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Pros and cons of mouthwashes in the prevention of Covid 19: A review

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Abstract

Despite several efforts to control the spread of corona virus, it still constitutes a public health emergency of international concern. Antiseptic-mouthwashes have been generally and gradually utilized as a standard measure before any routine dental treatment, particularly preoperatively because of fundamental role in decreasing the quantity and specificity of microorganisms in the oral cavity and thus helping in maintaining the oral hygiene. Many studies have proposed that antiseptic mouthwashes may control and diminish the danger and transmission of corona virus. However, the safety and efficacy for the utilization of antiseptic mouthwashes in COVID-19 positive patients is lacking and still unclear, therefore the main of this paper is to give a brief review on the current proposals for the utilization of mouthwashes against the COVID-19 pandemic and to justify the points of interest and drawbacks of most ordinary antiseptic mouthwashes particularly used in dentistry.

Keywords: Coronavirus, Chlorhexidene, Infection, Transmission.

Introduction

It's a well known fact that the saliva and oral cavity can be a reservoir for the virus has brought to the front the role and significance of the oral cavity as the portal of this disease. Various studies have justified the fact that due to the nearness of the dentists to the patient's oropharyngeal area and aerosol generating procedures, the dental surgeons are found to be at the highest risk sub-groups among the health-care services.1,2 This virus has entered the human ecosystem and new considerations have been created for us given that humans can host the virus. The angiotensin-converting enzyme 2, receptors of epithelial cells of the salivary glands is the main target of the SARS-covid 19 virus. Abundance of these receptors (ACE-2) in the tongue, indicate a high probability of infection in the oral cavity. According to research, there is 1.2 × 108 infective copies/mL of COVID-19 virus in the tested saliva of patients. Various papers have confirmed the shedding of the virus is very high in the early stages of the disease mainly in upper respiratory system. Acknowledging the importance of salivary glands and saliva in the entry of sars-cov2 virus into the body, the process of infection and the presence of the virus should be considered even in asymptomatic carriers. Saliva plays an important role in transmitting the infectionthrough the spread of virus infected droplets.3 Recently, the World Health Organization has also acknowledged the air-borne transmission risk of Covid-19 infection, and advised to postpone routine or non-urgent dental treatment. To decrease the chances of air-borne transmission, dentists have been advisedthe use of high efficacy particulate air (HEPA) filters, Ultraviolet-decontamination of air, and avoiding aerosol-generating procedures.[4]

Mode of Transmission	Characteristics
Direct	Through sneezing, droplets of saliva, other body secretions.
Through contact	With nasal, ocular and ocular mucous membrane
In dentistry	After touching contaminated surfaces with your hands and then scratching or touching eyes, nose or mouth.

Table 1: routes of transmission of virus.[5]

Various studies suggest that some mouthwashes may help reduce the spread of SARS-CoV-2, by temporarily reducing the amount of virus in the mouth. The virus spreads through respiratory droplets produced when an infected person sneezes, talks, coughs, or breathes, according to the US Centers for Disease Control and Prevention. So this paper gives the brief description of different types of mouthwashes which in-turn can reduce viral load in oral cavity, thus preventing its transmission.[6]

Different Types of Mouth Washes

- **Chlorhexidine (Chx)**

Chlorhexidine is biguanide, a gold standard mouth wash and has broad spectrum antiseptic and disinfectant properties and is thus being widely used. Earlier studies have shown it to be effective against a wide range of nicroorganism especially against Gram positive bacteria and to a lesser extent against Gram negative, aerobic and non-aerobic bacteria, which is highly superior and more effective than other mouthwashes in this respect. It inactivates the negatively charged microbial cell wall and causes cell leakage due to the presence of a positive charge. As an oral antimicrobial agent, its efficiency is well-established against many bacterial species correlated with periodontal disease, such as Fusobacterium

nucleatum, Porphyromonas, Streptococcus , Actinomyces, and Enterobacteria, .

Its virucidal action, however, is limited. In an in vitro study, Bernstein et al. 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. the authors opined that chlorhexidine formulations at a concentration of 0.02% could only weakly inactivate coronaviruses, even after an exposure of 10 min. Moreover, the component of ethanol in chlorhexidine mouthwash may contribute to the antiviral properties. Oral flora of patients with respiratory infections might be altered making the patient more vulnerable to systemic complications of the disease. This mouthwash helps in restoring the oral flora of the patients, both in hospital and non-hospital settings and can also be helpful in the improving symptoms even in COVID-19 patients. A meta-analysis has shown that this mouthwash reduces the hazard of ventilator-associated pneumonia in patients. Furthermore, based on the previous researches on the efficacy of chlorhexidine against human coronavirus, as laid down in Guidelines for the Diagnosis and Treatment of New Coronavirus Pneumonia of the NHC (National Health Commission) Republic of China, it can be said that chlorhexidine as mouth rinse is not proficient to kill SARS-CoV-2. Simillar results were found by Rajeev Chitguppi in April 2020 in which he analysed all the studies available on PUBMED on The effect of Chlorhexidine gluconate solution on inactivating novel coronavirus and found that Chlorhexidine mouthwashes are not effective against the novel coronavirus. However Prescribing CHX before dental procedures is a routine procedure that reduces the level of oral microorganisms in the aerosols generated during dental procedures[3,7,8,9]

Povidone-Iodine (PVP-I)

PVP-I, also known as betadiene, a broad-spectrum antimicrobial agent is a water-soluble complex with polyvinyl pyrrolidone and free iodine (usually 1 ppm) and has been widely used as a mouthwash along with pre-surgical skin antiseptic. PVP-I has 10% as the most common formulation with oxidation of amino acids and nucleic acids as its basic action but it is typically used in a concentration of 1% for prophylaxis of oropharyngeal infections, mucositis, and prevention of ventilator-associated pneumonia.. It damages the microorganism by perturbation of various metabolic pathways and destabilization of the cell membrane by iodine which rapidly penetrates microbes by disrupting protein structure and oxidising nucleic acids and finally leading to microbial death [10]

Studies have reported that PVP-I has more antiviral properties than other mouthwashes such as benzalkonium chloride and chlorhexidine.[11] In 2018, Eggers et al stated that both the strains of coronavirus (SARS and MERS) could be efficiently and rapidly inactivated by povidine iodine in concentration of 0.23% , which can be used for a period of 15 seconds.[12] A prevalence as low as 0.4% allergies, do not produce tongue or tooth

discolouration or taste disturbance, unlike alcohol-based products and thus can be used while using electrocautery. In cases of SARS CoV-2, Povidene iodine agents when used for 2 min reduced the virus infectivity from 1.17 x 10^6 TCID (50)/ml to below the detectable level. Povidene iodine when used as topical oronasal treatment, may be an effective method to immediately reduce the viral load of the upper aero-digestive tract and thus decrease the risk of inadvertent virus transmission.[13]

- **Cetylpyridinium Chloride**

Cetylpyridinium Chloride (CPC) is a well know quaternary ammonium compound that has been used for decades for many pathogens, including bacterial and fungal infections (Popkin et al., 2017) and is safe for human use. Various randomized clinical trials have been done which proved its worth as an antiplaque, oral antimicrobial, and anti-gingivitis agent at the concentration of 0.05% and is an effective alternative agent in patients who develop stains and mucosal irritation due to chlorhexidene. Regarding its virucidal activity, few in vitro studies have demonstrated that it has the potential to inactivate various strains of influenza virus, thus, significantly reducing the severity and duration of sore throat and cough. As this agent has the ability to disrupt the lipid envelope due to lysosomotropic mechanism of action, it was suggested that it may be beneficial against other enveloped viruses such as coronaviruses. 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 within influenza virus, rhinovirus, and adenovirus. It was evaluated that patients in experimental group showed shorter lasting and less severe 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.[14,15,16]

- **Hydrogen Peroxide (H_2O_2)**

Use of hydrogen peroxide in dentistry alone or combined with other salts started since centuries. When used as a mouthwash, it is a clear, odourless and colourless liquid. The antimicrobial action of this agent is based on its ability to disrupt the microbial lipid membrane by releasing free radicals. Lack of an adverse soft tissue effect was found in many studies of 1%–1.5% H_2O_2 used as a daily rinse over two years' follow-up. An in vitro study found that 3% H_2O_2 effectively inactivated adeno-associated virus type 4, rhinoviruses 1A, 1B, and type 7, adenovirus types 3 and 6, influenza A and B, myxoviruses, coronavirus strain 229E and respiratory syncytial virus, within 1–30 minutes, discovering that coronaviruses and influenza viruses were the most sensitive. Since SARS-CoV2 is vulnerable to oxidation, preprocedural mouthrinses containing oxidative agents such as 1% H_2O_2 have been suggested to reduce the salivary viral load. One of the major drawbacks of hydrogen peroxide mouthwash is found to be its limited substantivity, because it gets quickly deactivated because of bacteria and host originated catalase action in the saliva in the oral cavity.[17,18,19]

Authors	Year	Characteristics of Hydrogen Peroxide	Concentration of Hydrogen Peroxide	Action Time	Ventilation Time	Inactivation of Virus *
Kindermann et al.(Kindermann et al., 2020)	2020	Vapour	33.8%	11–55 min	—	BVDV, HAV,MVM, ReoIII
Holmdahl et al.(Holmdahl, Odenholt,Riesbeck, edstrand, &Widell, 019)	2019	Vapour	860 ppm	33 min	50 min	HuNoV
Montazeri et al.(Montazeri et al., 2017)	2017	Vapour	7.5%	5 min	20 min	FCV, HuNoV
Becker et al. (Becker,Bischo) Brill,Steinmann, &Steinmann, 2017)	2017	Solution	40%–60%	30 s–3 min	—	ADV, MNV,MVM,poliovirus,Vacciniavirus,
Baker et al. (Bakeret al., 2017)	2017	Foam	4.25%	40 and50 min	—	PEDV, PRCV
Holtkamp et al.(Holtkamp et al., 2017)	2017	Foam	4.25%	30 min	—	PEDV

Table 2: Earlier studies regarding the potrency of Hydrogen Peroxide as surface disinfectant.[20]

* Abbreviations: ADV, adenovirus; BVDV, bovine viral diarrhea virus; FCV, feline calicivirus; H1N1-influenza; hADV-1, humanadenovirus type1; HAV, hepatitis A virus; HPV, human papillomavirus; HuNoV, human noroviruses; MNV, Murinenorovirus; MVM, Minute virus of mice; PEDV, porcine epidemic diarrhea virus; PRCV, Porcine respiratory corona virus; Reo III, respiratory enteric orphan virus type III; SARS, severe acute respiratory syndrome virus; TGEV, transmissible gastroenteritis virus.

- **Herbal Mouthwashes**

Various attempts have been made to combine plant products with agents like chlorhexidene to obtain the desirable therapeutics agents to obstruct the activity of ACE-2 receptors for covid 19. Flavonoids, triphala, and thymol containing compounds are recently being studied for their possible role in reducing the risk transmission during the covid pandemic. Flavonoids have shown effective antiviral, anti-inflammatory and antibacterial activity and can impede the enzyme activity of MERSCoV/3CL pro. Triphala besides having an excellent antifungal and antibacterial action, it also demonstrates antiviral action against cytomegalovirus, HIV and HSV-1.

However numerous studies have been done which fail to demonstrate its efficacy against coronavirus strains. Recent studies have shown that biological substrates such as Limonene, Isothymol and thymol obtained from the essential oils can obstruct the ACE-2 receptors for coronavirus. These facts may be suggestive of a possible role of essential oils containing mouthwashes in reducing risk transmission during the present SARS-CoV-2 outbreak.[21, 22, 23]

- **Suggested Recommendations Of Various Mouthwashes[24]**

Mouth rinsing for 30 seconds in the oral cavity followed by 30 seconds in the back of the throat with any of the following agents:

- 1.5% or 3% H_2O_2 15 ml
- PVP-I, 0.2%, 0.4%, or 0.5% 9 ml
- 0.12% CHX 15 ml
- 0.05% CPC 15 ml.

Conclusion

About three different pathways are present forSARS CoV-2 in saliva, from lower and upper respiratory tract that enters the oral cavity together with the liquid droplet,from blood it can access the mouth via crevicular fluid, and finally occur in the oral cavity by major- and minor-salivary gland infection, with subsequent release of particles in saliva through salivary ducts. As most of the dental procedures are associated with aerosol production making the dentist more prone to cross infections. Thus a preprocedural mouthwash is highly recommended to limit the cross infection apart from following proper protocols. Clinical studies, including control subjects and in large scale, are required to evaluate the efficacy of antiseptic mouthwashes on SARS-CoV-2. Research is urgently needed to determine its potential for use against this new virus.

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