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Use of Mouthwash in Preventing Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

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Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a virus that enters the respiratory tract through the nose and mouth affects a wide range of cells and systems of the body, causing various types of symptoms. Therefore, the discovery that the use of mouthwash may help prevent COVID-19 from entering the body is a breakthrough and an area of interest for research. In this report, several research papers about the effects of mouthwash in preventing COVID-19 are evaluated and different types of mouthwash are discussed. In particular, one randomized prospective cohort study presented the promising result of chlorhexidine mouthwash and spray in preventing COVID-19. Despite the result, the number of clinical trials is lacking, and more clinical trials need to be performed to obtain more conclusive clinical evidence that the mouthwash indeed has a preventive effect on SARS-CoV-2 transmission.

Introduction:

First identified in Wuhan, China in December 2019, coronavirus disease 2019 (COVID-19) has since spread worldwide, leading to an ongoing pandemic. Efforts have been made around the world to discover ways to prevent the spread of the virus responsible for the disease. However, despite the development of several vaccines, the virus seems incapable of being restrained. It seems as if the virus cannot be eradicated, and it would be best to settle for alternative forms of control, such as wearing masks and keeping good personal hygiene. The virus SARS-CoV-2 enters the body through the respiratory tract, specifically the nose and mouth, and affects a wide range of cells and systems of the body, leading to various types of symptoms. This review paper investigates and examines the following question: Would the use of mouthwash help prevent transmission of SARS-CoV-2? Despite several efforts, such as the development of various vaccines, the virus persists and continues to spread. Similar to flu viruses, which are constantly mutating, SARS-CoV-2 comes in many variants, such as delta and omicron, making it much harder to eradicate the virus. Thus, it has been proposed that the best way to prevent the virus is to wear masks and keep good personal hygiene in addition to getting vaccines. Researchers have been studying further ways to prevent the spread of the virus. In this paper, several research articles on the effect of mouthwash in preventing virus transmission have been reviewed.

Pathogenesis of coronavirus disease 2019 (COVID-19):

Coronaviruses are enveloped RNA viruses that have "spike proteins" on the surface. The virus enters the cell by the interaction of its spike proteins and the angiotensin-converting enzyme 2 (ACE2) receptors present in different parts of the body, including oral mucosal tissue, gingiva, tongue, and salivary glands. In COVID-19 patients, high SARS-CoV-2 viral load has been detected in saliva, suggesting that the oral cavity may be a reservoir of the virus and that the virus is capable of being transmitted during coughing, sneezing, and talking. Thus, several studies have proposed that the use of mouthwash may help prevent transmission of the virus.

Literature Review:

In the research article "Use of Mouthwash against COVID-19 in Dentistry" by A. Vergara-Buenaventura and C. Castro-Ruiz (Vergara-Buenaventura & Castro-Ruiz, 2020), the authors analyzed the different types of mouthwashes used in dentistry. Antiseptic mouthwashes have been used in dentistry to reduce the number of microorganisms in the oral cavity and aerosols, hinting that rinsing the oral cavity with mouthwash may help reduce SARS-CoV-2 transmission. Notwithstanding the lack of clinical evidence, the American Dental Association (ADA) and the Center for Disease Control and Prevention (CDC) recommend the use of pre-procedural mouthwashes before dental procedures. The first antiseptic mouthwash discussed in the article is chlorhexidine (CHX), which is an antiseptic mouthwash that is renowned to be effective against both Gram-positive and negative bacteria. It is used in dentistry to reduce dental plaque and help treat periodontal disease. There is clinical evidence that CHX has an effect against enveloped viruses such as influenza A, parainfluenza, herpesvirus 1, cytomegalovirus, and hepatitis B. The authors alluded to a study by Yoon et al, which demonstrated that the use of 15mL of 0.12% CHX had an effect of suppressing the virus for two hours, suggesting its potential use for controlling the virus. Hydrogen peroxide (H2O2) is another mouthwash that is frequently used in dentistry. An

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in vitro study suggests that 3% H2O2 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. SARS-CoV-2 is vulnerable to oxidation, and since H2O2 is an oxidizing agent, the author suggests the use of mouthwash containing 1% H2O2 to reduce the salivary viral load. Cetylpyridinium chloride (CPC) is another alternative that has demonstrated its antiviral effect against influenza. CPC has a lysosomotropic mechanism, which enables it to destroy viral capsids, and it is hypothesized that CPC may have an effect against SARS-CoV-2 since it is an enveloped virus with viral capsids. The last mouthwash discussed is povidone-iodine (PVP-I). Previous research has demonstrated that PVP-I has a more effective antiviral effect compared to other common antiseptic agents, including CHX already discussed. It has an effect against multiple viruses such as SARS-CoV, MERS-CoV, and influenza virus A (H1N1). It has been proposed to use 0.23% PVP-I mouthwash for 15 seconds before dental procedures to reduce salivary viral load. Combining all the studies, the author suggests the following recommendations: gently gargle for 30 seconds in the oral cavity and 30 seconds in the back of the throat 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.

In response to the study mentioned above, authors Gururaj Arakeri and Vishal Rao US wrote a letter to the editor titled "Methylene blue as an anti-COVID-19 mouthwash in dental practice," suggesting methylene blue (MB) as an additional mouthwash to consider in reducing the viral load in the aerosol and oral cavity. They laid out three potential ways in which MB can have an effect against SARS-CoV-2. First, reduced MB can competitively inhibit the virus by occupying cellular sites where the virus attaches. Second, reduced MB has redox-potential properties, through which it can complete defective oxidative processes of cells and uncouple oxidation and phosphorylation. Lastly, MB has a direct and indirect virucidal effect and the ability to prevent the production of reactive oxygen species. Based on these effects, the authors recommend 0.5% MB oral rinse to be used every five to ten minutes during dental procedures to prevent viral transmission.

In the research article "Use of Chlorhexidine to Eradicate Oropharyngeal SARS-CoV-2 in COVID-19 Patients," written by Y. Hanna Huang and Jong T. Huang (Hanna & Huang 2020), the authors performed a randomized prospective cohort study using CHX as an oral rinse and posterior oropharyngeal spray in hospitalized COVID-19 patients. In this study, COVID-19 positive patients hospitalized in four community hospitals in Los Angeles, California were randomly assigned to the study and control groups. The study group was given 15 ml 0.12% CHX to use as an oral rinse whereas the control group was not. The study group patients were instructed to rinse the mouthwash for 30 seconds twice a day, and after 4 days, the patients were swabbed and tested for the presence of SARS-CoV-2. Since the oral rinse alone was unable to efficiently reach the posterior oropharynx, the researchers had a second study group, which received posterior oropharyngeal CHX spray in addition to the oral rinse, and the second study group was compared to the second control group. Lastly, a group of 15 healthcare workers used CHX as an oral rinse and oropharyngeal spray twice a day, and the rate of COVID-19 infection was compared to the other healthcare workers in their respective hospitals during the same period. The results revealed that SARS-CoV-2 was eliminated from the oropharynx in 62.1% of patients who used CHX oral rinse only, compared to the control group in which only 5.5% of the group had SARS-CoV-2 eliminated. In the second study group, 86.0% of the patients who used a combination of oral rinse and oropharyngeal spray had SARS-CoV-2 eliminated versus 6.3% of control patients. Overall, the results indicated the effectiveness of CHX as an oral spray and posterior oropharyngeal spray in preventing COVID-19.

Discussion:

The above-mentioned research has highlighted that mouthwashes are potentially effective ways to reduce SARS-CoV-2 salivary load and to prevent transmission of the virus. The article written by Vergara-Buenaventura and Castro-Ruiz detailed various mouthwashes of specific concentrations that may help prevent the viral transmission of SARS-CoV-2. The randomized prospective cohort study done by Hanna and Huang demonstrated the efficacy of chlorhexidine, as an oral spray and oral rinse, in significantly reducing the salivary load of SARS-CoV-2. In addition to the mouthwashes that were mentioned in the article written by Vergara-Buenaventura and Castro-Ruiz, Arakeri and Rao US proposed diluted methylene blue as another potential mouthwash for reducing the salivary viral load of SARS-CoV-2, and they also suggested three possible mechanisms by which methylene blue can help lower the viral load.

All the research that has been done so far has demonstrated a promising effect of mouthwash in

preventing transmission of SARS-CoV-2. However, it cannot be said with confidence that mouthwash has a definitive effect on preventing viral transmission of SARS-CoV-2 due to a lack of clinical evidence. More clinical studies, ideally randomized controlled trials, need to be performed to compile data to confirm the effectiveness of mouthwashes against SARS-CoV-2. Furthermore, besides having more clinical studies, more follow-up research needs to be done on the published studies to replicate the results, which will uphold the hypothesis that mouthwash is capable of hindering the transmission of SARS-CoV-2.

Recently, some researchers have taken a novel approach to curb the viral load of SARS-CoV-2 in saliva. Dr. Henry Daniell from the University of Pennsylvania School of Dental Medicine and his team conducted a study using a chewing gum that contains virus-trapping proteins called Cholera Toxin B Angiotensin-Converting Enzyme 2 (CTB-ACE2), which trap SARS-CoV-2 to debulk virus from the saliva. The surface of human epithelial cells is rich in ACE2 receptors, and the CTB-ACE2 chewing gum competes with the receptor by directly binding to the virus and preventing its entry into human cells. Through several clinical assays, the study successfully demonstrated the effectiveness of the CTB-ACE2 chewing gum in reducing SARS-CoV-2 viral load in saliva. The author notes that the CTB-ACE2 chewing gum is a novel, affordable and practical way to prevent the SARS-CoV-2 transmission during this pandemic, especially in places where vaccines are not available or affordable.

Considering the enormous impact that COVID-19 is causing globally, it was surprising to find such little clinical research on preventing the viral transmission of SARS-CoV-2. This literature review hopes that various mouthwashes as a way to prevent COVID-19 attract more attention from researchers and more clinical trials be performed.

Conclusion:

Research articles discussed in this literature review have demonstrated and concluded mouthwashes as a potential way to reduce the viral load of SARS-CoV-2 in saliva. However, some limitations need to be considered. Specifically, there is a need for more clinical trials to be performed to indicate that mouthwash has a definitive effect in preventing viral transmission. Additionally, after more research is compiled, there needs to be a specific guideline on using mouthwashes in preventing the transmission of SARS-CoV-2. All in all, mouthwashes, along with the ongoing research on chewing gum with ACE2, are promising areas of research. As more steps are taken to assure their effectiveness, along with the ongoing development of vaccines and treatments, it will be a matter of time before COVID-19 becomes a thing of the past.

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