COVID-19 - Mouthwash in dental clinical practice: review

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Abstract
Severe acute respiratory syndrome (SARS-CoV-2) is a highly infectious respiratory disease. Dental surgeons perform various procedures that generate aerosolization, leading to the dissipation of saliva and drops of blood. The indication during the COVID-19 pandemic in clinical practice is the use of mouthwashes to reduce the viral load of SARS-CoV-2. The present work brings the main rinses indicated in the literature to minimize the viral load of SARS-CoV-2 in clinical practice.

Descriptors: Mouthwash; SARS Virus; Coronavirus Infections.

INTRODUCTION
The severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) was first identified in the Chinese city of Wuhan in late 2019. As of November 22, 2020, there were more than 57.8 million cases and 1.3 million deaths reported globally since the pandemic began.

Infection with SARS-CoV-2 occurs through the transmission of respiratory droplets and direct or indirect contact. The infection occurs mainly through the coughing, sneezing, and saliva of an infected patient. Particles containing SARS-CoV-2 can remain suspended in the air, contaminating other individuals from points of entry such as mouth, nose, eyes, lesions on the skin, and mucous membranes, thus, interpersonal proximity becomes an important means of contagion for coronavirus 2. Dental work, in addition to being performed close to the patient, involves the production of aerosols. This characteristic may indicate that dentists represent the group with the highest risk of infection, among health professionals.

There are various guidelines to reduce the exposure of these professionals to direct or cross-contamination with the coronavirus. The recommendation is to use mouthwash or mouthwash before dental clinical procedures, to decrease the viral load in saliva. Currently, clinical research is underway to assess the power of mouthwashes to reduce the viral load of SARS-CoV-2.

Analyzing the possible consequences that SARS-CoV-2 can develop, the concern in the scenario of dental clinical practice becomes obvious. The use of personal protective equipment (PPE) is already a consensus among the dental population. The obstacle, however, becomes after-care since the virus can remain in the air and on the surfaces for several hours. Thus, even with all the care taken during care, the infection may occur at some point.

Given all this information, dental professionals go through a period of uncertainty and concerns. Reducing the patient's viral load would be an alternative to decrease the risk of infection, and thus make the profession safer. Among the recommendations for dental care, preoperative mouthwashes can help reduce viral load. Sarfaraz et al. reported that only 22.6% of dentists were aware of the antiviral action of povidone-iodine and 36.9% of the action of hydrogen peroxide.

Therefore, the objective of the present work is to make a brief narrative review of the mouthwashes recommended for the reduction of the viral load of COVID-19, making it possible to guide professionals.

RESULTS AND DISCUSSION

Mouthwash versus COVID-19

Dental surgeons perform numerous procedures that produce a lot of aerosolization in the clinical environment and present a high risk of contamination by COVID-19. The aerosol produced during dental procedures can travel between 1 and 3 meters, thus facilitating
contamination\textsuperscript{14}. All this information should be evaluated considering the premise that the salivary glands are in constant cyclic activity, so saliva is constantly renewed. With this salivary renewal, the virus becomes present, again in the oral cavity\textsuperscript{15}. Clinical research is currently underway to assess the power of mouthwashes to reduce the viral load of SARS-CoV-2\textsuperscript{9}. On November 29, 2020, only eighteen study protocols involving SARS-CoV-2 and mouthwashes are listed on (https://clinicaltrials.gov)\textsuperscript{16}.

- **Chlorhexidine (CHX)**
  Chlorhexidine gluconate (Chlorhexidine) is a cationic biguanide used as an antiseptic that has a broad spectrum with bactericidal and bacteriostatic properties\textsuperscript{17}. The chlorhexidine may not be effective in killing SARS-CoV-2\textsuperscript{6}. Chlorhexidine has shown limited effectiveness in relation to coronavirus\textsuperscript{9}. In a study by Yoon et al.\textsuperscript{18} it showed that the viral load of SARS-CoV-2 is high in saliva. In addition, he demonstrated that chlorhexidine (0.12%, 15 mL) for 30 seconds is effective in reducing viral load for two hours. Izzetti et al.\textsuperscript{19} argue that there is still a lack of systematic data on the use of chlorhexidine as a mouthwash to reduce the viral load of SARS-CoV-2.

- **Povidone-iodine**
  Povidone-iodine (PVP-I) is a stable chemical complex of polyvinylpyrrolidone and elemental iodine, being a broad-spectrum antimicrobial that is used in the control and prevention of infections\textsuperscript{23,24}. Parhar et al.\textsuperscript{22} believe that the topical application of povidone-iodine (PVP-I) ranging from 0.23% to 7% may help to reduce the viral load and the aerosolization potential of SARS-CoV-2. In a study carried out by Kariwa et al.\textsuperscript{23}, the authors observed that the PVP-I products used for two minutes reduced the infectivity of SARS-CoV by completely inactivating the virus, thus gargling or spraying the throat would have a prophylactic effect.

The use of PVP-I as a mouthwash to reduce viral load in the oral cavity has been studied since the outbreak of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), showing good results in the concentration of 1% of PVP-I with 30-second exposure\textsuperscript{25}. Gargling or rinsing with 0.23% PVP-I has effective bactericidal activity against SARS-CoV, MERS-CoV, and the influenza A (H1N1) virus\textsuperscript{26}. The use of PVP-I is well tolerated by patients and has a low cost and can be used in prophylaxis before patients undergo procedures\textsuperscript{26}. In a review of the literature Farzan and Firouzi\textsuperscript{27} evaluated which mouthwash was most appropriate for the elimination of coronavirus, in this review four studies were found, of which three attest to the efficiency of PVP-I as an effective mouthwash for coronavirus.

Arefin et al.\textsuperscript{28} reported a new approach combining polyethylene protection fields with PVP-I-based mouthwashes. According to the authors, both health professionals and patients should perform preoperative mouthwashes with 10 mL of 1% PVP-I solution, for 1 minute. The authors recommend that, in patients with impaired consciousness, a sponge soaked in 2.5 mL of 1% PVP-I should be used to carefully clean the surface of the oral cavity. Khan and Parab\textsuperscript{29} proposed in their study a similar pre-procedure oral hygiene regime, however with the use of 10 mL of 0.5% PVP-I solution, with mouthwashes for 30 seconds, followed by a 30 second period in which the solution remains at the back of the throat. The authors recommended that health professionals perform this procedure every 2-3 hours. This study showed that both professionals and patients did not report discomfort or allergy to the solution. Meister et al.\textsuperscript{30} reported that Iso-Betadine mouthwash 0%, a product based on iodopolividone, is capable of significantly reducing the infectivity of SARS-CoV-2 to undetectable levels. Imran et al.\textsuperscript{31} suggests that the use of PVP-I has its toxic effects depending on the dose and the contraindications should be evaluated before the prescription. In a review carried out by Burton et al.\textsuperscript{32} he showed concern about the studies on mouthwashes in progress and does not declare whether he will assess adverse effects or changes in the oral or nasal microbiota.

- **Hydrogen peroxide (H\textsubscript{2}O\textsubscript{2})**
  Peng et al.\textsuperscript{33} recommend the use of oxidizing agents to perform mouth rinses before dental procedures, to reduce viral load. In the sequence, other authors reinforced the use of 0.5-1% hydrogen peroxide in reducing the viral load of SARS-CoV-2\textsuperscript{34}. Hydrogen peroxide decomposes to form water, oxygen, and hydroxyl free radicals, which can cleave biomolecules\textsuperscript{17}.

Kampf et al.\textsuperscript{10} reported in a recent review that hydrogen peroxide was effective against coronavirus at a concentration of 0.5%. Catalases present in the patient’s oral environment can inactivate hydrogen peroxide. Therefore, O’Donnell et al.\textsuperscript{35} suggests that this action can be reduced by pre-washing with water. This would increase the effectiveness of hydrogen peroxide. Ortega et al.\textsuperscript{36} question the use of 1% hydrogen peroxide or 0.2% povidone as a mouthwash, so that, so far, these conduct are not based on scientific studies and can cause harm to patients. Most published studies recommend the use of 1% hydrogen peroxide or 0.2% PVP-I as a preoperative mouthwash\textsuperscript{37}.

Gottsauner et al.\textsuperscript{38} evaluated the efficacy of mouthwashes with 20 mL of 1% hydrogen peroxide, with gargling for 30 seconds, through a prospective pilot clinical study. Ten patients were included in the sample, and the authors concluded that there were no significant differences between baseline viral load and viral load after mouthwash with 1% hydrogen peroxide, that is, this solution did not affect reducing intraoral viral load of patients tested positive for...
SARS-CoV-2.

- **Cetylpyridinium chloride (CPC)**
  
  N-hexadecyl pyridinium chloride or cetylpyridinium chloride (CPC) is a water-soluble quaternary ammonium compound, non-oxidizing or corrosive and highly cationic at neutral pH. The CPC works by promoting the inactivation of the virus by destroying the capsid, as well as by its lisosomotropic action. CPC (0.05 ± 0.1%) showed effective activity against MERS-CoV. The 0.05% CPC can be used as a mouthwash using 15ml for 30 seconds due to its oxidizing action.

- **Statin-Based Mouthwashes**

  Statin-based drugs are safe and effective, with antimicrobial, antiviral, antifungal, anti-inflammatory, immunomodulatory and antioxidant properties. Based on these principles Abdulrab et al. raised the hypothesis that the pre-procedure mouthwash of 1% simvastatin solution (dissolution of simvastatin 20 mg tablets in distilled water), used for 15-20 seconds can minimize the risks of transmission of SARS-CoV-2.

**CONCLUSION**

In conclusion, studies on the effectiveness of mouthwashes in reducing the viral load of SARS-CoV-2 are reduced, and so far, the different protocols and substances studied have shown some level of reduction in viral load from saliva. Therefore, the use of PVP-I and the use of cetylpyridinium chloride are the substances that showed the most effective results against SARS-CoV-2; however, more in vitro and in vivo work must be performed.

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CONFLICTS OF INTEREST
The authors declare no conflicts of interests.

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