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Review Article

Preventive role of mouthwashes in COVID-19 disease transmission: An overview

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ABSTRACT

The current COVID-19 pandemic has changed the face of the health and medical care services. Due to the nature of dental treatment, which involves a very close proximity to patient's oropharyngeal region and production of aerosols the dental healthcare providers, and dental patients are at a very high risk of getting or transmitting the virus. Efforts are being made to reduce the viral load in patient's oral cavity, as well the dental clinic. For this, the role of mouthwashes has also been suggested. The aim of the present paper is to discuss the various mouthwashes, which exhibit virucidal actions, especially in relation to COVID-19.

Keywords: COVID-19, Mouthwashes, Oral antiseptics

INTRODUCTION

The current COVID-19 pandemic has brought the whole world together against fighting it.[1] All across the globe various governments, healthcare providers, non-government organizations, and individuals are doing whatever possible to break the chain of infection. Hand-hygiene, social distancing, face-coverings, and respiratory etiquettes have become an inevitable part of the lifestyle. With no definite drugs or vaccine against it yet, these safety measures seem to be the only weapon against this deadly virus presently.

First reported in the city of Wuhan, China, this highly contagious infectious disease is now known to be caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) of the Coronaviridae family.[2] It has exhibited an alarmingly rapid spread in a very short time, affecting approximately 185 countries currently. The intra-human contamination is largely due to direct inhalation of cough or sneeze droplets from an infected person; or indirect transmission through contaminated surfaces and fomites.[3] There is ample evidence that SARS-CoV-2 demonstrates a high affinity for angiotensin-converting enzyme (ACE-2). The epithelial lining of the salivary glands, oral mucosa (specially the tongue mucosa), and the lungs exhibit a high expression of ACE-2. Besides this, it also expresses in intestines, hearts, and kidneys.[4] In a very recent research, To *et al.*[5] concluded that there may be as high as 1.2×10^8 infected copies of the COVID-19 virus in the saliva of the patients; and a very high virus shedding in the upper respiratory system during the initial period of infection, while the patient maybe completely asymptomatic.

The fact that the oral cavity and saliva can be a major reservoir for the virus has brought to the front the role and significance of the oral cavity as the portal of this disease. Many recent papers have

highlighted the fact that due to the nearness of the dentists to the patient's oropharyngeal area and aerosol generating procedures, the dental surgeons are among the highest risk sub-groups among the health-care services.[6,7] Aerosols refer to liquid or solid particles of <5 μm dimension, which remain suspended in air for longer periods, and can be carried away to farther distances.[8] Prominent health agencies such as the American Dental Association, Centre for Disease Control and the Indian Dental association have issued advisories regarding how to curtail the viral load and subsequent risk of transmission. These mainly focus on reduction of viral load in the aerosols, as aerosols are lighter in weight, remain suspended in the air for a very long time and can lead to airborne transmission of the disease.[9,10] Recently, the World Health Organization has also acknowledged the air-borne transmission risk of SARS-CoV-2 infection, and advised to postpone routine or non-urgent dental treatment.[11] To decrease the chances of air-borne transmission, dentists have been advised the use of high efficacy particulate air (HEPA) filters, Ultraviolet-decontamination of air, and avoiding aerosol-generating procedures.[12]

One of the suggested methods of reducing viral load in dental environment is the practice of an effective pre-procedural mouthwash, as anti-septic mouthwashes used as a pre-procedural rinse have shown the ability to reduce bacteria in the aerosols in few previous studies.[13] Prominent mouthwashes which have been studied are chlorhexidine, Povidone-iodine, and cetylpyridinium chloride. During the earlier SARS outbreaks, research has proven that the human coronavirus is vulnerable to oxidation. Presently also, their potential role in inactivation of SARS-CoV-2 is being recognized and explored.[14]

Keeping in mind the potential of oral cavity to act like a reservoir for coronavirus, the present paper attempts to review the possible role of pre-procedural rinses/mouthwashes in reducing the aerosol viral load and subsequent airborne risk of transmission of COVID-19.

MATERIAL AND METHODS

An electronic literature search was conducted pertaining to articles related to the role of mouthwashes or antiseptic oral rinses advised in COVID-19, using the keywords "SARS-CoV-2" AND "pre-procedural mouthwashes;" "COVID-19" AND "pre-procedural mouthwashes;" and "anti-viral mouthwashes."

RESULTS

The search "SARS-CoV-2" AND "pre-procedural mouthwashes" resulted in ten items; "COVID-19" AND "pre-procedural mouthwashes" resulted in 186 items; and "COVID-19" AND "pre-procedural mouthwashes" resulted in 1330 items. Finally, only pertinent articles in English language, up to August 2020, were included in the review.

DISCUSSION

Both dental health-care personnel and patients are exposed to aerosol during dental treatment as most of the dental treatment involves use aerosol generating equipment such as high-speed airotors, ultrasonic scalars, and water-air sprays.[6] This equipment receives water through tubes called the dental unit water lines and produces aerosol, which is a combination of air, water from dental unit water lines, and the patient's saliva.[15] Moreover, certain patients with respiratory diseases such as tuberculosis, SARS, or Legionnaires disease may harbor microbes in the oropharyngeal region.[16] Thus, decontamination and disinfection of the air in the dental clinics are of paramount importance to stop cross infection. Use of UV-irradiation, HEPA filters, heavy-duty exhausts, and fumigation is among few methods to achieve this goal.[17]

Apart from these methods, which decontaminate the air after it has been laden with microbes; there is a suggested role of pre-procedural oral antiseptics in reducing the viral load reaching outside the oral cavity. The results of a recent meta-analysis by Marui *et al*. in 2019, prove that oral antiseptics such as chlorhexidine, Povidone-iodine, and few essential oils have shown to be efficacious in reducing the viral load in the aerosols coming out of the patient's oral cavity.[18] Although, the previous results have largely analyzed the effect of the oral antiseptics against bacterial microbes, and there is no clear confirmation of their effect on SARS-CoV-2. Considering the vulnerability of human coronavirus to oxidizing agents, use of hydrogen peroxide and Povidone-iodine containing oral antiseptics has gained momentum and needs to be explored further.

POVIDONE-IODINE

Povidone-iodine (PVI) is a broad-spectrum antimicrobial mouthwash. It is a water-soluble compound of the iodine and the carrier molecule Povidone. On interaction with the tissue, the carrier complex gradually releases free iodine. This steady release helps to reduce tissue irritation, diminishes possible harmful effects, and also maintains its germicidal activity. Povidone-iodine is effective against Gram-positive and Gram-negative bacteria, fungi, and viruses. Its antimicrobial effect is attributed to is destabilization of the cell membranes and disruption of certain metabolic pathways.[19] It has been found to be effective against SARS-CoV, MERS-CoV, influenza virus A (H1N1), and rotavirus *in vitro* and in 1% concentration inactivates MERS-CoV and that a concentration of 0.23% inactivates SARS-CoV, H1NI, and rotavirus within 15 s of exposure.[20] Apart from these, it also exhibits virucidal activity against adenovirus, rhinovirus,

rubella, measles, and human immunodeficiency virus (HIV). Kariwa *et al*.[21] in their study showed that PVP in 0.23% concentration has equivalent virucidal efficacy against SARS-CoV *in vitro*. Based on its promising results, in Japan, the government has supported daily gargling as a preventive approach to curtail upper respiratory tract infections.[20]

CHLORHEXIDINE

Chlorhexidine is biguanide based broad spectrum antiseptic and disinfectant. It has proven to be effective against a wide range of bacteria especially against Gram positive and to a lesser extent against Gram negative too. Being positively charged, it inactivates the negatively charged microbial cell wall and causes cell leakage.[22] As an oral antiseptic, its efficiency is well-established against bacterial species correlated with periodontal disease, such as *Enterobacteria*, *Porphyromonas*, *Fusobacterium nucleatum*, *Actinomyces,* and *Streptococcus*.[23] Its virucidal action, however, is limited. In an *in vitro* study, Bernstein *et al*.[24] established that at a concentration of 0.12%, it can inactivate enveloped (herpes simplex virus [HSV], HIV, Influenza virus, and cytomegalovirus) but not non-enveloped viruses (enterovirus, poliovirus, and papilloma virus). In a recent review by Kampf *et al*.,[25] the authors opined that chlorhexidine formulations at a concentration of 0.02% could only weakly inactivate coronaviruses, even after an exposure of 10 min. However, the ethanol component of the chlorhexidine mouthwash may contribute to the antiviral properties. It is a known fact that the oral flora of patients with respiratory infections might be altered and makes a patient more vulnerable to systemic complications of the disease. Chlorhexidine mouthwash can help to restore the oral flora of the patients, both in hospital and non-hospital settings and may be helpful in improving symptoms even in COVID-19 patients. A meta-analysis has already proven that chlorhexidine does reduce the hazard of ventilator-associated pneumonia in patients who are on mechanical ventilation.[26] However, based on the previous researches on efficacy of chlorhexidine against human coronavirus, as laid down in Guidelines for the Diagnosis and Treatment of New Coronavirus Pneumonia of the National Health Commission of the Republic of China, it can be said that chlorhexidine as mouth rinse is not proficient to kill SARS-CoV-2.[3]

HYDROGEN PEROXIDE

Hydrogen peroxide, a popular bleaching agent used in dentistry produces free radicals of oxygen, which help in lightening of discolored teeth. The antimicrobial action of hydrogen peroxide is also based on the ability of the free radicals to disrupt the microbial lipid membrane.[27] Few *in vitro* studies conducted during earlier coronavirus pandemics have shown it to be effective against coronavirus 229E and other enveloped viruses at a concentration of 0.5%.[28] A potential drawback of hydrogen peroxide mouthwash is very limited substantivity, as it is very quickly deactivated because of host and bacteria originated catalase action in the saliva in the oral cavity.[25]

CETYLPYRIDINIUM CHLORIDE

This belongs to the class of cationic quaternary ammonium compound disinfectants. Various randomized clinical trials have proved its worth as an oral antiseptic as an antiplaque and anti-gingivitis agent.[29] Regarding its virucidal activity, few *in vitro* studies have demonstrated that it has the potential to inactivate different strains of influenza virus. As this agent has the ability to disrupt the lipid envelope, it was suggested that it may be beneficial against other enveloped viruses such as coronaviruses.[30] A double-blinded, placebo-controlled randomized control trial in humans assessed a cetylpyridinium chloride based inhalation agent, when used in patients with the upper respiratory tract infections associated with influenza virus, rhinovirus, and adenovirus. It was seen that patients in experimental group showed less severe and shorter lasting symptoms when compared to placebo group. Based, on these facts, it has been projected as a possible oral antiseptic of use against SARS CoV-2.[31]

HERBAL/PLANT BASED MOUTHWASHES

Flavonoids

Flavonoids are a group of phytochemicals with a broad range of biological actions, primarily because of its antioxidant potential and capacity to control numerous cell receptors or enzymes. They also show antiviral, antibacterial, and anti-inflammatory activities.[32] Some flavonoids (Isobavachalcone, herbacetin, helichrysetin, quercetin, and 3-β-d-glucoside) can impede the enzyme activity of MERS-CoV/3CLpro.[33] Attempts are being made to combine plant products with other agents like chlorhexidine to obtain the desirable therapeutics of both of them.

Triphala

Triphala is a dried powder of three fruits: Indian gooseberry (*Emblica officinalis*), black myrobalan (*Terminalia chebula*) and belleric myrobalan (*Terminalia bellirica*).[34] Srikumar *et al*.[35] in a study observed that Triphala possesses antibacterial activity against the bacterial isolates (*Klebsiella pneumoniae*) of HIV infected patients. Besides having an excellent antibacterial and antifungal action, Triphala has demonstrated antiviral action against HSV-1, cytomegalovirus, and HIV. *T. chebula*, an active component in Triphala inactivates hepatitis B virus DNA polymerase.[36] However, studies have not been conducted

to demonstrate its efficacy against any of the human coronavirus strains.

Thymol containing compounds/essential oils

In an a recent study, it was seen that that biological substrates such as thymol, Limonene, and Isothymol obtained from the essential oil of the plant *Ammoides verticillata* can obstruct the activity of the ACE-2 as a receptor for SARS-CoV-2.[37] This fact may be suggestive of a possible role of thymol containing mouthwashes in reducing risk transmission during the present SARS-CoV-2 outbreak.

CONCLUSION

Although the studies indicate the impending use of mouthwashes in reducing viral load in oral cavity and saliva, still no clinical trials have been conducted to prove the same. However, it would be pertinent to carry out studies to find out the probable role of mouthwashes in diminishing the transmission of SARS-CoV-2. In the near future, it would be useful to study their role both as a method for reducing disease transmission, and also extending these guidelines to the community in general.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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