**Povidone–Iodine Solution: A Potential Antiseptic to Minimize the Risk of COVID-19? A Narrative Review**

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**Objectives:** Patients are mask-free during dental attention. In addition, dentists and dental staff after working for hours need to hydrate or eat. Removing the mask makes them vulnerable to the risk of contamination. For those cases, a prophylactic decontamination protocol could be useful as an adjunct to the most recommended biosecurity protocols. This article aims to provide a comprehensive review of the published evidence about the use of povidone–iodine (PVP-I) against SARS-CoV-2 and to propose a prophylactic protocol for dental attention using PVP-I during the COVID-19 pandemic. **Materials and Methods:** An electronic search in Medline via PubMed, Scopus, Cochrane Library and Scielo databases was performed up to July 24, 2020, to identify relevant literature focusing on Povidone Iodine, SARS-CoV-2, COVID-19, SARS-COV, MERS, antiviral mouthwashes, and oral cavity. **Results:** Clinical studies on the virucidal effectiveness of PVP-I against SARS-CoV-2 have not yet been reported. We identify a recent *in vitro* study showing PVP-I effectiveness at 0.5, 1, and 1.5% within 15 s of contact. Moreover, another *in vitro* study has shown ≥99.99% virucidal activity as 1% mouthwash and 0.45% throat spray. The only study in SARS-CoV-2 confirmed patients reported a significant 3 h drop in viral load after rinsing with 15 mL of 1% PVP-I for 1 min. **Conclusions:** Although no clinical trials have reported the efficacy of PVP-I on SARS-CoV-2, recent studies in patients with positive PCR to SARS-CoV-2 found a significant 3-h drop in viral load. We believe that an oral prophylactic protocol with PVP-I for dental healthcare workers and patients as an adjunct to the current biosecurity protocol could minimize the transmission risk during COVID-19 pandemic. **KEYWORDS:** COVID-19, dentistry, mouthwashes, povidone–iodine, cross-infection

**INTRODUCTION**

The short distance between patients and dentists during dental treatment has an obvious concern in the setting of COVID-19. It has been reported that SARS-CoV-2 can stay in the air for hours, indicating that aerosolizing procedures made during routine dental practice represent a high risk for transmission of SARS-CoV-2. Additionally, some studies have revealed that nasopharynx and oral mucosa epithelium have high expression of the main receptor of SARS-CoV-2, the angiotensin-converting enzyme 2 (ACE2). Moreover, another research has found high viral loads in human saliva, turning the oral cavity into a potential reservoir for aerosolized transmission, and progression of pulmonary diseases. Furthermore, it has been indicated that aerosols of asymptomatic patients also...
contain SARS-CoV-2,[8] suggesting that infection from a nonsymptomatic patient during dental care is highly probable.[2,8]

In a daily routine, dentist and dental staff work for hours needing to stop for hydrating or eating. These moments where they are mask-free could be potentially risky.[9] On the other hand, patients are mask-free during the whole dental treatment.

On the basis of these arguments, the use of preprocedural mouthwash, including oxidative agents, has been suggested to control cross-infection during dental practice.[10] Povidone–iodine (PVP-I) has shown a virucidal activity against the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV).[11,12] In addition, recent evidence has demonstrated its in vitro and in vivo effectiveness against the new SARS-CoV-2,[13-15] encouraging its use for COVID-19 outbreak.

Thus, this article aims to provide a comprehensive review of the published evidence about the use of PVP-I against SARS-CoV-2 and to propose a prophylactic protocol for the dental practice to be easily implemented during the COVID-19 pandemic.

**REVIEW**

**SEARCH STRATEGY**

An electronic search in Medline via PubMed, Scopus, Cochrane Library and Scielo databases was performed up to July 24, 2020, to identify relevant literature focusing on PVP-I, SARS-CoV-2, COVID-19, SARS-CoV, MERS, antiviral mouthwashes, and oral cavity. The search did not apply language or time restrictions. Furthermore, the references of selected articles were hand-searched.

**Povidone–Iodine**

PVP-I is an iodine complex with the water-soluble polymer polyvinylpyrrolidone, developed in the 1950s. It has widely been used as a presurgical antiseptic in the skin and as a mouthwash.[16] The antimicrobial action of PVP-I occurs after free iodine dissociates from the polyvinylpyrrolidone. Then, iodine rapidly penetrates microbes, disrupts proteins, and oxidizes nucleic acid structures causing microbial death.[17]

**THE USE OF PVP-I AGAINST CORONAVIRUSES**

PVP-I has a strong virucidal action that inhibits N1, N2, and N3 neuraminidases and hemagglutinin. PVP-I actively inactivate viral attachment to cell receptors and prevent viral spread.[18] PVP-I has higher virucidal activity than other commonly used antiseptic agents, including chlorhexidine (CHX) and benzalkonium chloride.[19]

In the past, some prophylactic protocols using PVP-I have been suggested to protect highly exposed health care workers (HCW). The Committee for the Japanese Respiratory Society guidelines recommended that hospital patients and HCW should rinse with PVP-I four times per day to reduce the risk of hospital-acquired pneumonia.[20] Given the high homology of SARS-CoV-2 and SARS-CoV,[21] it could be suggested that PVP-I could be effective against the new SARS-CoV-2.[3]

Additionally, many in vitro studies demonstrated its positive effect against multiple coronaviruses, influenza virus A (H1N1), and rotavirus.[16,19,22] In the past, PVP-I oral rinses of 0.23% PVP-I after 15 s of exposure revealed a valuable bactericidal result against Klebsiella pneumoniae and Streptococcus pneumoniae, and inactivation of SARS-CoV, MERS-CoV, influenza virus A (H1N1), and rotavirus.

**Virucidal Activity against SARS-CoV-2**

Clinical studies on the virucidal effectiveness of PVP-I against SARS-CoV-2 have not yet been reported. Recent in vitro studies have shown PVP-I effectiveness at 0.5%, 1%, and 1.5% within 15 s of contact.[13] Anderson et al.[14] have shown ≥99.99% virucidal activity as 1% mouthwash and 0.45% throat spray.

Martinez-Lamas et al.[15] evaluated the effect of PVP-I in four SARS-CoV-2-confirmed patients after rinsing with 15 mL of 1% PVP-I for 1 minute and found a significant 3-h drop in viral load.

**Safety and Tolerance**

Prolonged use of PVP-I does not exhibit adverse side-effects, such as irritation of oral mucosa, discoloration of teeth/tongue, or changes in taste sensation, as seen with CHX.[23]

In the oral mucosa, it has been used safely at doses from 1% to 10% for infection prophylaxis and prevention in upper respiratory tract surgical procedures.[24] Typically, commercial over-the-counter oral mouth rinse formulations are of 1% PVP-I.[25]

Although detectable systemic iodine absorption may happen with long-term use of PVP-I, thyroid disturbances are infrequent.[23] Besides, being a non-alcohol-based solution, its nonflammable property is suitable for electrocautery procedures. Gargled PVP-I is very well tolerated when compared with other oral antiseptic agents.[26]

The recommended daily dose of iodine for an adult is 0.15 mg.[27] Additionally, allergy to PVP-I is extremely
The nasal use of PVP-I was reported in a phase 1 study. The nasal spray of PVP-I did not result in any harm of nasal function or detectable damage to the multilayer ciliated epithelium.[16] As well, the prolonged use up to 28 months of 1% to 1.25% PVP-I mouthwash did not cause adverse effects in the oral mucosa of patients.[3,31] Furthermore, it has been documented that intranasal and oral use of 1.25% to 5% PVP-I is safe up to 5 and 6 months, respectively.[3]

**Preventive protocols for healthcare workers during COVID pandemic that could be applied to dentistry**

It has been suggested that the application of PVP-I to the nasal and oral mucosa of COVID-19 patients may significantly reduce the viral load.[17,31,32]

Challacombe et al.[33] proposed the use of PVP-I for patients before dental treatment. Additionally, a dose of 0.23% PVP-I mouthwash for at least 15 s before procedures has been suggested to reduce the viral load in the patient’s saliva.[12] Moreover, a pre-and postprocedural preventive protocol of PVP-I mouthwash and nasal spray in dental surgeons and dental staff have been recommended as an adjunct to reduce the cross-infection risk during the pandemic.[19,31,33,34]

Mady et al.[31] suggested that PVP-I nasal and oral rinses may be implemented as a complementary form of the personal protective equipment (PPE) currently recommended, especially for frontline HCW exposed to high risk during oncology patients care.

However, it was mentioned that nasal irrigation could be a potential risk of increasing “susceptibility to SARS-CoV-2 infection by affecting mucociliary function or local immunity” of HCW.[34] Kirkley et al.[17] suggested another protocol to be applied during the attention of COVID-19 patients, especially in procedures of the upper aerodigestive tract. Furthermore, they emphasized that, during COVID-19 pandemic, all patients should be considered as infected.[17] They suggested the use of this protocol every 2–3 h up to four times a day while treating patients during the pandemic.

**Preventive protocol for dental healthcare workers and dental patients during COVID pandemic**

Due to the nature of dental treatment and how dental care dynamics are implemented, the authors suggest a variation of the previously cited protocols. We believed that this protocol would offer a potential prophylactic effect with the difference that is easier to implement in dental practice and more comfortable to the patient/dentist.

Like other authors, we recommend concentrations of PVP-I of 1% that are proven to be safe[34,25] when using PVP-I as a repeated application.

For dental patients, the use of this protocol is recommended in the dental office before and after dental treatment. For dental health care workers, it is recommended before hydrating or eating in working hours. Moreover, it is advisable after any accidental mask removal during patient attention. The use of this protocol is an adjunct to the recommended PPE:

1. **Intranasal application[17,31,33]:** gently cleaning each nostril with a cotton swab embedded with 1%[15] PVP-I solution.
2. **15 mL of 1% PVP-I solution as a mouthwash:** disperse all over the mouth, including the back of the throat for 60 s.[15]

**Conclusions**

Although no clinical trials have reported the efficacy of PVP-I on SARS-CoV-2, recent studies in patients with positive PCR to SARS-CoV-2 found a significant 3-h drop in viral load. We believe that an oral prophylactic protocol with PVP-I for dental healthcare workers and patients as an adjunct to the current biosecurity protocol could minimize the transmission risk during COVID-19 pandemic. Meanwhile, clinical research is needed to identify the efficacy of PVP-I against SARS-CoV2.
DATA AVAILABILITY STATEMENT
Not applicable.

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