Review Article

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

Carmen Castro-Ruiz, Andrea Vergara-Buenaventura

Department of Periodontology, School of Dentistry, Universidad Científica del Sur, Lima, Peru

Abstract

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*

Received : 29-06-20
Revised : 28-07-20
Accepted : 02-08-20
Published : 19-10-20

Introduction

The short distance between patients and dentists during dental treatment has an obvious concern in the setting of COVID-19.[1] It has been reported that SARS-CoV-2 can stay in the air for hours,[2,3] indicating that aerosolizing procedures made during routine dental practice represent a high risk for transmission of SARS-CoV-2.[4]

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).[5-7] 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.[2] Furthermore, it has been indicated that aerosols of asymptomatic patients also

Access this article online

Quick Response Code:

Website: www.jispcd.org

DOI: 10.4103/jispcd.JISPCD_304_20

Address for correspondence: Dr. Carmen Castro Ruiz, Universidad Científica del Sur, Calle Cantuarias 398, 15048, Miraflores, Lima, Perú.
E-mail: ccastro@ucientifica.edu.pe

How to cite this article: Castro-Ruiz C, Vergara-Buenaventura A. Povidone–iodine solution: A potential antiseptic to minimize the risk of COVID-19? A narrative review. J Int Soc Prevent Communit Dent 2020;10:681-5.

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* effectivity 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.[25] 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

rare, with a prevalence of 0.4%[28] and reports of type 1 allergy are considered exceptional.[29]

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.[30] 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.[31] 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[24,25] 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.

Acknowledgement

Not applicable.

Financial support and sponsorship

This research received no external funding.

Conflicts of interest

The authors declare that they have no conflicts of interest

Author contribution

CCR: conception. AVB and CCR: design of the manuscript, review for relevant intellectual content, writing-review and editing, and final approval of the version to be published. CCR and AVB Writing-original draft

Ethical policy and institutional review board statement

Not applicable.

Patient declaration of consent

Not applicable.

Data availability statement

Not applicable.

References

1. Dexter F, Parra MC, Brown JR, Loftus RW. Perioperative COVID-19 defense: An evidence-based approach for optimization of infection control and operating room management [published online ahead of print, March 26, 2020]. Anesth Analg 2020. doi:10.1213/ANE.0000000000004829
2. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, *et al*. SARS-COV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 2020;382:1177-9.
3. Frank S, Capriotti J, Brown SM, Tessema B. Povidone-Iodine use in sinonasal and oral cavities: A review of safety in the COVID-19 era [published online ahead of print June 10, 2020]. Ear Nose Throat J 2020. doi:10.1177/0145561320932318
4. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, *et al*. Molecular and serological investigation of 2019-ncov infected patients: Implication of multiple shedding routes. Emerg Microbes Infect 2020;9:386-9.
5. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, *et al*. SARS-cov-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020;181:271-280.e8.
6. Kronbichler A, Effenberger M, Eisenhut M, Lee KH, Shin JI. Seven recommendations to rescue the patients and reduce the mortality from COVID-19 infection: An immunological point of view. Autoimmun Rev 2020;19:102570.
7. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, *et al*. High expression of ACE2 receptor of 2019-ncov on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:8.
8. Al-Sadeq DW, Nasrallah GK. The incidence of the novel coronavirus SARS-CoV-2 among asymptomatic patients: A systematic review [published online ahead of print July 2, 2020]. Int J Infect Dis 2020. doi:10.1016/j.ijid.2020.06.098
9. Cheung SSL, Wong CYK, Chan JCK, Chan CKM, Lam NM, Yuen HKL, *et al*. Ophthalmology in the time of COVID-19: Experience from Hong Kong Eye Hospital. Int J Ophthalmol 2020;13:851-9.
10. Herrera D, Serrano J, Roldán S, Sanz M. Is the oral cavity relevant in SARS-cov-2 pandemic? Clin Oral Investig 2020;24:2925-30.
11. Eggers M, Eickmann M, Zorn J. Rapid and effective virucidal activity of povidone-iodine products against middle east respiratory syndrome coronavirus (MERS-COV) and modified vaccinia virus ankara (MVA). Infect Dis Ther 2015;4:491-501.
12. Eggers M, Koburger-Janssen T, Eickmann M, Zorn J. In vitro bactericidal and virucidal efficacy of povidone-iodine gargle/mouthwash against respiratory and oral tract pathogens. Infect Dis Ther 2018;7:249-59. doi:10.1007/s40121-018-0200-7
13. Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B. Rapid in-vitro inactivation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using povidone-iodine oral antiseptic rinse. J Prosthodont 2020. [published online ahead of print, 2020 Jun 8] doi:10.1111/jopr.13209
14. Anderson DE, Sivalingam V, Kang AEZ, Ananthanarayanan A, Arumugam H, Jenkins TM, *et al*. Povidone-iodine demonstrates rapid in vitro virucidal activity against SARS-CoV-2, the virus causing COVID-19 disease [published online ahead of print July 8, 2020]. Infect Dis Ther 2020;1-7. doi:10.1007/s40121-020-00316-3
15. Martínez Lamas L, Diz Dios P, Pérez Rodríguez MT, *et al*. Del Campo Pérez V, Cabrera Alvargonzalez JJ, López Domínguez AM, *et al*. Is povidone-iodine mouthwash effective against SARS-CoV-2? First in vivo tests [published online ahead of print July 2, 2020]. Oral Dis 2020. doi:10.1111/odi.13526d
16. Parhar HS, Tasche K, Brody RM, Weinstein GS, O'Malley BW Jr, Shanti RM, *et al*. Topical preparations to reduce SARS-CoV-2 aerosolization in head and neck mucosal surgery. Head Neck 2020;42:1268-72.
17. Kirk-Bayley J, Sunkaraneni V, Challacombe S. The Use of Povidone Iodine Nasal Spray and Mouthwash During the Current COVID-19 Pandemic May Reduce Cross Infection and Protect Healthcare Workers. 2020 May [cited June 7, 2020]. Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3563092 [Last accessed on 2020 Sep 14].
18. Sriwilaijaroen N, Wilairat P, Hiramatsu H, Takahashi T, Suzuki T, Ito M, *et al*. Mechanisms of the action of povidone-iodine against human and avian influenza A viruses: Its effects on hemagglutination and sialidase activities. Virol J 2009;6:124.
19. Kariwa H, Fujii N, Takashima I. Inactivation of SARS coronavirus by means of povidone-iodine, physical conditions and chemical reagents. Dermatology (Basel) 2006;212(Suppl 1):119-23.
20. Committee for the Japanese Respiratory Society Guidelines in Management of Respiratory. Prevention of hospital-acquired pneumonia (strategies for prevention of hospital-acquired infections). Respirology 2004;9:48-50.
21. Yu F, Du L, Ojcius DM, Pan C, Jiang S. Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in wuhan, china. Microbes Infect 2020;22:74-9.
22. Eggers M. Infectious disease management and control with povidone iodine. Infect Dis Ther 2019;8:581-93.
23. Slots J. Selection of antimicrobial agents in periodontal therapy. J Periodontal Res 2002;37:389-98.
24. Tsuda S, Soutome S, Hayashida S, Funahara M, Yanamoto S, Umeda M. Topical povidone iodine inhibits bacterial growth in the oral cavity of patients on mechanical ventilation: A randomized controlled study. BMC Oral Health 2020;20:62.
25. Ader AW, Paul TL, Reinhardt W, Safran M, Pino S, McArthur W, *et al*. Effect of mouth rinsing with two polyvinylpyrrolidone-iodine mixtures on iodine absorption and thyroid function. J Clin Endocrinol Metab 1988;66:632-5.
26. Shiraishi T, Nakagawa Y. Evaluation of the bactericidal activity of povidone-iodine and commercially available gargle preparations. Dermatology (Basel, Switzerland) 2002;204(suppl):37-41. doi:10.1159/000057723
27. World Health Organization, ICCIDD U. Recommended iodine levels in salt and guidelines for monitoring their adequacy and effectiveness. 1997. Available from: https://apps.who.int/iris/bitstream/handle/10665/63322/WHO_NUT_96.13.pdf?ua=1 (accessed June 11 2020).
28. Lachapelle JM. Allergic contact dermatitis from povidone-iodine: A re-evaluation study. Contact Dermatitis 2005;52:9-10.
29. Lachapelle JM. A comparison of the irritant and allergenic properties of antiseptics. Eur J Dermatol 2014. doi:10.1684/ejd.2013.2198

30. Gluck U, Martin U, Bosse B, Reimer K, Mueller S. A clinical study on the tolerability of a liposomal povidone-iodine nasal spray: Implications for further development. ORL J Otorhinolaryngol Relat Spec 2007;69:92-9.
31. Mady LJ, Kubik MW, Baddour K, Snyderman CH, Rowan NR. Consideration of povidone-iodine as a public health intervention for COVID-19: Utilization as "personal protective equipment" for frontline providers exposed in high-risk head and neck and skull base oncology care. Oral Oncol 2020;105:104724.
32. Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int J Oral Sci 2020;12:9. doi:10.1038/s41368-020-0075-9
33. Challacombe SJ, Kirk-Bayley J, Sunkaraneni VS, Combes J. Povidone iodine. Br Dent J 2020;228:656-7. doi:10.1038/s41415-020-1589-4
34. Pattanshetty S, Narayana A, Radhakrishnan R. Povidone-iodine gargle as a prophylactic intervention to interrupt the transmission of SARS-CoV-2 [published online ahead of print, 2020 Apr 30]. Oral Dis 2020. doi:10.1111/odi.13378