



Review Article

Effect of chlorhexidine on covid 19 virus

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ABSTRACT

High generation of aerosols, and the presence of SARS-CoV-2 in saliva have suggested oral cavity as a reservoir for COVID-19 transmission. COVID-19 can penetrate the human body. The transmission can occur during coughing, sneezing, talking and even during dental care. SARS-CoV-2 is an enveloped virus, characterized by an outer lipid membrane. It has been seen that preprocedural rinses with mouthwash reduces the viral load. Chlorhexidine gluconate has been used in the clinical practice since ages. It is a broad spectrum antimicrobial agent, causing destruction of cellular membranes. It acts against gram positive and gram negative bacteria, aerobes, facultative anaerobes and fungus. It is also seen to be effective against viruses. Therefore, this review focuses on the role of chlorhexidine in COVID-19.

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1. Introduction

The microorganism found in the oral cavity have been referred to as the oral microbiome. The term microbiome was coined by Joshua Lederberg. This signifies the ecological community of commensal, symbiotic and pathogenic microorganism that share the body space. The oral cavity includes several microbial habitats. These include the teeth, gingival sulcus, attached gingiva, tongue, cheek, lip, hard palate and soft palate. Therefore, the oral cavity is the major gateway to the human body.¹

The hazards to which the dental clinicians are exposed in the dental office includes pathogenic microorganism (viruses, bacteria and fungi). Microorganisms can spread easily in the closed spaces. During any dental procedure, microorganism can be transferred from the patient's oral cavity onto the doctor and other way round. In dental office, the routes of spreading biological factors include blood borne route, direct contact with the patient and contamination of instruments and through emission of aerosols.²

Aerosols are liquid or solid units that remains in air for a longer period of time.³ These aerosols which are produced from the working handpiece are of serious concern to the dentist as it contains saliva with microorganisms that come from the oral cavity and the respiratory tract of the patient. Procedures performed with these handpieces may introduce bacteria present in the oral cavity of the patient to their blood and lymphatics leading to bacteremia.²

In late 2019, there was a sudden outbreak of COVID-19 virus producing widespread complications.⁴ COVID-19 belongs to coronavirus family. Only α and β family coronaviruses can infect humans, and COVID-19 is from β family coronaviruses.⁵ The transmission of COVID-19 happens due to close interaction with an ill person, exposure to coughing, sneezing and airborne particles.⁶

Saliva plays a key role in the transmission of COVID-19 through infected droplets.⁷ Aerosols carrying the virus can penetrate the human respiratory system during normal breathing and can cause COVID-19 disease.⁸

One of the way to decrease viral load in dental atmosphere is with usage of mouthwashes earlier to the treatment.⁹

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2. Pathogenesis of Coronavirus Disease 2019

Coronaviruses are a group of enveloped RNA viruses. It has a typical structure with the spike protein in its membrane envelope.¹⁰ The interaction of the virus protein and angiotensin-converting enzyme 2 (ACE-2) receptor makes it possible for the virus to enter the cell.¹¹ The distribution of ACE-2 receptor in different parts of the body may indicate possible routes of infection. The ACE-2 receptor of epithelial cells of the salivary glands is the chief target of the COVID-19 virus. This receptor is found in abundance in tongue, representing a high chance of infection in the oral cavity.¹²

After the contamination with SARS-CoV-2 genome host cell starts innate and adaptive immune response which characterizes the first line of defence against the viral infection. The innate immune response is activated by interferon (IFN) type I. Also, Th1 mediated immune response plays a predominant role in adaptive immunity against viral infections. Cytokine storm that is high levels of chemokines and plasma cytokines like interleukins (IL) are also seen in the COVID-19 patients. This cytokine storm leads to the viral sepsis which is followed by lung injury brought by inflammation. Severity of the disease in patient is related with noticeable reduction in the amount of circulating B cells, CD8+ cells, CD4+ cells, natural killer cells as well as reduction in eosinophils, monocytes and basophils. (Figure 1)¹³

A high SARS-CoV-2 viral load is seen in saliva and as well as periodontal pockets.^{14,15} These findings suggest oral cavity to be a reservoir for transmission of SARS-Cov-2.

3. Chlorhexidine

Chlorhexidine gluconate, a biguanide compound, has been used in the clinical practice since ages. It is a broad spectrum antimicrobial agent, causing destruction of cellular membranes.¹⁶ It acts against gram positive and gram negative bacteria, aerobes, facultative anaerobes and fungus.

The antiplaque effect of chlorhexidine makes it a gold standard and can be attributed to its substantivity. Substantivity can be defined as an ability of an agent to adhere to soft and hard tissues and then be released over the time with retention of potency. The antibacterial effect of chlorhexidine can be explained by its superior persistence at the tooth and the mucosal surface.¹⁷

3.1. Antimicrobial activity

At low concentration chlorhexidine causes displacement of calcium and magnesium and loss of potassium for the cell wall, resulting in a bacteriostatic effect.¹⁸ At high concentrations chlorhexidine causes leakage of all the intercellular components out of the cell resulting in cell lysis and death.¹⁹ The antiviral effect of chlorhexidine is also due to altered cell membrane permeability and also it can

inactivate enveloped viruses.²⁰

3.2. Uses

1. Management of oral hygiene.
2. Management of gingivitis, periodontitis and peri-implantitis.
3. Irrigant in root canal therapy.
4. Pre rinse to reduce aerosolisation of microbes during dental procedure.

3.3. Oral hygiene

Chlorhexidine can be used as a mouthwash in reducing the amount of plaque on teeth.²¹ Along with mouthwash, mechanical toothbrushing and interdental cleaning aids are the preferred method for the effective plaque removal.

3.4. Gingivitis and periodontitis

Gingivitis is a gum disease whereas periodontitis is an inflammatory condition characterized by loss of attachment apparatus leading to bone loss and eventually tooth loss. The most significant levels of disease involve gram negative anaerobic species.²² For established periodontitis chlorhexidine mouthrinses for a specific limited period of time must be employed alongside mechanical measures.²³

3.5. Peri-implantitis

3.6. Irrigant in root canal therapy

Irreversible pulpitis and periapical periodontitis are caused by bacteria entering the root canal system.²⁴ Gram positive *Enterococcus faecalis*, is a most resistant bacteria to disinfection and unresolved periapical infection. 0.2% of chlorhexidine for whole mouth oral disinfection can be used as an adjunct to healing of perio-endo lesions after RCT is completed.²⁵

3.7. Preprocedural mouthwash in dental setting

Dental procedures such as high-speed drill and ultrasonic scalers, microorganisms can aerosolise and splatter upto 6 feet away from the dental chair.²⁶ It has been found that preprocedural rinse with mouthwash can lessen dentally produced aerosolisation of viral microorganisms.²⁷ 0.2% chlorhexidine reduces the number of colony forming units (CFUs) of bacteria produced due to ultrasonic scaling.²⁸

3.8. Side effects

Chlorhexidine with its advantages also has some side effects which include tooth staining, dry mouth, altered taste sensations and discoloured or coated tongue.²⁹ The other less common side effects include burning sensation, desquamation of the oral mucosa, swelling of the parotid

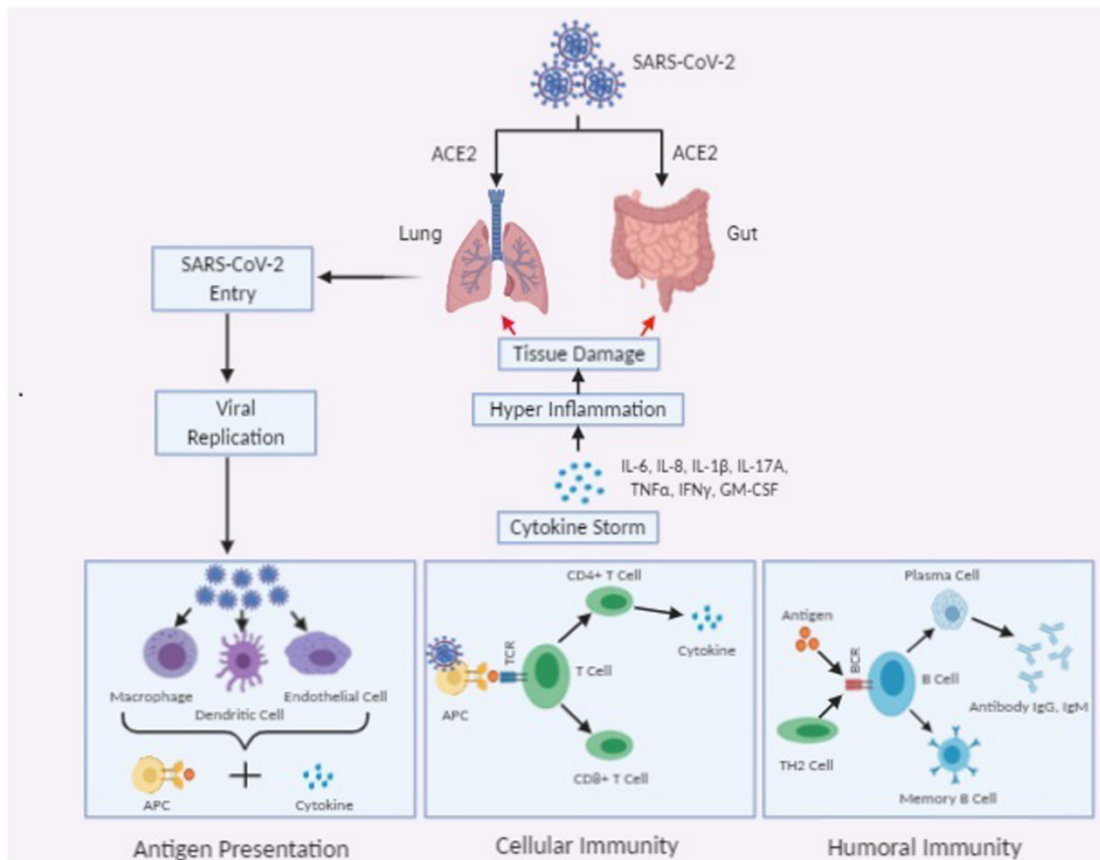


Fig. 1:

gland and oral paraesthesia.³⁰ The reason for tooth staining after beyond the specified time period is due to non-enzymatic browning (Maillard reaction) and production of the pigmented metal sulphide formation in the pellicle.³¹

4. Importance of Chlorhexidine against Covid-19

Chlorhexidine is more effective against enveloped than non-enveloped viruses.³² Yoon et al¹⁰ concluded the suppression of SARS-CoV-2 for two hours after using 15ml 0.12% chlorhexidine once. Therefore its use will be beneficial for the control of COVID-19 transmission.

It is seen that patients with lung infections have different oral flora and when these patients are exposed to infective microorganism leads to alteration in the patients's systemic symptoms. Efforts to reinstate the normal flora in patients with lung infections decrease the systemic complications of the disease and hasten the recovery course.³³ Use of chlorhexidine in COVID-19 patients with different oral flora, reduces the symptoms in these patients.⁵ Likewise, in critically ill patients, it has been found that chlorhexidine mouthwash or gel can assist to cut the rate of ventilator associated pneumonia from 24% to about 18%.³⁴ Use of chlorhexidine ensures superior care of caregivers and staff in

the health care organization and who are in direct interaction with these patients.³⁵

5. Conclusion

The effect of occurrence and progression of SARS-CoV-2 on the interaction among the virus and the individual's immune system. The various viral factors include virus category, mutation, viral load, viral titer and viability of the virus in vitro. The individual's immune factors include genetics, age, gender, nutritional status. All these factors play important role in the infection with the virus, the duration and severity of disease. This brief review suggests that use of preprocedural rinse in dental clinics reduces SARS-CoV-2 viral load from previous dental procedure and reduces the cross infection risk while treating patients during the pandemic. Also, need for proper hand hygiene, personal protective equipment (PPE) and protective measures in the aerosol production, should be considered.

6. Source of Funding

None.


7. Conflict of Interest

The authors declare that there is no conflict of interest.

References

- Dewhirst FE, Chen T, Izard J, Paster BJ, Tanner ACR, Yu WH, et al. The Human Oral Microbiome. *J Bacteriol.* 2010;192(19):5002–17. doi:10.1128/jb.00542-10.
- Szymanska J, Sitkowska J. Bacterial hazards in a dental office: An update review. *Afr J Microbiol Res.* 2012;6(8):1642–50.
- Jayaweera M, Perera H, Gunawardana B, Manatunge J. Transmission of COVID-19 virus by droplets and aerosols: A critical review on the unresolved dichotomy. *Environ Res.* 2020;188:109819. doi:10.1016/j.envres.2020.109819.
- Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Emergence, transmission, and characteristics of human coronaviruses. *J Adv Res.* 2020;24:91–8. doi:10.1016/j.jare.2020.03.005.
- Moosavia MS, Aminishakibb P, Ansari M. Antiviral mouthwashes: possible benefit for COVID-19 with evidence-based approach. *J Oral Microbiol.* 2020;12:1794363.
- Li Q, Guan X, Wu P. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med.* 2020;382:1199–1207.
- Yan J, Grantham M, Pantelic J. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc Natl Acad Sci.* 2018;115(5):1081–6.
- Schroter RC. Social distancing for covid-19: is 2 metres far enough? *BMJ.* 2020;369:m2010. doi:10.1136/bmj.m2010.
- Wirthlin MR, Marshall GW. Evaluation of Ultrasonic Scaling Unit Waterline Contamination After Use of Chlorine Dioxide Mouthrinse Lavage. *J Periodontol.* 2001;72(3):401–10. doi:10.1902/jop.2001.72.3.401.
- Yoon JG, Yoon J, Song JY. Clinical significance of a high SARS-CoV-2 viral load in the saliva. *J Korean Med Sci.* 2020;35:195.
- Chen Y, Guo Y, Pan Y. Structure analysis of the receptor binding of 2019-nCoV. *Biochem Biophys Res Commun.* 2020;525:135–40.
- Vinayachandran D, Balasubramanian S. Salivary diagnostics in COVID-19: Future research implications. *J Dent Sci.* 2020;15(3):364–6. doi:10.1016/j.jds.2020.04.006.
- Chatterjee SK, Saha S, Munoz MNM. Molecular Pathogenesis, Immunopathogenesis and Novel Therapeutic Strategy Against COVID-19. *Front Mol Biosci.* 2020;7:196. doi:10.3389/fmolb.2020.00196.
- Li Y, Ren B, Peng X. Saliva is a non-negligible factor in the spread of COVID-19. *Mol Oral Microbiol.* 2020;35:141–5.
- Badran Z, Gaudin A, Struillou X, Amador G, Soueidan A. Periodontal pockets: A potential reservoir for SARS-CoV-2? *Med Hypotheses.* 2020;143:109907. doi:10.1016/j.mehy.2020.109907.
- Gilbert P, Moore LE. Cationic antiseptics: diversity of action under a common epithet. *J Appl Microbiol.* 2005;99(4):703–15. doi:10.1111/j.1365-2672.2005.02664.x.
- Mathur S, Mathur T, Srivastava R, Khatri R. Chlorhexidine: The gold standard in chemical plaque control. *Nat J Physiol Pharm Pharmacol.* 2011;1(2):45–50.
- Cieplik F, Jakubovics NS, Buchalla W, Maisch T, Hellwig E, Al-Ahmad A. Resistance Toward Chlorhexidine in Oral Bacteria – Is There Cause for Concern? *Front Microbiol.* 2019;10:587. doi:10.3389/fmicb.2019.00587.
- Wood A, Payne D. The action of three antiseptics/disinfectants against enveloped and non-enveloped viruses. *J Hosp Infect.* 1998;38(4):283–95. doi:10.1016/s0195-6701(98)90077-9.
- McDonnell G, Russell AD. Antiseptics and Disinfectants: Activity, Action, and Resistance. *Clin Microbiol Rev.* 1999;12(1):147–79. doi:10.1128/cmr.12.1.147.
- James P, Worthington HV, Parnell C, Harding M, Lamont T, Cheung A, et al. Chlorhexidine mouthrinse as an adjunctive treatment for gingival health. *Cochrane Database Syst Rev.* 2017;3:8676. doi:10.1002/14651858.cd008676.pub2.
- Bartold PM, Dyke TEV. An appraisal of the role of specific bacteria in the initial pathogenesis of periodontitis. *J Clin Periodontol.* 2019;46(1):6–11. doi:10.1111/jcpe.13046.
- Herrera D, Alonso B, León R, Roldán S, Sanz M. Antimicrobial therapy in periodontitis: the use of systemic antimicrobials against the subgingival biofilm. *J Clin Periodontol.* 2008;35:45–66. doi:10.1111/j.1600-051x.2008.01260.x.
- Wang Z, Shen Y, Haapasalo M. Effectiveness of Endodontic Disinfecting Solutions against Young and Old Enterococcus faecalis Biofilms in Dentin Canals. *J Endod.* 2012;38(10):1376–9. doi:10.1016/j.joen.2012.06.035.
- Haapasalo M, Shen Y, Wang Z, Gao Y. Irrigation in endodontics. *Br Dent J.* 2014;216(6):299–303. doi:10.1038/sj.bdj.2014.204.
- Harrel SK, Molinari J. Aerosols and splatter in dentistry: a brief review of the literature and infection control implications. *J Am Dent Assoc.* 2004;135:429–37.
- Marui VC, Souto MLS, Rovai ES, Romito GA, Chambrone L, Pannuti CM. Efficacy of preprocedural mouthrinses in the reduction of microorganisms in aerosol. *J Am Dent Assoc.* 2019;150(12):1015–26.e1. doi:10.1016/j.adaj.2019.06.024.
- Prasad MGS, Satish K, Bhowmik N, Reddy S, Kaul S, Kakarala S. Efficacy of 0.2% tempered chlorhexidine as a pre-procedural mouth rinse: A clinical study. *J Indian Soc Periodontol.* 2012;16(2):213–7. doi:10.4103/0972-124x.99264.
- Zanatta FB, Antoniazzi RP, Rösing CK. Staining and calculus formation after 0.12% chlorhexidine rinses in plaque-free and plaque covered surfaces: a randomized trial. *J Appl Oral Sci.* 2010;18(5):515–21. doi:10.1590/s1678-77572010000500015.
- Tartaglia GM, Tadakamadla SK, Connelly ST, Sforza C, Martín C. Adverse events associated with home use of mouthrinses: a systematic review. *Ther Adv Drug Saf.* 2019;10. doi:10.1177/2042098619854881.
- Addy M, Moran J. Mechanisms of Stain Formation on Teeth, in Particular Associated with Metal Ions and Antiseptics. *Adv Dent Res.* 1995;9(4):450–6. doi:10.1177/08959374950090041601.
- Farzan A, Firoozi P. Common Mouthwashes for Pre-procedural Rinsing in Dental Practice: Which One is Appropriate for Eliminating Coronaviruses? A Mini Literature Review. *J Regen Reconstr Restoration.* 2020;5:2.
- Tomás I, Cousido MC, García-Caballero L, Rubido S, Limeres J, Diz P. Substantivity of a single chlorhexidine mouthwash on salivary flora: Influence of intrinsic and extrinsic factors. *J Dent.* 2010;38(7):541–6. doi:10.1016/j.jdent.2010.03.012.
- Hua F, Xie H, Worthington HV, Furness S, Zhang Q, Li C. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev.* 2016;(10). doi:10.1002/14651858.cd008367.pub3.
- Dexter F, Parra MC, Brown JR, Loftus RW. Perioperative COVID-19 Defense: An Evidence-Based Approach for Optimization of Infection Control and Operating Room Management. *Anesth Analg.* 2020;131(1):37–42. doi:10.1213/ane.0000000000004829.

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