker of SARS-CoV-2 infection, and suggests that olfactory testing can predict not only the existence of COVID-19 in patients, but in some cases will help prevent the spread and aggression SARS-CoV-2 in the body. Summarizing the review, we can confidently say that absolutely a new direction in scientific research, with the identification features of damage to the structures of the oral cavity, related neurostomatological and some biochemical changes in saliva in COVID-19. Similar work will allow developing

diagnostic algorithms for early detection, prevention, treatment and rehabilitation of injuries oral cavity of its consequences in coronavirus infection, on the basis of which paths of optimal drug therapy.

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