

Loss of Taste, Smell and Oral Manifestations in COVID-19

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1. Abstract

COVID 19 mainly affects the respiratory, gastrointestinal and neurological systems but it also involves the oral cavity, olfactory and integumentary system. The oral manifestations of COVID 19 along with inflammatory response of surrounding tissues are due to angiotensin converting enzymes (ACE 2) and Trans membrane serine protease (TMPRSS 2). ACE 2 and TMPRSS 2 play a key role in virus transmission through saliva and shows its expression in the salivary glands, oral mucosal epithelium. The reported oral manifestation of COVID 19 are Xerostomia, loss of taste, smell, COVID tongue, halitosis and mucosal lesions. The exact mechanism how these structures are involved are not known that whether these manifestations are the result of direct infection or secondary manifestations. This review will discuss the oral manifestations of COVID 19 along with its possible mechanism.

2. Introduction

SARS-CoV-2 is a pandemic infectious disease threatening the World today [1] having many clinical manifestations such as fever, dry cough, viral pneumonia, shortness of breath, myalgia, headache, sore throat, rhinorrhea, chest pain, nausea, vomiting and diarrhea, conjunctiva, nasal congestion, fatigue, Hemoptysis, chill, loss of taste and smell. SARS-CoV-2 can infect the mouth, raising the possibility that saliva can play a major role in the transmission of virus. Thus oral cavity is important site for SARS-CoV-2 [2, 3]. The researchers hypothesized that salivary glands, barrier epithelial cells of the oral cavity and oropharynx can be infected by SARS-

CoV-2 contributing to the spread of the infection. Two human oral single –cell RNA sequencing (ScRNA – seq) atlases to predict cell specific susceptibilities to SARS-CoV-2 infection. RNA or two key viral entry proteins the ACE2 and TMPRSS2 are found in the salivary gland and lining of the oral cavity plus in gingival cells indicating higher vulnerability to SARS-CoV-2 infection. There is correlation between oral symptoms and saliva containing SARS-CoV-2 suggesting oral infection may play a role in COVID 19 oral symptoms [4, 5].

Thus mouth is considered as prime site for COVID 19 infection even before symptoms and the occurrence of loss of taste (aguesia) and loss of smell occur in many patients. These oral lesions due to COVID 19 occur in both gender approximately 52 years of age. The ulcerated lesions are most common may be erosions, petechial, macules and blisters. The main site is palate and the tongue followed by gums and the lips. There is Orofacial pain in 75% cases while taste alterations occur in 25% of the reported cases. The exact etiology of these manifestations are unknown but may be multifactorial it may be due to direct or indirect action of SARS-CoV-2 over oral mucosa to cells to the hypersensitivity of drugs used in the treatment of COVID 19 or general state of health of patient due to disease or to long period of hospitalization. Oral manifestations due to hypersensitivity reactions of drugs are not unknown in case of COVID 19 but may be due to the cytokines storm [6].

Saliva is a common transient medium for transmitting virus by

breathing, talking and sneezing by droplets. It can pass on the infection this indicates that saliva as a potential route of SARS-CoV-2 transmission and can be used for diagnosis of COVID 19 - a reliable tool to detection of SARS-COV-2 [7]. The COVID 19 also migrates from the naso pharynx to the lower respiratory tract to the oral cavity but it can't be excluded that a role may be played by the secretory activity of salivary gland. As There is high expression of ACE2 receptors of 2019-n COV on the epithelial cells of oral mucosa with high tendency on tongue (13 times) this ACE2 expressing cells in oral tissues especially in epithelial cells of tongue than mucosal and gingival tissues might pass vide possible route of entering for 2019-n-COV which proves that oral cavity might be potential risk route of 2019-n-COV [8].

There appear many oral manifestations in Corona patients which may be due to predisposing factors such as poor oral hygiene, stress, opportunistic infection, immunosuppression, vasculitis, hyper inflammatory response secondary to COVID 19. There is oral dryness, Vesiculo bullous lesions, Aphthous like ulceration, Dysgnesia and anosmia [9]. The main stimulants of taste are saliva formation Xerostomia may be caused in nasal congestion and rhinorrhea which lead to dysgnesia [10]. Xerostomia also contributes to burning mouth syndrome.

The Corona patients also complain of fore head pain which is explained by patients as inability to differentiate between facial pain and headache. It is due to nasal congestion which occurs in URTI as result of dilatation of veins in the nasal epithelium with added secretion s in the sinuses which puts pressure in trigeminal nerves endings causing pain. The bruxism due to stress and psycho emotional status in COVID 19 result in TMD symptoms with Orofacial pain [11].

There are taste buds widely distributed in the oral cavity containing taste receptors but mainly concentrated in the papilla on the dorsum of tongue with ACE2 which are diffusely expressed on the mucous membrane of the whole oral membrane [12]. There are ACE2 receptors on the tongue to which SARS-Cov-2 binds as compared to buccal and gingival tissues of oral cavity in order to gain entry into host cells/highly expressed in the epithelial cells of tongue hence it could be possible reason for taste disturbance in all viral infections including COVID 19 infection [13]. The Taste loss can occur due to damage of taste pores because of the destruction of taste buds.

Loss of taste can be due to damage of neural pathway innervating the taste buds subsequent to viral infection in the oral cavity as the cranial nerve V11,IX an X which transmit information from mouth and pharynx to brain are involved .Taste loss can occur due to damage of taste pores because of the destruction or loss of taste buds .Corona virus binds to their target cell through angiotensin converting enzyme 2(ACE2) which are also expressed by epithelial cells of the lungs ,intestine, Kidneys ,blood vessels so affecting these systems of the body The enzyme TMPRSS (trans membrane

protease ,serine2)allows the virus to fuse to membrane with that of host cell and slip inside [14].

The general health state of the COVID 19 patients are degraded which predisposes the appearance of oral manifestations. The patients are hospitalized and different procedures are performed the opportunist infections such as thrush and herpes so oral care hygiene is important in hospitalization.

The Oral lesions in diagnosis of COVID 19 are controversial. Taste alterations may be considered most relevant oral manifestations off COVID 19. Oral lesions due to COVID 19 occur in both genders approximately 52 years of age. (2, 15) The ulcerated lesions are most common which may be erosions, petechial, macules and blisters. The main site is palate and tongue followed by gums and the lips. There is pain in 75% while taste alterations in 25% of reported cases.

The mostly reported five oral manifestations associated with COVID 19 are as under:

1. Gingival inflammation. This is due to cytokine storm particularly interleukin 6 (IL 6)
2. Xerostomia (Dry mouth) There are many causes of Xerostomia such as auto immune diseases drugs, viral infection and now COVID 19. Xerostomia may cause oral ulceration, halitosis caries and fungal infection, candidiasis. The quantity and quality of salivary flow is decreased in corona due to viral entry into salivary gland [16].
3. COVID Tongue

The association between erythema migrans (Geographic tongue) and SARS-CoV-2 is termed as COVID tongue [17]. Geographic tongue is a benign condition which has positive association between SARS-CoV-2. In COVID tongue there is swelling with bumps on the left side and swelling with patchy red spot on the right side of tongue. COOVID tongue is the result of inflamed disease ACE2 receptors enzymes that act as point of entry for SARS-CoV-2 AND exist in large number on the tongue and mucous membrane o mouth resulting in swelling, bumps and patchiness associated with COVID tongue [18]. The other theory is corona virus causes inflammation of blood vessels and the virus is messing with blood vessels in the tongue and mouth resulting in COVID tongue so much research is needed.

The COVID tongue has two types of symptoms: Patient may complain of discoloration, enlargement and other mouth problems "Furry coating" can be white or yellow cannot be scrubbed of with brush, Scalloped tongue which is painful; the other group had inflammation of small bumps on tongue surface which may be swollen and inflamed, mouth ulcers and patchy area on tongue and swelling in mouth [19, 20].

4. Cracked teeth There is increase in bruxism due to stress sleep deprivation or obstructive sleep apnea result in cracked teeth and bruxism with TMD and Orofacial pain [21, 22].

5. Loss of taste and smell which observed in many patients with COVID 19 but not clear that these manifestations are due to Covid 19 or secondary manifestations due to patients systemic conditions.

ACE2 receptors which are diffusely expressed on the mucous membrane of the whole oral cavity particularly on the tongue. The role of ACE2 in modulating taste perception due to chemo sensitive side effects of ACE2 inhibitors and angiotensin II blockers.

There is reduction in sialic acid in saliva which is a fundamental component of salivary mucin and its glycoproteins that convey gustatory molecule inside taste pore from premature enzyme degradation, so there is an increase gustatory threshold, SARS-CoV-2 occupy the binding sites of sialic acid on taste buds accelerating degradation of gustatory particles plus olfactory disturbances. Viral disruption of cranial nerves 1,7,9 and 10 as well as the supporting cells of neural transmission [23].

The inflammation can induce expression of ACE2 in human cells not neuron might under represent the cells types that express ACE2 under CoV-2 INFECTION Abundance of ACE2 receptor direct.

3. Anosmia (Loss of Smell)

The loss of smell result from diseases which causes the disease of pathways which transmit smell to the brain by use of drugs as decongestants, nasal sprays, nifedipine and prothiazines. There is close relationship between taste and smell as olfactory sensory neurons, sensory cells detect odors and these neurons are present in nasal lining. The infection or swelling of these blockage prevent odor messages to the brain. The ability to taste food is tiedly connected to sense of smell so there is loss of taste [24, 25]. The tongue is the not only an organ involved in taste but throat, roof of mouth and nose. Loss of taste also occur in upper respiratory tract such as common cold, sinus infection, middle ear infection, poor oral hygiene, anti-fungal drugs, macrolides, proton pump inhibitors, ACE etc also affect the person ability to taste.

Taste disturbances mainly occur in oral infection, oral appliance such as dentures, bell's palsy and old age. It is an early warning system against toxins, polluted air, smoke and spoiled food products. It has significant impact on quality of life. Taste receptors are in taste buds not only on the tongue but also on the soft palate, pharynx, epiglottis, uvula and first one third of esophagus. These are bathed by salivary gland and dryness distort perception.

The exact etiology or loss of smell is unknown the damage of olfactory system is either due to primary infection or secondary inflammation. It is possible that cells infected with COV-2 can form syncytia with cells that do not express the ACE2 such a mechanism can damage neuron adjacent to infected cells. The inflammation can induce expression of expression of ACE2 in human cells so stem cells not neurons might under represent the cells types that express ACE2 under COV-2 [26].

4. Conclusion

Loss of taste and smell is first recognized symptom of COVID 19 but most common oral symptoms are on the tongue, aphthous like ulcers, herpetic form lesions, Xerostomia and candidiasis which occur in old people either due to previous underlying disease stress, trauma, hyper inflammatory response of COVID 19 or drug allergy which may be aggravating factor in the development of oral lesions.

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