

Primljen/ Received on: 23.08.2021.
Revidiran / Revised on: 30.08.2021.
Prihvaćen/ Accepted on: 13.09.2021.

INFORMATIVNI RAD
INFORMATIVE
ARTICLE
doi: 10.5937/asn2184334Z

ORALNE MANIFESTACIJE KOD PACIJENATA OBOLELIH OD KOVIDA-19

ORAL MANIFESTATIONS IN PATIENTS INFECTED WITH COVID-19

Emilija M. Živković Marinkov^{1,2}, Dušan R. Milisavljević^{1,2}, Milan D. Stanković^{1,2}, Gordana Lj. Filipović^{1,3}, Mila R. Bojanović^{1,2}, Nikola D. Nikolić², Snežana S. Babac^{4,5}

¹UNIVERZITET U NIŠU, MEDICINSKI FAKULTET

²KLINIK ZA OTORINOLARINGOLOGIJU, UNIVERZITETSKI KLINIČKI CENTAR NIŠ, SRBIJA

³KLINIK ZA DENTALNU MEDICINU, ORTOPEDIJA VILICA, NIŠ, SRBIJA

⁴KLINIK ZA OTORINOLARINGOLOGIJU, KLINIČKO BOLNIČKI CENTAR ZVEZDARA, BEOGRAD, SRBIJA

⁵UNIVERZITET U BEOGRADU, FAKULTET ZA SPECIJALNU EDUKACIJU I REHABILITACIJU

¹UNIVERSITY OF NIŠ, FACULTY OF MEDICINE

²CLINIC OF OTORHINOLARYNOLOGY, UNIVERSITY CLINICAL CENTER OF NIŠ, NIŠ, SERBIA

³DEPARTMENT OF ORTHODONTICS, DENTAL MEDICINE CLINIC, NIŠ, SERBIA

⁴CLINIC OF OTORHINOLARYNOLOGY, CLINICAL AND HOSPITAL CENTRE ZVEZDARA, BELGRADE, SERBIA

⁵UNIVERSITY OF BELGRADE, FACULTY OF SPECIAL EDUCATION AND REHABILITATION, BELGRADE

Sažetak

Uvod: Kod pacijenata obolelih od KOVID 19, se pored karakteristične kliničke slike respiratorne infekcije, mogu se dijagnostikovati i oralne manifestacije.

Cilj: Cilj rada je bio da se pregledom savremene literature sagleda zastupljenost promena u usnoj duplji odnosno prisustvo oralnih simptoma kod obolelih od KOVID-19, kako bi se ukazalo da oralne manifestacije mogu nastati usled virusne infekcije SARS-CoV-2.

Metode: Do relevantnih informacija koje su bitne za rad, došli smo pretragom dostupne elektronske baze podataka PubMed-a i Google Scholar.

Rezultati: Utvrđena je raznovrsna lokalizacija oralnih lezija kod obolelih od KOVID-19: sluzokoža jezika (dorzuma i bočne strane jezika), bukalna sluzokoža, tvrdo i meko nepce, unutrašnja strana usana i gingive. Najčešće su evidentirane ulceracije u različitim delovima usne duplje. Još uvek je kontraverzno pitanje da li su oralne lezije kod infekcije SARS-CoV-2 virusa nastale kao posledica primarnog dejstva samog virusa ili kao sekundarna manifestacija infekcije. Visoka zastupljenost receptora za angiotenzin-konvertujući enzim 2 na oralnim epitelnim ćelijama jezika i pljuvačnih žlezdi ukazuje da usna duplja može biti posebno podložna infekciji SARS-CoV-2. Disfunkcija čula ukusa je najčešći oralni simptom kod pacijenata obolelih od KOVID-19.

Zaključak: Oralne lezije, ksarostomija, poremećaji čula ukusa mogu se javiti kod pacijenata kod kojih je dijagnostikovana infekcija KOVID-19, zbog čega je bitno načiniti iscrpan intraoralni pregled da bi se utvrdile promene u usnoj duplji i primenila adekvatna terapija.

Cljučne reči: KOVID-19, SARS-CoV-2, oralne manifestacije, poremećaj ukusa

Corresponding author:

Emilija Živković – Marinkov, MD, PhD
Faculty of Medicine, University of Niš
dr Zoran Djindjića Blvd. 81, 18000 Niš,
E-mail: emilijazm@gmail.com

Abstract

Introduction: In addition to the characteristic clinical picture of respiratory infection, patients with COVID-19 can also be diagnosed with oral manifestations.

Aim: The aim of this study was to review current literature for the prevalence of changes in the oral cavity i.e., the presence of oral symptoms in patients with COVID-19, in order to indicate that oral manifestations may occur due to viral infection with SARS-CoV-2.

Methods: Important information relevant to the study was obtained by searching the available electronic PubMed and Google Scholar database.

Results: Oral lesions were found in different locations in patients with COVID-19: tongue mucosa (dorsum and lateral sides of the tongue), buccal mucosa, hard and soft palate, inner lip and gingiva. The most common were ulcerations in different parts of the oral cavity. It is still unclear whether oral lesions in SARS-CoV-2 virus infection were a consequence of the primary effect of the virus itself or a secondary manifestation of the infection. The high presence of angiotensin-converting enzyme 2 in oral epithelial cells of the tongue and salivary glands indicates that the oral cavity may be particularly susceptible to SARS-CoV-2 infection. Taste disorder is the most common oral symptom in patients with COVID-19.

Conclusion: Oral lesions, xerostomia, taste disorders can occur in patients diagnosed with COVID-19. Therefore, a comprehensive intraoral examination is necessary in order to determine changes in the oral cavity and apply proper treatment.

Key words: COVID-19, SARS-CoV-2, oral manifestations, taste disorders

2021 Faculty of Medicine in Niš. Clinic of Dentistry in Niš. All rights reserved / © 2021. Medicinski fakultet Niš. Klinika za stomatologiju Niš. Sva prava zadržana.

Uvod

Bolest KOVID-19 prvi put je registrovana krajem 2019. godine u Kini, a uzročnik je novi koronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2). Bolest se veoma brzo proširila na sve kontinente i Svetska zdravstvena organizacija (SZO) proglasila je globalnu pandemiju 11 marta 2020. godine. Virus se prenosi kapljičnim, kontaktnim putem i aerosolom, a dominantno je zahvaćen respiratorni sistem¹. Najčešći simptomi SARS-CoV-2 infekcije su: suvi kašalj, povišena telesna temperatura, problemi sa disanjem, bolovi u mišićima, nešto ređe se javljaju dijareje, glavobolje, hemoptizije, gubitak čula mirisa i ukusa^{2,3,4}. Do sada opisane kliničke manifestacije infekcije SARS-CoV-2 virusa su raznovrsne i kreću se od blage do vrlo teške kliničke slike. Procenjuje se da 80% obolelih imaju blagu kliničku sliku bez potrebe za hospitalizacijom, 15% bolesnika zahteva bolničko lečenje i primenu kiseonika, a kod 5 % obolelih je neophodno lečenje u jedinicama intenzivne nege uz respiracijsku potporu i mehaničku ventilaciju⁵. Kliničke studije ukazuju da su predisponirajući faktori za razvoj teže kliničke slike: uzrast (>65 godina), kardiovaskularne bolesti, dijabetes melitus, hipertenzija, hronična opstruktivna bolest pluća, pušenje cigareta, imunodeficijencija i maligna oboljenja².

Osnovni princip delovanja SARS-CoV-2 virusa zasniva se na vezivanju za receptore angiotenzin-konvertujući enzim 2 (ACE2), koji su široko rasprostranjeni u organizmu. ACE2 receptori su potvrđeni u različitim epitelnim ćelijama kože, sluzokože usne i nosne duplje, različitim endotelnim ćelijama. Princip po kome deluje SARS-CoV-2 virus zasniva se na izazivanju preterane imunološke reakcije, pri čemu dolazi do nastanka leukocitne oluje. Skoro istovremeno se javlja i citokinska oluja koja oslobađanjem proinflammatory hemo-kina, dovodi do proinflammatory kaskadne reakcije, što za posledicu ima aktivaciju koagulacije i stvaranje mikro-tromba⁶.

Introduction

COVID-19 disease was first recorded in China in late 2019 and the cause was the new coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2). The disease spread to all continents very quickly and the World Health Organization (WHO) declared a global pandemic on March 11, 2020. The virus is transmitted by droplets, contact and aerosols and it predominantly affects the respiratory system¹. The most common symptoms of SARS-CoV-2 infection are: dry cough, fever, breathing problems, muscle pain, whereas somewhat rare symptoms include diarrhea, headaches, hemoptysis, loss of smell and taste^{2,3,4}. The clinical manifestations of SARS-CoV-2 virus infection described so far are diverse and range from mild to very severe cases. It has been estimated that 80% of cases are mild and do not require hospitalization, 15% of patients require hospital treatment and oxygen therapy, and 5% of patients require treatment in the intensive care units with respiratory support and mechanical ventilation⁵. Clinical studies indicate that predisposing factors for the development of severe clinical picture include age (>65 years), cardiovascular diseases, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, smoking, immunodeficiency and malignancies².

The basic principle of action of SARS-CoV-2 virus is based on binding to angiotensin-converting enzyme 2 (ACE2) receptors, which are widely distributed in the body. ACE2 receptors have been confirmed in various cells of the skin, mucous membrane of the oral and nasal cavity, and various endothelial cells. The principle by which the SARS-CoV-2 virus works is based on causing an excessive immune response which triggers a leukocyte storm. Almost simultaneously, a cytokine storms occurs, which causes a release of proinflammatory chemokines thus provoking a proinflammatory cascade reaction the result of which is activation of coagulation and formation of microthrombi⁶.

Oralne manifestacije

Pored zahvaćenosti donjih respiratornih puteva, virus SARS-CoV-2 može dovesti do pojave simptoma infekcije gornjih disajnih puteva, pri čemu je prisutan bol u grlu, nazalna kongestija i sekrecija iz nosa. Evidentirano je da gubitak čula mirisa može biti prvi simptom infekcije KOVID-19, dok se još nisu razvili drugi simptomi, zbog toga otorinolaringolog može biti prvi lekar koji sagledava pacijente^{7,8}.

Podaci iz literature ukazuju da su kod pacijenata obolelih od KOVID 19 pored karakteristične kliničke slike respiratorne infekcije dijagnostikovane i oralne manifestacije⁹⁻¹¹. Neophodna su dalja ispitivanja da bi se utvrdilo da li su oralne lezije kod SARS-CoV-2 virusa nastale kao posledica primarnog dejstva samog virusa ili kao sekundarna manifestacija infekcije¹². U prilog činjenici da oralne manifestacije nastaju kao direktna posledica virusa je i to što je usna duplja prvo mesto kontakta sa SARS-CoV-2 virusom. Istraživanja ukazuju da veća prisutnost receptora za ACE2, u respiratornom tkivu i drugim organima, može da uslovi veću sklonost da se virus veže za te organe i dovede do njihovog oštećenja. To može da objasni nastanak disgeuzije i oralnih lezija kod pacijenata sa COVID-19, jer je utvrđena veća zastupljenost ACE2 u epitelnim ćelijama jezika i pljuvačnim žlezdama^{13,14}. Histopatološka istraživanja ukazala su da postoji sličnost između trombon oštećenih krvnih sudova usne duplje i pluća, što takođe govori u prilog primarnoj manifestaciji SARS-CoV-2 virusa^{6,15}. Sa druge strane oralne lezije mogu imati i sekundarni karakter, što ukazuje da nastaju kao: posledica terapije SARS-CoV-2 infekcije, usled primene imunosupresivne terapije koja predisponira nastanak sekundarnih bakterijskih infekcija, loše oralne higijene kao posledica intubacije⁶.

Oralne manifestacije virusom nisu česte, međutim, u odsustvu uobičajenih simptoma mogu ukazivati na početak SARS-CoV-2 infekcije. Posebnu pažnju treba posvetiti gubitku čula mirisa i ukusa, koje kod asimptomatskih pacijenata mogu biti jedini znak bolesti^{4,16}. Veća prevalencija oralnih lezija utvrđena je kod starije populacije pacijenata i kod prisustva teže kliničke slike, dok nije utvrđena predispozicija prema polu^{9,10}. Evidentirana je raznovrsna lokalizacija oralnih lezija nastalih kod obolelih od KOVID-19. Sluzokoža jezika, pre svega dorzuma i bočne strane jezika, ali i bukalna sluzokoža, tvrdo i meko nepce, unutrašnja strana usana i gingiva su samo neke od opisanih mesta oralnih manifestacija SARS-CoV-2 infekcije^{10,11}.

Oral manifestations

In addition to lower respiratory tract, SARS-CoV-2 virus can also cause infection of the upper respiratory tract, with symptoms such as sore throat, nasal congestion and nasal discharge. It has been documented that loss of smell may be the first symptom of COVID-19 infection, occurring before other symptoms, so an otorhinolaryngologist may be the first physician to examine patients^{7,8}.

Literature data indicate that in addition to the characteristic clinical picture of respiratory infection, COVID-19 patients were also diagnosed with oral manifestations⁹⁻¹¹. Further research is needed in order to determine whether oral lesions in SARS-CoV-2 virus are a consequence of the primary action of the virus itself or a secondary manifestation of the infection¹². The oral cavity is the first point of contact with the SARS-CoV-2 virus which supports the fact that oral manifestations are a direct consequence of the virus. Studies indicate that a higher presence of ACE2 receptors in the respiratory tissue and other organs may be the reason why there is a greater tendency of the virus to bind to these organs causing their damage. This may explain the development of dysgeusia and oral lesions in COVID-19 patients because of a higher presence of ACE2 receptors in the epithelial cells of the tongue and salivary glands^{13,14}. Histopathological studies have shown a similarity between thrombus-damaged blood vessels of the oral cavity and lungs, which also speaks in favor of the primary manifestation of the SARS-CoV-2 virus^{6,15}. On the other hand, oral lesions can also have a secondary character, which indicates that they occur as a consequence of SARS-CoV-2 infection treatment, due to immuno-suppressive treatment which predisposes to the development of secondary bacterial infections, poor oral hygiene and as a consequence of intubation⁶.

Oral manifestations of the virus are not frequent but in the absence of common symptoms, they may indicate the onset of SARS-CoV-2 infection. Special attention should be paid to the loss of smell and taste which may be the only signs of the disease in asymptomatic patients^{4,16}. A higher prevalence of oral lesions was found in older patient population and in patients with more severe clinical picture, whereas no predisposition was determined in relation to patients' sex^{9,10}. Different locations of oral lesions in COVID-19 patients have been reported.

Iranmanesh i sar.¹⁰ su analizom 35 radova o oralnim manifestacijama kod infekcije KOVID-19 utvrdili da je najčešća lokalizacija oralnih lezija na jeziku (38%), labijalnoj sluzokoži (26%) i nepcu (22%).

Opisani su različiti oblici oralnih lezija SARS-CoV-2 infekcije: eritematozni plak, ulceracije, vezikule, bule, petehije, mukozitis i deskvamativni gingivitis^{10,16}. Najčešće opisivane promene su u vidu solitarnih ili multiplih ulceracija¹¹. Vezikulobulozne lezije se često pojavljuju zajedno sa kožnim promenama, kao što su vezikule i petehije. Pojava eritroplakija i leukoplakija je uglavnom u korelaciji sa padom imunoloških odgovora organizma. Ređe se javljaju angina bulosa, reaktivacija herpes simpleks virusa tip 1, različite promene na gingivi, suvoća usne duplje, pojava bola i otoka jezika⁴.

Kod pacijenata evidentirana je velika distribucija vremena od dijagnoze KOVIDA-19 do pojave oralnih lezija i kreće se u rasponu od 4 do 90 dana¹⁷. Amorim Dos Santos i sar.¹² su u svom istraživanju utvrdili da kod blage kliničke slike oralne lezije se manifestuju pre ili u isto vreme sa početnim respiratornim simptomima, ali kod težih oblika kod kojih je potrebno bilničko lečenje i primena medikamentne terapije, lezije nastaju otprilike od 7 do 24 dana nakon pojave simptoma.

Još uvek nije dovoljno jasno koji je tačan patogenetski mehanizam nastanka suvoće usne šupljine, odnosno kserostomije kod obolelih pacijenata od KOVID-19. Pretpostavlja se da dolazi do smanjenog lučenja pljuvačke¹⁸. U brojnim prikazima slučaja pretpostavljena je korelacija između kserostomije i aftoznih promena¹¹. Pojedini autori su potvrdili da postoji i povezanost kserostomije sa disfunkcijom čula ukusa¹⁰.

Utvrđeno je da hiposekrecija pljuvačke može povećati rizik od infekcije SARS-CoV-2, jer je izmenjena zaštita oralne sluzokože koju ostvaruje pljuvačka. Usled hiposalivacije smanjena je fizička barijera u odnosu na viruse i time je povećana mogućnost adhezije i kolonizacije virusima. Takođe dolazi do smanjene produkcije antimikrobnih proteina i peptida¹⁸.

Prisustvo velike koncentracije ACE-2 u epitelnim ćelijama pljuvačnih žlezda, može biti razlog pojave infekcije i nastanka akutnog sialadenitisa, koji može usloviti i nastanak hroničnog sialadenitisa, kao i destrukciju žlezdanog tkiva usled dejstva zapaljenskog procesa^{19,20}.

Potrebno je naglasiti da oralne patološke promene kod pacijenata sa KOVIDOM-19 nisu uvek direktno uzrokovane infekcijom SARS-CoV-2, već mogu da nastanu kao jatrogene komplikacije tokom lečenja KOVID-19.

Some of the described locations of oral manifestations of SARS-CoV-2 infection include the mucous membrane of the tongue, primarily the dorsum and lateral sides of the tongue, as well as buccal mucosa, hard and soft palate, inner lip and gingiva^{10,11}. Iranmanesh et al.¹⁰ analyzed 35 studies on oral manifestations in COVID-19 infection and found that the most common location of oral lesions was the tip of the tongue (38%), labial mucosa (26%) and palate (22%).

Various forms of oral lesions of SARS-CoV-2 infection have been described: erythematous plaque, ulcerations, vesicles, bullae, petechiae, mucositis and desquamative gingivitis^{10,16}. The most commonly described changes were solitary or multiple ulcerations¹¹. Vesiculobullous lesions often appear with skin changes such as vesicles and petechiae. The occurrence of erythroplakia and leukoplakia is mainly correlated with a decrease in the body's immune response. Angina bullosa, reactivation of herpes simplex virus type 1, various changes in the gingiva, dryness of the oral cavity, pain and swelling of the tongue occur less frequently⁴.

A long time distribution from the COVID-19 diagnosis to the appearance of oral lesions has been reported and it ranges from 4 to 90 days¹⁷. Amorim Dos Santos et al.¹², found that in mild cases oral lesions developed before or at the same time as the initial respiratory symptoms but in severe cases that required hospitalization and medication treatment, the lesions occurred approximately 7 to 24 days after the onset of symptoms.

The precise pathogenetic mechanism of the dryness of the oral cavity, i.e., xerostomia in COVID-19 patients is still not completely clear. It is assumed that it is a consequence of decreased salivary flow¹⁸. Numerous case studies assume a correlation between xerostomia and aphthous changes¹¹. Some authors have also confirmed a correlation between xerostomia and taste disorder¹⁰.

It has been determined that hyposalivation of the saliva can increase the risk of SARS-CoV-2 because of the changes in the protection of the oral mucosa provided by saliva. Due to hyposalivation, the physical barrier against viruses is lowered whereby the possibility of adhesion and colonization by viruses is increased. There is also a reduced production of antimicrobial proteins and peptides¹⁸.

The presence of a high concentration of ACE-2 in the epithelial cells of the salivary glands can be the reason for the occurrence of infection and development of acute sialadenitis, which can also cause chronic sialadenitis as well as the destruction of glandular tissue due to the inflammatory process^{19,20}.

Usled produžene intubacije i primene drugih invazivnih postupaka, mogu da nastanu mehaničke traume i pojave oralnih lezija kod pacijenata^{21,22}. Utvrđeno je i da kao reakcija nakon primene određenih lekova mogu se javiti propratne promene u usnoj duplji²³. Kod pacijenata sa COVID-19 evidentirane su i oralne infekcije koje su ustvari oportunističke infekcije, koje se javljaju i kod drugih bolesti gde nastaje stečena imunodefijencija. Kandidijaza i herpes simpleks infekcije nisu direktno povezane sa patološkim procesima infekcije SARS-CoV-2²⁴⁻²⁶. U nastanku oralne kandidijaze kod obolelih od COVID-19, veliku ulogu ima imunokompromitovani status, kserostomija, primena kortikosteroida kod pacijenata sa teškom kliničkom slikom i korišćenje antibiotika kod koinfekcije i nastanka bakterijske pneumonije.

Neophodno je dalje ispitivanje patofiziološkog mehanizma promena u usnoj duplji. Odnosno potrebno je utvrditi da li je njihov nastanak uslovljen direktnim dejstvom virusne infekcije COVID-19, koinfekcije, reakcije na lekove, uticaj stresa ili nastaju kao jatrogene komplikacije⁹⁻¹¹.

Poremećaj ukusa

Prevalenca je disfunkcija čula ukusa je od 4,9% do 69,8% kod pacijenata obolelih od COVID-19²⁷. Poremećaji ukusa se češće javljaju kod žena, bele rase, praćeni su lakšom kliničkom slikom i boljom prognozom¹². S obzirom na afinitet, koji SARS-CoV-2 virus ispoljava ka nervnom tkivu, mirisni i gustatorni nervi nisu izuzetak. Iako tačna patogeneza poremećaja čula mirisa i ukusa nije u potpunosti razjašnjena, pretpostavlja se da uloga ACE-2 inhibitora, koji se posebno nalaze na jeziku, ima ključnu ulogu. Na početku infekcije COVID-19 se obično javlja anosmija i ageusija, što može pomoći u dijagnozi same bolesti. Faridi sar.⁴ su ukazalida ukoliko pacijenti sa SARS-CoV-2 infekcijom imaju i gustatorne i olfaktivne smetnje, poremećaj čula mirisa se smatra primarnim. Preko 95% disgeuzija u korelaciji je sa poremećajem čula mirisa. Do sada je u literaturi opisano malo slučajeva disgeuzija u odsustvu olfaktornih disfunkcija. Zato su potrebna dodatna istraživanja, koja bi dala važne podatke o samoj prirodi gustatornih poremećaja, lokalizaciji oštećenja, kao i pragu čula ukusa.

It should be emphasized that oral pathological changes in COVID-19 patients are not always directly caused by SARS-CoV-2 infection but can occur as iatrogenic complications during COVID-19 treatment. Mechanical trauma and oral lesions can occur in patients due to prolonged intubation and other invasive procedures^{21,22}. It has also been determined that accompanying changes in the oral cavity can appear as a reaction after the application of certain medications²³. COVID-19 patients can also develop opportunistic infections of the oral cavity which occur with other acquired immunodeficiency diseases. Candidiasis and herpes simplex infections are not directly related to the pathological processes of SARS-CoV-2 infection²⁴⁻²⁶. Immuno-compromised status, xerostomia, the use of corticosteroids in severe cases and the use of antibiotics in coinfection and bacterial pneumonia all play an important role in the development of oral candidiasis in COVID-19 patients.

Further research of the pathophysiological mechanism of changes in the oral cavity is necessary. In other words, it is necessary to determine whether their development is caused by direct action of the COVID-19 viral infection, coinfection, drug reactions, the effect of stress or if they occur as iatrogenic complications⁹⁻¹¹.

Taste disorder

The prevalence of taste disorders in COVID-19 patients ranges from 4.9% to 69.8%²⁷. Taste disorders are more common in Caucasian women and are accompanied by mild symptoms and better disease outcomes¹². Considering the affinity that SARS-CoV-2 exhibits towards the nervous tissue, the olfactory and gustatory nerves are no exception. Although the precise pathogenesis of the smell and taste disorders is not completely clear, it is assumed that ACE2 inhibitors, which are especially located on the tongue, play an important role. Anosmia and ageusia commonly occur at the onset of COVID-19 infection, which can help in the diagnosis of the disease itself. Farid et al.⁴ indicated that if SARS-CoV-2 patients have both gustatory and olfactory disorders, the olfactory disorder is considered primary. Over 95% of dysgeusia cases are correlated with olfactory disorders. So far, few cases of dysgeusia in the absence of olfactory disorders have been described in the literature. Therefore, additional research is needed in order to obtain important data on the very nature of gustatory disorders, location of damage as well as the threshold of the sense of taste.

Terapija

Tretman oralnih lezija kod pacijenata sa SARS-CoV-2 virusom, najviše zavisi od vrste i težine same lezije. U brojnim radovima naznačeno je da kod pacijenata sa blagom do umerenom kliničkom slikom, kao i kod asimptomatskih pacijenata nije primenjivana nikakva terapija. Kao glavni razlog navodi se sama priroda promena i njihova tendencija brze regresije. U slučajevima težih formi oralnih lezija najčešće primenjivani lekovi su antivirusici u kombinaciji sa antibioticima, antipireticima i analgeticima, ali je bitno multidisciplinarno sagledavanje pacijenta. Zbog antinflatoatnog efekta primenjuju se i kortikosteroidi i antihistaminici. Prisustvo bola, hiperemije i edema oralne sluzokože mogu otežati ishranu i govor pacijenta, zbog čega je potrebno pored sistemske terapije uključiti i lokalnu terapiju odnosno anti-septike, antimikotike, obezbediti adekvatnu ishranu i sprovesti oralnu higijenu^{28,29}.

Zaključak

Ulceracije oralne sluzokože, ksero-stomija, disfunkcija čula ukusa mogu se javiti kod pacijenata kod kojih je dijagnostikovana infekcija KOVID-19 zbog čega je bitno načiniti iscrpan intraoralni pregled da bi se utvrdile promene u usnoj duplji i primenila adekvatna terapija. Pored toga značajna je i adekvatna oralna higijena pacijenata sa KOVID-19 jer ona može znatno uticati na pogoršanje simptoma oralnih lezija.

Treatment

The treatment of oral lesions in SARS-CoV-2 patients mostly depends on the type and severity of the lesion itself. Numerous studies have indicated that no treatment was applied in mild to moderate cases as well as asymptomatic cases. The main reason is the nature of the changes and their tendency to regress rapidly. In severe forms of oral lesions, the most commonly applied medications were antivirals in combination with antibiotics, antipyretics and analgesics but a multi-disciplinary examination of patients is also important. Due to their anti-inflammatory effect, corticosteroids and antihistamines are also used. The presence of pain, hyperemia and edema of the oral mucosa can make nutrition and speech more difficult for patients, which is why it is necessary to include local therapy in addition to systemic therapy i.e., antiseptics, antifungals, to provide adequate nutrition and implement appropriate oral hygiene^{28,29}.

Conclusion

Ulcerations of the oral mucosa, xerostomia, and taste disorders can occur in patients diagnosed with COVID-19 and a comprehensive intraoral examination is therefore necessary in order to determine the changes in the oral cavity and apply proper treatment. In addition, appropriate oral hygiene of COVID-19 patients is also important as it may have a significant impact on the worsening of symptoms of oral lesions.

LITERATURA / REFERENCES

1. World Health Organization. Coronavirus Disease (COVID-19) Advice For The Public. Geneva: World Health Organization (2020a).
2. Salian VS, Wright JA, Vedell PT, et al. COVID-19 Transmission, Current Treatment, and Future Therapeutic Strategies. *Mol Pharm* 2021;18(3):754-71
3. Burić N, Stojanović S. Occupational hazard for Dental staff exposed to the SARS-CoV-2 virus during Dental procedures. *Acta Stom Naissi*2020;36(81): 2051-62.
4. Farid H, Khan M, Jamal S, Ghafoor R. Oral manifestations of Covid-19-A literature review. *Rev Med Virol* 2021; 24:e2248
5. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report – 56. Geneva: World Health Organization (2020b).
6. Etemad-Moghadam S, Alaeddini M. Is SARS-CoV-2 an Etiologic Agent or Predisposing Factor for Oral Lesions in COVID-19 Patients? A Concise Review of Reported Cases in the Literature. *Int J Dent* 2021:6648082.
7. El-Anwar MW, Elzayat S, Fouad YA. ENT manifestation in COVID-19 patients. *Auris Nasus Larynx* 2020; 47(4):559-64.
8. Lovato A, de Filippis C. Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms. *Ear Nose Throat J* 2020;99(9):569-76.
9. Riad A, Klugar M, Krsek M. COVID-19-Related Oral Manifestations: Early Disease Features? *Oral Dis* 2020; 13516
10. Iranmanesh B, Khalili M, Amiri R, Zartab H, Aflatoonian M. Oral manifestations of COVID-19 disease: A review article. *Dermatol Ther* 2021;34(1):e14578.
11. Aragonese J, Suárez A, Algar J, Rodríguez C, López-Valverde N, Aragonese JM. Oral Manifestations of COVID-19: Updated Systematic Review With Meta-Analysis. *Front Med (Lausanne)* 2021; 8:726753.
12. Amorim Dos Santos J, Normando AGC, Carvalho da Silva RL, Acevedo AC, De Luca Canto G, Sugaya N, Santos-Silva AR, Guerra ENS. Oral Manifestations in Patients with COVID-19: A Living Systematic Review. *J Dent Res* 2021; 100(2):141-54
13. Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 2020; 12(1):8.
14. Dziedzic A, Wojtyczka R. The impact of coronavirus infectious disease 19 (COVID-19) on oral health. *Oral Dis* 2021; 27 (Suppl 3):703-6
15. Soares CD, Carvalho RA, Carvalho KA, Carvalho MG, Almeida OP. Letter to Editor: Oral lesions in a patient with Covid-19. *Med Oral Patol Oral Cir Bucal* 2020; 25(4):e563-e564
16. Bhujel N, Zaheer K, Singh RP. Oral mucosal lesions in patients with COVID-19: a systematic review [published online ahead of print, 2021 Jun 25]. *Br J Oral Maxillofac Surg* 2021; S0266-4356(21)00243-6.
17. La Rosa GRM, Libra M, De Pasquale R, Ferlito S, Pedullà E. Association of Viral Infections With Oral Cavity Lesions: Role of SARS-CoV-2 Infection. *Front Med (Lausanne)*2021;7:571214
18. Farshidfar N, Hamedani S. Hyposalivation as a potential risk for SARS-CoV-2 infection: Inhibitory role of saliva. *Oral Dis* 2021; 27 (Suppl 3):750-1
19. Tsuchiya H. Oral Symptoms Associated with COVID-19 and Their Pathogenic Mechanisms: A Literature Review. *Dent J (Basel)* 2021;9(3):32.
20. Wang C, Wu H, Ding X, Ji H, Jiao P, Song H, Li S, Du H. Does infection of 2019 novel coronavirus cause acute and/or chronic sialadenitis? *Med Hypotheses* 2020; 24(140) :109789.
21. Ramires MCCH, Mattia MB, Tateno RY, Palma LF, Campos L. A combination of phototherapy modalities for extensive lip lesions in a patient with SARS-CoV-2 infection. *Photodiagnosis Photodyn Ther* 2021; 33:102196.
22. Singh C, Tay J, Shojirat N. Skin and Mucosal Damage in Patients Diagnosed With COVID-19: A Case Report. *J Wound Ostomy Continence Nurs* 2020; 47(5):435-438.
23. Sakaida T, Tanimoto I, Matsubara A, Nakamura M, Morita A. Unique skin manifestations of COVID-19: is drug eruption specific to COVID-19? *J Dermatol Sci* 2020; 99:62–4.
24. Riad A, Gad A, Hockova B, Klugar M. Oral Candidiasis in Non-Severe COVID-19 Patients: Call for Antibiotic Stewardship. *Oral Surg* 2020; 10.1111/ors.12561.
25. Salehi M, Ahmadikia K, Badali H, Khodavaisy S. Opportunistic fungal infections in the epidemic area of COVID-19: a clinical and diagnostic perspective from Iran. *Mycopathologia* 2020; 185:607–11.
26. Kitakawa D, Oliveira FE, Neves de Castro P, Carvalho L. Short report – Herpes simplex lesion in the lip semimucosa in a COVID-19 patient. *Eur Rev Med Pharmacol Sci* 2020; 24:9151–3.
27. Vaira LA, Hopkins C, Salzano G, et al. Olfactory and gustatory function impairment in COVID-19 patients: Italian objective multicenter-study. *Head Neck* 2020; 42(7):1560-9.
28. Eghbali Zarch R, Hosseinzadeh P. COVID-19 from the perspective of dentists: A case report and brief review of more than 170 cases. *Dermatol Ther* 2021; 34(1):e14717.
29. Irmadani Anwar A, Ayu A, Yusriyanti Yusu M, Zulkifli Abdullah A, Ruslin M. Oral health knowledge, attitude and practice among people in monitoring during COVID-19 pandemic in Makassar. *Acta Stom Naissi* 2021; 37(83):2158-67