Prophylactic Oral Rinse Usage Against Transmission of COVID 19 – A Comprehensive Review

Sharika Gopinath, 1 Rithesh Kulal 1

1Department of Periodontology, Rajarajeswari Dental College and Hospital, Bangalore, Karnataka, India.

INTRODUCTION

The COVID-19 pandemic has united the whole world in its battle against it. All across the globe various governments, healthcare providers, non-governmental organisations, and individuals are working around the world to break the infection chain. Hand washing, social distancing, face coverings, and respiratory etiquette have also been ingrained in our culture.1

Aerosols are generated during routine dental procedures, posing possible health risks to the dental care personnel as well as patients. Although, no cases of coronavirus transmission have been reported in a dental setting, considering the disease’s high transmissibility, dental teams should be vigilant and maintain a safe atmosphere for both their patients and themselves.2

One of the most important strategies for reducing the proportion of microorganisms in oral aerosols is to use a pre-procedural mouth rinse (Samaranayake and Peiris, 2004; Feres et al., 2010). A meta-analysis found that using a pre-procedural mouth rinse containing chlorhexidine (CHX), essential oils, and cetylpyridinium chloride (CPC), povidone-iodine (PVP-I), and hydrogen peroxide (H2O2) and certain herbal products can be suggested as a possible solution to reduce the viral load in the oral cavity. This paper aims to provide a comprehensive review on certain mouthwashes, their antiviral activity against Covid-19.
have been widely used as a standard measure.\textsuperscript{4,5} They play an important role in lowering the number of microorganisms in the mouth.\textsuperscript{6} Recent publications indicate that rinsing the oral cavity may minimise the risk of SARS-CoV-2 transmission.\textsuperscript{7,8} However, there is no clear evidence for the safety and efficacy of this method.

The aim of this paper is to provide a comprehensive analysis of existing guidelines for the use of mouthwashes in the fight against the COVID-19 pandemic, as well as to analyse the benefits and drawbacks of most antiseptic mouthwashes used in dentistry.

**PATHOGENESIS**

SARS-CoV-2 viruses are enveloped RNA viruses possessing a spike protein in its membrane envelope. ACE2 (angiotensin-converting enzyme 2) has recently been reported as the SARS-CoV-2 receptor, establishing a crucial connection between immunity, inflammation, ACE2, and cardiovascular disease. ACE2 act as a negative regulator of the renin-angiotensin system, facilitator of amino acid transport, and the severe acute respiratory syndrome-coronavirus (SARS-CoV) and SARS-CoV-2 receptor. ACE2 is widely distributed in the lungs, cardiovascular system, gut, kidneys, central nervous system, and adipose tissue indicating possible routes of infection. Thus, the interaction of this protein with angiotensin-converting enzyme 2 (ACE2) receptors is responsible for the entry of virus into cells.\textsuperscript{9} Mucosal tissues, gingiva, non-keratinising squamous epithelium, epithelial cells of the tongue, and salivary gland epithelial cells all have membranes bound to ACE2. In addition, a strong SARS-CoV-2 viral load has been observed in saliva, and its existence in periodontal pockets has been suggested.\textsuperscript{10} Recent studies suggest virus transmission is closely linked to saliva interactions, suggesting that oral tissues may be a reservoir from which SARS-CoV-2 transmission could occur during coughing, sneezing, or talking and even during dental care.\textsuperscript{2,11}

**MOUTHWASHES IN PREVENTION OF VIRAL INFECTIONS**

Studies suggest mouthwashes possess antiviral properties. Due to their ability to reduce the number of microorganisms in the oral cavity and colony-forming units in dental aerosols, mouthwashes are commonly used solutions for rinsing the mouth, especially before oral surgery.\textsuperscript{4} They can decrease airborne respiratory infections, including infections from the flu virus and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), the causative agent responsible for the current coronavirus disease 2019 (COVID19) pandemic.

If further more studies show that mouthwashes have antiviral properties, they may be a powerful and cost-effective tool for combating the pandemic. Mouthwashes would be a low-cost, readily available strategy that could be implemented quickly. The transmission chain can be slowed by lowering viral loads in the mouth. Mouthwashes are also available as oral sprays, so they can be used by the elderly population as it is more convenient for them. While studies have shown that various oral products have antiviral activity in vitro, it is unknown which components in mouthwashes are responsible for the antiviral activity or what mechanism of action they use.\textsuperscript{12}

**Cetylpyridinium chloride (CPC)**

CPC is a quaternary ammonium compound with antimicrobial and antiseptic properties. In patients who experience mucosal irritation and stains due to CHX, CPC 0.075% has been used as an alternative to minimise dental plaque and gingivitis. It acts by penetrating the cell membrane, causing cell components to leak, which eventually leads to cell death.\textsuperscript{13}

CPC has been shown to have an antiviral effect in influenza patients, reducing the duration and severity of cough and sore throat.\textsuperscript{14} Studies report that antiviral activity of CPC disrupts the viral envelope, by lysosomotropic mechanism of action indicating protection against SARS-CoV2. SARS-CoV2 is primarily transmitted via the upper respiratory tract, nasal sprays containing CPC may be more effective in preventing or reducing infection. Recent study concludes addition of 0.28% zinc increases the efficacy of CPC in reducing plaque, gingivitis, oral halitosis in turn inhibits the progression of periodontitis, which is a risk factor for covid 19.\textsuperscript{15}

**Chlorhexidine**

Chlorhexidine is a biguanide, broad spectrum antiseptic that act against Gram-positive and Gram-negative bacteria, aerobes, facultative anaerobes, and fungus. Chlorhexidine alters cell membrane permeability due to its antibacterial effects. It possesses both bacteriostatic and bactericidal actions depending on the concentrations. CHX causes Ca2+ and Mg2+ displacement and K+ removal from the cell wall at low concentrations (0.02%-0.06%), resulting in a bacteriostatic effect. On other side CHX cause
leakage of all major intracellular components out of the cell at high concentrations (>0.1 percent), resulting in a bactericidal (cell lysis and death) effect.\(^1\)

Evidence suggest 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).\(^1\) The antiviral properties of chlorhexidine mouthwash may be aided by the ethanol component. CHX can restore the altered oral flora of the patients with respiratory infections, thereby helps in improving symptoms even in COVID-19 patients. When compared to other mouthwashes, 0.12 % CHX gluconate was suggested to have little or no impact against coronaviruses, despite the fact that COVID-19 is an enveloped virus.\(^7,18\) However, after using 15 ml of 0.12 % CHX once, Yoon et al discovered that SARS-CoV-2 was suppressed for two hours, implying that its use could help regulate COVID-19 transmission.

**Hydrogen peroxide (H2O2)**

Hydrogen peroxide, a popular bleaching agent has been using as a temporary oral debriding agent since many years. Hydrogen peroxide can destroy bacterial cell walls by breaking the slime barrier that protects the biofilm. It releases oxygen and provides an unfavourable environment for anaerobic bacteria.\(^19\) Many studies report daily rinsing of 1% –1.5 % H2O2 over a two-year period give no adverse effects on soft tissue.\(^20,21\) In an in vitro analysis, researchers discovered that 3 % \(\text{H}_2\text{O}_2\) effectively inactivated adenovirus types 3 and 6, adeno-associated virus type 4, rhinoviruses 1A, 1B, and type 7, myxoviruses, influenza A and B, respiratory syncytial virus, strain long, and coronavirus strain 229E within 1–30 minutes, where coronaviruses and influenza viruses being the most susceptible.\(^22\)

Pre procedural mouthrinses containing oxidative agents such as 1% H2O2 have been suggested to reduce the salivary viral load because SARS-CoV2 is susceptible to oxidation. A major disadvantage of hydrogen peroxide mouthwash is its low substantivity, as it is easily deactivated by catalase activity in the oral cavity caused by the host and bacteria.\(^23\)

**Povidone-iodine**

Povidone - iodine (PVI) is water soluble iodine complex with iodine as soluble compound and povidone, the carrier molecule. The carrier complex steadily releases free iodine after interacting with the tissue. This consistent release reduces tissue inflammation, mitigates potentially harmful effects, and retains germicidal activity. PVI is effective against gram positive and gram-negative bacteria, fungi, and viruses. It’s usually used in a 1% concentration for mucositis, oropharyngeal infection prophylaxis, and ventilator-associated pneumonia prevention.

PVP-I has been shown to have higher virucidal activity than other widely used antiseptics like CHX and benzalkonium chloride in previous studies. It is safe, with prevalence of 0.4 % allergy cases, does not cause tooth or tongue discoloration or taste disturbances, and can be used with electrocautery, unlike alcohol-based products. In vitro, it has been shown to be effective against MERS-CoV at 1% and influenza virus A (H1N1), SARS-CoV, H1NI, and rotavirus at 0.23 % concentration within 15 seconds of exposure.\(^24\) Thus, pre procedural rinsing with 0.23% PVP-I mouthwash for at least 15 seconds may reduce salivary viral load indicating its use in COVID-19– positive patients.\(^25\)

**HERBAL MOUTHWASHES**

**Flavonoids**

Flavonoids are naturally occurring organic compounds having variable phenolic structures. Fruit, grains, bark, herbs, roots, flowers, tea, wine, and stems are the most common sources.

They possess anti-inflammatory, antiviral, antiallergic, anticancer effects. Some flavonoids have antioxidant and vitamin C-sparing properties. The antiviral effects of flavonoids were investigated by Wang et al. Respiratory syncytial virus, herpes simplex virus, parainfluenza virus, influenza virus, and adenovirus are among the viruses thought to be affected by flavonoids in large numbers.\(^26\) Due to the presence of polyphenols including catechins, tannins, and flavonoids, in herbal products which is acidic in Ph can affect viral proteins.\(^27\) Some flavonoids; such as isobavachalcone, herbacetin, helichrysetin, querce tin, and 3-9-glucoside, can inhibit MERS-CoV/ 3CLpro enzyme activity. Plant products are being combined with other agents such as chlorhexidine in an attempt to achieve the therapeutic benefits of both.\(^28\)

**Triphala**

In Traditional Ayurvedic Medicine, “triphala” is one of the most popular formulas. Triphala is made up of the fruits of three trees: Indian gooseberry Amalaki (Embilica of/ cinalis),...
Bibhitaki (Terminalia belerica), and Haritaki (Terminalia chebula). It is listed in Ayurvedic medicine’s ancient literature as a tonic, highly valued for its ability to regulate the digestive and elimination processes.28

Various studies have listed a number of uses of Triphala. Triphala have hypercholesteremic, anti-inflammatory, Gastrointestinal, stress reducing, antiobesity, antidiabetic, anti-inflammatory, antimutagenic and bronchodilator effects.29 It possess antibacterial activity against bacterial isolates of HIV-infected patients (Klebsiella pneumoniae). Triphala has shown antiviral activity against HSV-1, cytomegalovirus, and HIV, in addition to possessing excellent antibacterial and antifungal properties. Hepatitis B virus DNA polymerase is inactivated by T. chebula, an active ingredient in Triphala.30 Evidence indicates that 0.6% Triphala and 0.1% Chlorhexidine have an inhibitory effect on plaque, gingivitis, and growth of Streptococcus mutans and Lactobacillus. Considering all the effects triphala can be used as a preventive measure of Covid-19.28

Mouthwashes containing essential oils

Biological substrates such as thymol, Limonene, and Isothymol obtained from the essential oil of the plant Ammoides verticillata have been shown to inhibit the function of the ACE-2 as a SARS-CoV-2 receptor in a recent report. This fact may point to thymol-containing mouthwashes playing a role in reducing risk transmission during the current SARS-CoV-2 outbreak.31

Current usage guidelines for the pre-procedural mouthrinses against COVID-19

Gently gargle with 1.5% or 3% H2O2 15 ml; PVP-I, 0.2%, 0.4%, or 0.5% 9 ml; 0.12% CHX 15 ml; or 0.05% CPC 15 ml for 30 seconds in the oral cavity and 30 seconds in the back of the throat.

CONCLUSIONS

We recommend the use of pre procedural mouthwash in dental practise to minimise SARS-CoV-2 viral load and to reduce the risk of cross infection when treating patients during the pandemic. Antiseptic mouthwashes must be evaluated in clinical trials with control subjects on a broad scale to determine their effectiveness against SARS-CoV-2. It’s important to do research to see how it can be used to protect from this new virus and also their role as a tool for reducing disease transmission in the immediate future.

ACKNOWLEDGEMENTS – Nil

REFERENCES


9. Yushun Wan, Jian Shang, Rachel Gra-
Prophylactic Oral Rinse Usage Against Transmission of COVID-19 – A Comprehensive Review


27. Supriya, Lakshmi. “Green tea and some fruit juices inhibit SARS-CoV-2 in vitro”. News-Medical. 27 April 2021. [Full Text]

28. Bajaj N, Tandon S. The effect of Triphala and

