

Review

Prevention of oral cross-infection by using povidone-iodine compared with other antiseptic agents for orally transmitted diseases: A Review

Ala'a Saif Alqhtani^{1,*}, Abdulkarem Ali Ali Mohammed^{2,3}, Farouk Al-ghazaly⁴, Ahmed Alareqi⁵ and Anis Irmawati⁶

¹Department of Oral Medicine, College of Dentistry, Jibla University for Medical and Health Science, Ibb, Yemen

²Department of Periodontology, Thamar (Dhamar) University, Yemen

³Dental Department, Al-Jazeera University, Ibb, Yemen

⁴Doctoral Study Program, Department of Dental Public Health, Faculty of Dentistry, Universitas Airlangga, Surabaya, Indonesia

⁵Jordan University of Science and Technology, Irbid, Jordan

⁶Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia

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*Correspondence:

Ala'a Saif Alqhtani

Address: Ibbo City, Yemen.

Email: alqhtanialaa@gmail.com

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ABSTRACT

The oral cavity is a high-risk infective site, and highly contagious diseases like viral infections are confirmed to be transmitted through it. Oral rinses are a very important and one of the most important objective methods and topical essential strategies to decrease the spread and transmission of contagious diseases. There is a gap in the literature regarding a comprehensive comparison between povidone-iodine and other formulations in terms of their effectiveness in preventing oral cross-infection and transmission of orally transmitted diseases. The authors performed a comprehensive literature review utilizing Google Scholar, PubMed, and Science Direct to review relevant studies over the previous years on the effectiveness of povidone-iodine in preventing oral cross-infection and transmission of orally transmitted diseases by using these keywords: oral transmitted diseases, povidone-iodine, cross-infection, and antiseptic. This article includes a comprehensive overview of the existing knowledge regarding the effectiveness of povidone-iodine compared with other antiseptic agents in preventing oral cross-infection and transmission of orally transmitted diseases. Povidone-iodine has shown effective antiseptic properties in the oral cavity without disrupting its natural balance. It is a valuable anti-septic preventive oral-transmitted disease for patients and healthcare providers, and there is no evidence to show the side effects over a long time. Povidone-iodine can be safely used as antiseptics for the oral cavity for the prevention of orally transmitted diseases as personal prophylaxis, and it's the most effective mouth rinse for viral infection in the oral cavity due to its fast action.

Keywords: Cross-transmission; cross-infection; antiseptic; COVID-19; oral transmitted diseases; povidone-iodine

1. INTRODUCTION

The oral cavity contains the various anatomical components (tongue, oral mucosa, teeth, saliva, periodontium, etc.) and microbiota that build up the microecosystem in the oral cavity. However, there is a complex ecosystem balance between health and disease, both locally and systemically. On the other hand, infectious agents enter to and from the oral cavity and spread to the digestive and respiratory systems and the oral cavity itself. Moreover, oral microbes have been linked to several epidemiologically contagious diseases.^(1,2)

Highly contagious diseases like viral infections are confirmed to be transmitted by various routes, for example, airborne, droplets, mass gatherings, or touching surfaces (fomites) contaminated by the virus and then touching the mouth or eyes or kissing others, like Ebola or SARS-CoV-2 viral infections.⁽³⁾ Medical care facilities may be hotspots for virus spread, most orally transmitted diseases are pandemics, like COVID-19, and hepatitis B, which puts healthcare and medical workers like dentists, oral and maxillofacial surgeons, ear, nose, and throat surgeons, and anesthesiologists in a critical position. Taking into consideration that Saliva and blood are the main components for viral and bacterial spread, so some infectious diseases are transmitted by saliva mononucleosis that the healthcare and medical workers have direct contact with furthermore, spread through contact with body fluids infected with the virus, such as direct contact with blood or open wounds.⁽⁴⁾

Manner of speaking, Environmental factors are often important for a virus's survival like the ambient humidity, temperature, and pH of the environment they are in, so many viruses survive only a few hours in the environment and are often readily inactivated by common hygiene techniques, using soap and water, and some detergents, disinfectants, and antiseptics. Hence, the use of chemical and mechanical control of contagious viruses is recommended synchronously to guarantee good oral hygiene and potentiate a good oral health state.⁽⁵⁾ Referring to the previous transmission risks, Topical preparations of the oral cavity could be utilized to decrease the infection from and to the oral cavity, potentially reducing the risks of viral and bacterial transmission. The oral rinse is a very important and essential strategy to decrease the spread

and transmission of infectious diseases like viral and bacterial infections. The most important topical method for antiseptics of the oral cavity is using oral rinses.⁽⁶⁾

The oral rinses are a very important and one of the most important objective methods and topical essential strategies to decrease the spread and transmission of contagious diseases such as viral infections for antiseptics of the oral cavity using oral rinses like chemicals containing chlorhexidine can effectively decrease the level of transmission of contiguous diseases but continuous use can cause several local side effects.⁽⁷⁾ On the other hand, Povidone-iodine is a well-known antiseptic agent with broad-spectrum antibacterial, antiviral, and antifungal activity against bacteria, viruses, and fungi respectively. It works particularly well against oral pathogens linked to cross-infections. A promising option for decreasing the spread of oral diseases, povidone-iodine demonstrates excellent and quick bactericidal and virucidal activity.⁽⁸⁾

According to studies the use of povidone-iodine as a pre-procedural rinse helps reduce the oral transmission of COVID-19 when used as an oral rinse, and its actions to decrease the salivary load are noted for up to 6 hours.⁽⁹⁾ Nowadays, the oral rinses used to decrease oral transmission of contagious diseases are an effective strategy. The use of oral raises containing chemicals like chlorhexidine, hydrogen peroxide, etc. agonists for a broad range of viruses, continuous for a long period can cause several local side effects like staining (discolouration on teeth), allergic reaction, irritation of oral mucosa, burning sensation, change taste and in some cases peeling of the gingiva and desquamation of oral mucosal membrane and unpleasant or discomfort after gargling. Furthermore, onset of action, price, concentration, duration of exposure, and availability, etc. The researcher calls to compare the effectiveness of povidone-iodine with other antiseptic agents in preventing oral cross-infection and transmission of orally transmitted diseases and performed a comprehensive comparison between povidone-iodine and other formulations in terms of their effectiveness in preventing oral cross-infection and transmission of orally transmission diseases.

2. METHODS

A literature search in English was performed, comprehensive literature review utilizing Google Scholar and PubMed, ResearchGate and ScienceDirect base to identify relevant studies over the previous years on the effectiveness of povidone-iodine in preventing oral cross-infection and transmission of orally transmitted diseases. This present re-included a comprehensive overview of the existing knowledge regarding the effectiveness of povidone-iodine with other antiseptic agents in preventing oral cross-infection and transmission of orally transmitted diseases. Studies that directly address or contribute to the research topic, and reputable journal articles were included in this study.

3. ORAL CROSS-INFECTION

The oral cavity is a high-risk infective site. Most viral particles are seen in saliva and oral mucosa because the ACE2 receptors are famous in the oral cavity and salivary gland. These receptor-binding domains make orally transmitted diseases like SARS-CoV-2 able to bind to human Angiotensin-converting Enzyme 2 (ACE2) receptors; thus, we see the viral component in saliva and oral mucosa.⁽¹⁰⁾

Saliva is one of the primary modes for transmitting viral infectious particles and a source for the community-wide spread of infection because saliva contains the most viral nucleic acid in diagnostic testing. Salivary droplets can cause infection at a short distance during talking, coughing, and sneezing. Dentists and medical / health workers are at high risk for exposure to contagious diseases like COVID-19 because they are in direct contact with oral mucosa and saliva during the diagnosis and treatment of diseases.⁽¹¹⁾

The use of pre-procedural oral rinses has been investigated to decrease the number of viral particles and bacteria in aerosols, potentially decreasing the risk of cross-infection from SARS-CoV-2 during medical and dental procedures. One of the popular rinses is povidone-iodine, which is effective against SARS-CoV-2 in saliva and could be implemented as an oral rinse before interventions to decrease the risk of cross-infection in healthcare settings.⁽⁹⁾

Most orally transmitted diseases, such as SARS-CoV-2 particles, remain airborne for 3–4 hours. To reduce the incidence of airborne oral and respiratory

viral infections, it is recommended to take povidone-iodine for more than 2 minutes, up to four times a day. Povidone-iodine is a guideline for operative and surgical room care during a viral pandemic for any patient. Variant types such as solutions, swab sticks, and scrubs that are used in external sites must be avoided for the oral cavity because of their co-solvents and minerals.⁽¹²⁾

4. AGENTS FOR ORAL CROSS-INFECTION PREVENTION

Antiseptic agents used for the prevention of oral cross-infection can be categorized based on their chemical structure. This classification helps identify the different groups of antiseptics commonly utilized in oral healthcare. This part presents examples of the most antiseptic groups and highlights their significance in combating orally transmitted diseases.⁽¹³⁾

Antiseptic agents play a pivotal role in the prevention of oral cross-infection, effectively reducing the oral transmission of diseases. Commonly utilized in oral healthcare settings, antiseptic agents such as povidone-iodine, chlorhexidine, hydrogen peroxide, and benzalkonium chloride possess distinct properties and mechanisms of action that contribute to their efficacy in preventing oral cross-infection. These agents act as a defence against the transmission of infectious (contagious) agents through various routes, including inhalation, injection, ingestion, and contact with mucosa or skin. The implementation of infection prevention and control measures is paramount to minimizing the transmission of pathogenic agents between individuals, including patients, healthcare workers, and vice versa. Standard precautions should be universally applied to all patients, while transmission-based precautions are specifically employed when patients are at a heightened risk of transmitting contagious diseases, particularly those that are airborne.⁽¹³⁾

Some orally transmitted infections, including the cross-infection of SARS-CoV-2, may be caused by virus particles in respiratory droplets and aerosols produced during medical/dental treatments. On the other hand, some national COVID-19 advice documents for health and dental settings propose oral decontamination as a valuable adjunct to personal protective equipment in the health and dental field, for instance.⁽¹⁴⁾

SARS-CoV-2 can spread through direct contact, saliva, or respiratory droplets. Controlling the viral load in respiratory secretions and saliva is crucial. The practice of good oral and throat hygiene is one of the most straightforward and economical steps that the general public and healthcare professionals can take to stop cross-contamination and community transmission. Thus, using povidone-iodine mouthwash as a preventative strategy has been encouraged all over the world to lessen the spread of disease. On the other hand, povidone-iodine is recommended for people who are travelling to or coming from a virally infected hotspot.⁽¹¹⁾

Povidone-iodine oral rinse has highly effective virucidal activity against a broad range of viruses, like coronavirus, and is relatively innocent to use in the oral and upper airways. Furthermore, has been decreasing the risk of SARS-CoV-2 aerosolization during oral and upper airway mucosal surgery.⁽¹⁵⁾ The antiseptic povidone-iodine, when used as an oral rinse, has been found to exhibit complete effectiveness in inactivating

the SARS-CoV-2 virus across all concentrations following a 60-second exposure time. In vitro studies have demonstrated the rapid virucidal effect of povidone-iodine oral rinses, with the lowest concentration and shortest contact time of 15 seconds still being effective in inactivating the virus. These findings suggest that povidone-iodine can serve as a valuable personal prophylactic, acting as a protective tool in mitigating the transmission of COVID-19 during the ongoing pandemic.⁽¹⁵⁾

The efficacy of povidone-iodine against oral bacteria and viruses orally transmitted diseases has been studied. Povidone-iodine, specifically at a concentration of 1%, has been considered effective in preventing the spread of COVID-19 during dental procedures and has been proposed as a preventive measure to mitigate the transmission of COVID-19 infections.⁽¹⁶⁾ The role of povidone-iodine in prevention of oral microbial transmission have been represented in Table 1.

Table 1. Role of povidone-iodine in prevention of oral microbial transmission

Microorganism	Route of transmission	Role of povidone-iodine in prevention	Authors
<i>Streptococcus mutans</i>	Direct contact through saliva	Povidone-iodine successfully decreases the microbial burden, prevents <i>Streptococcus mutans</i> from growing, and decreases the chance of transmission.	Yuki Ito <i>et al.</i> , 2020 ⁽¹⁹⁾
<i>Candida albicans</i>	Indirect contact through contaminated surfaces	Povidone-iodine has antifungal properties, effectively killing <i>Candida albicans</i> and preventing its transmission.	Rufino <i>et al.</i> , 2022 ⁽²⁰⁾
Herpes simplex virus (HSV)	Direct contact through oral lesions or saliva	Povidone-iodine decreases the risk of transmission and recurrence by exhibiting virucidal action against HSV.	Khalifa <i>et al.</i> , 2022 ⁽²¹⁾
Human papillomavirus (HPV)	Direct contact through oral-genital contact or saliva	Povidone-iodine has shown efficacy in decreasing the viral load and inhibiting the transmission of HPV.	Capriotti <i>et al.</i> , 2015 ⁽²²⁾
<i>Treponema pallidum</i> (syphilis)	Direct contact through oral lesions or saliva	Povidone-iodine has demonstrated antimicrobial activity against <i>Treponema pallidum</i> , offering potential prevention against syphilis transmission.	Kramer <i>et al.</i> , 2010 ⁽²³⁾
<i>Staphylococcus aureus</i>	Direct contact through saliva or contaminated surfaces	Povidone-iodine exhibits bactericidal activity against <i>Staphylococcus aureus</i> and decreases the risk of transmission and infection.	Lepelletier <i>et al.</i> , 2020 ⁽⁸⁾

Several studies have reported that the use of povidone-iodine mouth rinse in COVID-19 patients did not lead to statistically significant changes in salivary viral load. This was determined by testing the patient's saliva using quantitative polymerase chain reaction (qPCR) at baseline as well as at 30, 60, and 120 minutes

after the oral rinse. Although the viral component appeared to be inactive, the presence of viral RNA was still detectable in vivo through PCR testing. Therefore, further research is warranted to investigate the efficacy of povidone-iodine in reducing the viral load in saliva and the oral cavity following oral rinsing. It is worth

noting that in vitro studies have demonstrated the virucidal effects of povidone-iodine oral antiseptics.⁽¹⁷⁾

The utilization of povidone-iodine in patients undergoing mechanical ventilation, following oral cleaning with water and hydrogen peroxide (H₂O₂) irrigation, has shown potential for effectively managing bacterial growth in oral or pharyngeal fluids. Importantly, this approach has been observed to have minimal impact on the equilibrium of the oral microbiota.⁽¹⁸⁾

As noted, chlorhexidine is another widely used antiseptic agent known for its broad-spectrum antimicrobial properties. It has been extensively studied and shown to effectively decrease the oral microbial load and prevent cross-infection. However, prolonged use of chlorhexidine has been associated with adverse effects such as oral mucosa irritation, tooth and tongue discolouration, rare but fatal allergic reactions to chlorhexidine, and alterations in taste sensation. Conversely, evidence for the effectiveness of chlorhexidine in managing or preventing orally transmitted diseases such as aerosolized viruses remain less certain.⁽²⁴⁾

Another popular antiseptic agent for oral cross-infection prevention is hydrogen peroxide, frequently employed as an antiseptic agent owing to its broad-spectrum antimicrobial activity against various microorganisms. It is sometimes used in oral rinsing and wound irrigation procedures. Nevertheless, the effectiveness of hydrogen peroxide in preventing oral cross-infection may fluctuate based on the concentration utilized and the duration of exposure. Furthermore, prolonged utilization of hydrogen peroxide can result in mucosal irritation, manifesting as redness, a stinging or mild burning sensation, oedema, scaling, crusting, pruritus, and, albeit rarely, hypersensitivity reactions.⁽²⁵⁾

In general terms, benzalkonium chloride is a surfactant with antibacterial characteristics. It has antibacterial properties that can be used to treat a variety of pathogens, including those that are linked to transmitted diseases. However, there is little information on its effectiveness, specifically in the prevention of orally transmitted infections. The Environmental Protection Agency classifies benzalkonium chloride as belonging to toxicity categories II and III, depending on the route of exposure (oral, inhalation, and cutaneous).⁽²⁶⁾

5. POVIDONE-IODINE MECHANISM OF ACTION

Povidone-iodine is a water-soluble iodine complex that has been widely used as a pre-surgical skin antiseptic and as a vaginal and oral rinse.⁽⁸⁾ Povidone-iodine is a mixture of elemental hydrogen iodide, iodine, and povidone. It is considered to oxidize cell membrane lipids and combine with microbial proteins to produce salts through the process of iodination, a type of halogenation. Microbicidal activity against gram-positive and gram-negative bacteria (including spores and *M. tuberculosis*), fungi, protozoa, and the virus's povidone-iodine are broad-spectrum antiseptics. Furthermore, unlike chlorhexidine, this antibiotic acts quickly after application and retains little activity. In one study, it was thought to be a safer alternative to chlorhexidine as a face antiseptic.⁽²⁵⁾

One of the studies that explain the action against a virus is iodine dissociated from polyvinylpyrrolidone, then, iodine rapidly penetrates viral cells to disrupt proteins and oxidize nucleic acid structures, causing viral death. So, most studies recommended mouth rinses with povidone-iodine to reduce the SARS-CoV-2 cross-infection.⁽²⁷⁾

6. COMPARATIVE ANALYSIS OF POVIDONE-IODINE

In vitro and in vivo studies have indicated that povidone-iodine solutions, at concentrations of 10% and 7.5%, exhibit rapid and superior bactericidal activity compared to chlorhexidine and mupirocin, respectively, against certain oral microbially transmitted diseases. Additionally, povidone-iodine solutions at concentrations of 10% and 5% have demonstrated effectiveness against strains that are resistant to both chlorhexidine and mupirocin. These findings highlight the potential of povidone-iodine as an effective antimicrobial agent for combating oral microbial-transmitted diseases, including those caused by resistant strains.⁽⁸⁾

Povidone-iodine oral antiseptic mouth rinse in vitro is fully inactivated SARS-CoV-2 virus at the lowest contact time, so it's preferred use during the COVID-19 pandemic more than hydrogen peroxide.⁽²⁸⁾ In the context of decreasing the transmission of viral infections, such as the SARS-CoV-2 virus, among young and healthy men, the utilization of povidone-iodine as

a chemoprophylaxis has demonstrated superior effectiveness compared to Vitamin C. Notably, povidone-iodine exhibits higher viricidal activity when compared to other commonly recommended antiseptic agents, including chlorhexidine, hydrogen peroxide, and benzalkonium chloride.⁽²⁹⁾

Comparative studies have been carried out to assess how well various antiseptic substances guard against oral cross-infection. These investigations have demonstrated that, when compared to benzalkonium chloride, hydrogen peroxide, chlorhexidine, and povidone-iodine, they demonstrate superior and faster bactericidal and virucidal activity. In contrast to several other antiseptic agents, povidone-iodine has been reported to have a negligible effect on the equilibrium of the oral microbiota. On the other hand, the present studies do not properly support or provide evidence for oral antiseptics' capacity to reduce human virus loads or the rate at which viral diseases advance.⁽³⁰⁾

7. SAFETY AND SIDE EFFECTS

Some studies found no significant impact of povidone-iodine on viral RNA quantification. Moreover, minimal differences were observed in viral titers between baseline and day 1, and thyroid-stimulating hormone levels exhibited changes in all patients after 5 days of povidone-iodine exposure, returning to the normal range after 7–12 days. No discernible differences were observed in T3, T4 thyroid hormone, or creatinine levels.⁽³¹⁾

Povidone-iodine allergy and contact sensitivity are rare when using up to a concentration of 5% in oral mucosa; additionally, no clinical thyroid disease is shown in chronic mucosal use. We can use povidone-iodine for up to 6 months in the oral cavity as a mouth rinse.⁽³²⁾ Extended utilization of povidone-iodine does not demonstrate any unfavourable side effects, including oral mucosa irritation, teeth or tongue discolouration, or alterations in taste perception, which are commonly associated with the use of chlorhexidine.⁽²⁷⁾

Povidone-iodine consumption when pregnant is related to neonatal hypothyroidism, which is defined by inadequate thyroid activity in neonates and has been related to a potential risk of neonatal. Povidone-iodine overexposure can interfere with the production of thyroid hormones and affect the thyroid gland's proper operation in both the mother and the growing fetus.

This raises questions about possible negative consequences for prenatal thyroid function. Hypothyroidism in newborns can have a substantial impact on their growth, development, and general health. Therefore, to reduce the risk of neonatal hypothyroidism, healthcare and dental hygiene professionals should carefully consider the advantages and dangers and use caution when prescribing or suggesting povidone-iodine or any antiseptic agent to pregnant persons.⁽³³⁾

8. RECOMMENDATIONS AND FUTURE DIRECTIONS

Povidone-iodine has to be more effective at preventing oral transmission diseases, and there are many ways to do this, including carrying out carefully planned clinical trials to gauge its efficacy in a range of populations and oral healthcare settings. Research must be done thoroughly to establish the ideal povidone-iodine concentration and exposure duration. Povidone-iodine's relative effectiveness can be better understood by doing comparative research with different antiseptics.⁽³⁴⁾

Future research should focus on examining its mechanisms of action, considering combination therapy, evaluating long-term safety, boosting patient education and compliance, creating new formulations and delivery systems, and performing cost-effectiveness assessments. The outcomes of public health initiatives aimed at avoiding or reducing oral transmitting illnesses will be improved as a result of these efforts, which will also help to optimize the usage of povidone-iodine in this regard.⁽³⁵⁾

9. CONCLUSION

Povidone-iodine oral rinses have the potential to decrease and prevent oral cross-infection pathogens and is a very important and essential strategy to prevent the spread and transmission of contagious diseases like viral and bacterial infections. Furthermore, can be safely used as an antiseptic for a long period in the oral cavity for the prevention of oral transmission of contagious diseases as personal prophylaxis, before any medical, and dental operation like maxillofacial surgeries, nose, and throat surgeries, and intubation procedures and it's the most effective oral rinse for viral infection in the oral cavity due to its fast action when

compare with others antiseptic agents. Shortly, researchers hope that this literature review can carry out further tests including in vitro, and in vivo tests as well as clinical trials to evaluate long-term safety, boost patient education and compliance, create new formulations and delivery systems, and perform cost-effectiveness assessments. Additionally, researcher hopes that further Povidone-iodine oral rinses can be produced and used by dentists, surgeons and the public to prevent the transmission of contagious diseases with minimal side effects.

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Conflict of Interest

The authors declare no conflict of interest.

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