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Am J Otolaryngol 41 (2020) 102618

Contents lists available at ScienceDirect

Am J Otolaryngol

journal homepage: www.elsevier.com/locate/amjoto

Repurposing 0.5% povidone iodine solution in otorhinolaryngology practice in Covid 19 pandemic

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ARTICLE INFO

Keywords:
Povidone iodine
SARS Cov
SARS CoV 2
MERS
Prophylaxis
Gargles
Nasal spray

ABSTRACT

SARS CoV 2 is very much homologous in structure to SARS CoV. Review of literature suggests the in-vitro virucidal action of povidone iodine in SARS CoV and MERS. The oropharynx and nasopharynx are target sites of SARS CoV 2. A significant proportion of COVID 19 sufferers are asymptomatic, but shedding these viral particles, PVP-I has been shown to be a safe therapy when used as a mouthwash or taken nasally or used during ophthalmic surgeries.

Aims:

1. To propose the use of 0.5% Povidone iodine gargles and nasal drops as prerequisite for office based nose and throat examination and procedures during COVID 19 pandemic.
2. To assess tolerability of 0.5% PVP-I in patients and in healthcare workers.

Materials and methods: 0.5% PVP-I solution is prepared from commercially available 10% PVP-I solution. Patients were instructed to put 0.5% PVP-I drops in nose and rinse mouth with gargle prior examinations for 30 s. For endoscopic procedure (nasal and throat) nasal douching and gargling to be started one day prior. Douching and rinsing to be repeated just before procedures. Nasal packing with 0.5% PVP-I along with 4% xylocaine/adrenaline solution, tolerability and any allergic reaction noted.

Results: The patient and health care workers tolerated the 0.5%. No allergy was noted.

Conclusion: We propose the use of 0.5% PVP-I in healthcare workers and their patients to minimise the risk of spread of the disease in addition to the recommended PPE.

1. Introduction

Iodine has been recognized as an effective bactericidal agent since the 1800s. Povidone-iodine (iodine with the water-soluble polymer polyvinylpyrrolidone, PVP-I) was discovered in 1955 at the Industrial Toxicology Laboratories in Philadelphia by H. A. Shelanski and M. V. Shelanski. It was developed so as to find an alternative form of antimicrobial iodine complex that was less toxic than tincture of iodine. The onset of antimicrobial action of PVP-I starts when free iodine [1] dissociates from the polymer complex. The free form of iodine rapidly penetrates microbes disrupting proteins and oxidising nucleic acid structures resulting ultimately in microbial death. PVP-I antibacterial activity is enhanced by dilution of the usually available 10% w/w cutaneous solution, from 1:2 dilution up to a 1:100 dilution (0·1%), with a reduction in activity occurring beyond 1:100 [2,3]. PVP-I has higher virucidal activity than other commonly used antiseptic agents including chlorhexidine [4] and benzalkonium chloride. PVP-I has been shown to be active in-vitro against the coronaviruses that have caused epidemics of SARS (severe acute respiratory syndrome epidemic of 2002–2003) and MERS (Middle East respiratory syndrome epidemic of 2012–2013) [5,6].

SARS-CoV-2 causing the COVID 19 Pandemic is highly homologous with SARS-CoV [7]. In-vitro study by Eggers et al. [5] on the virucidal activity of PVP-I against MERS-CoV showed that the lowest concentration of PVP-I to be effective was 1% when used for 30 s under "dirty" conditions, leading to a reduction of viral activity of ≥99.99%; but not effective at 0·1% [5]. In subsequent in-vitro work by Eggers et al. [6], the lowest concentration tested and effective against coronaviruses, was 0·23%. Kariwa et al. showed that in vitro treatment of SARS-CoV with various preparations of PVP-I for 2 min reduced the viral activity to untraceable levels [8]. The lowest concentration throat spray (Isodine Nodo Fresh®) of 0.23% was used in Japan. In many orthopaedic and ophthalmic surgeries PVP-I is used as preoperative agent for Decolonization of Nasal *Staphylococcus aureus* and many infections

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https://doi.org/10.1016/j.amjoto.2020.102618
Received 5 June 2020

[9–11]. In many ophthalmic surgeries, different dilutions of PVP-I are used for avoiding contamination and it is well tolerated [12].

The oropharynx and nasopharynx are the target sites of novel coronavirus with the result that saliva contains a high viral load of COVID 19 with up to 1.2×10^8 infective copies/per ml [13]. As an otorhinolaryngologist is closely working in this area, there is a significant risk of exposure during routine office based examinations of Ear, Nose and Throat and many endoscopy procedures. Even a few microliters of saliva contamination of surfaces or instruments may carry many thousands of infectious viral particles. Though asymptomatic, the viral shedding initial phase of COVID 19 is highly infectious [14]. At present there are no universal guidelines either for preoperative testing or for treatment of for COVID 19, and individual hospitals are creating their own protocols of treatment and prophylaxis. Povidone Iodine (PVP-I) has better antiviral activity than other antiseptics such as chlorhexidine [4] and has already been proven to be an effective virucidal in vitro against similar coronaviruses (SARS –CoV and MERS-Cov) [5,6,8] although it has not been tested directly with COVID 19. Hence, we propose the use of 0.5% PVP-I as gargles and nasal drops as a prerequisite for patients attending ENT Out-Patient department and health care workers attending these patients.

2. Methods and materials

All health care workers and patients attending out-patient department for consultations and for ENT endoscopies in the month of May were included in the study. This included patients with no symptoms of COVID-19 having procedures in or around the mouth and nose or procedures that transit those areas and the healthcare professionals carrying out those procedures due to the high incidence of asymptomatic infection.

2.1. Exclusion criteria

Patients with history of allergy to PVP-I, all forms of thyroid disease or on radioactive iodine treatment, lithium therapy, known pregnancy, renal failure and dermatitis were excluded from the study. The protocol can be used in children as a single application for Nose, Throat examination after excluding allergy.

The detailed protocol adopted is as follows:

In the hospital setting, we propose application of 0·5% PVP-I solution (0·55 mg/mL available iodine) as gargles onto the oral, oropharyngeal mucosa and as nasal drops onto nasal and nasopharyngeal mucosa of patients with suspected/confirmed COVID-19 and the healthcare workers in close contact with such patients and all routine patients seeking ENT consultation whose COVID 19 status is unknown. Additionally, the application of 0.5% PVP-I can be used for oral surgery, ENT examination and treatment, *endo*-tracheal intubation, endoscopy and bronchoscopy as a preoperative preparation.

Preparation of 0.5% solution of PVP-I from commercially available solution:

A. Povidone Iodine IP 10% v/w in purified water IP q.s.: Use 1 ml of PVP-I in 20 ml of sterile water/purified water.
B. Povidone Iodine IP 5% v/w in purified water IP q.s.: Use 1 ml of PVP-I in 10 ml of sterile water/purified water.
C. Povidone Iodine IP 7.5% v/w in purified water IP q.s.: Use 1 ml of PVP-I in 15 ml of sterile water/purified water.
D. Povidone Iodine IP 2.5% v/w in purified water IP q.s.: Use 1 ml of PVP-I in 5 ml of sterile water/purified water.

Method of application:

1. For ENT Examination and for endoscopies
   Step 1 – for all patients/healthcare professionals: The 0·5% PVP-I solution is administered in a dose of 4–5 drops into each nostril 10 min prior to examination. For endoscopic procedure, nasal pack with PVP is used and prior nasal douching 2 times prior day.
   Step 2 – conscious patients and healthcare professionals: 10 ml of the 0·5% PVP-I solution is then introduced into the oral cavity and used as a mouthwash. Care is taken to ensure the solution is distributed throughout the oral cavity for 30 s and then gently gargled or held at the back of the throat for another 30 s before spitting out.
2. For hospitalised patients: Patients hospitalised for confirmed/suspected COVID 19 and the involved healthcare workers: Steps 1 & 2 should be undertaken every 6 h for patients and up to four times per day for healthcare workers (maximal frequency two hourly). For healthcare workers, it is advised that steps 1 & 2 are performed prior to contact with the patients and if repeated contact is occurring, steps 1 and 2 are at a frequency up to 4 times in a day or repeated every 2–3 h.
3. Endoscopy and bronchoscopy and any other action to be carried out close to or in the mouth or nose: The patient should undergo steps 1 & 2 prior to examination or treatment. Healthcare workers conducting the procedure or in close proximity should perform steps 1 & 2 prior to contact with the patient and if multiple patients are being seen, repeat every 2–3 h, up to 4 times a day. Dosages are the same as above, but are single exposures for patients.

3. Results

All the patients and the health care workers were enquired for any irritation or discomfort following nasal douching and gargling. A total of 315 patients were evaluated and underwent nose and throat endoscopies. All except 7 were comfortable with PVP-I gargles and nasal drops (Table 1). 17 health care workers used the 0.5% PVP-I nasal drops and gargles. No allergy was reported by any of the patients and health care workers.

4. Discussion

PVP-I is being extensively used worldwide as a handwashing agent (usually a 7·5% solution containing foaming agents), for pre-procedural skin antisepsis [15] (usually simply as a 10% solution), in ophthalmic surgery [10,12] (often diluted to 5%) and in oral surgery as 10%. The PVP-I is commercially available in the Far East as a 1% w/v mouthwash for use every 2–4 h [16]. It is assumed that using a concentration twice as strong as that found to be virucidal in vitro (0·5% versus 0·23% [5,8]) will be effective to allow for dilution due to saliva as the exact effective concentration of PVP-I in the presence of mucins and saliva is not known.

The intranasal topical application of 0.08% solution of iodine for the treatment of recalcitrant chronic rhinosinusitis has been described by the St. Paul's Sinus Centre team in Vancouver [17,18]. This application did not cause any significant effect on thyroid function, mucociliary clearance or olfaction. PVP-I use in the nasal cavity to reduce infection or spread is rational for COVID-19 after two recent trials have demonstrated higher viral load there when compared with the oral cavity [5,6,8].

PVP-I gargles are very well tolerated as compared to other antiseptic agents gargles [4]. It has been demonstrated in clinically successfully

Table 1
Procedure wise age -gender distribution of the study population.

Age in years	Nasal endoscopy		Throat endoscopy		Total
	Male	Female	Male	Female	
18 to 30	32	27	26	15	100
31 to 45	26	39	17	20	102
> 45	39	25	25	24	113
Total	97	91	68	59	315

trials that nasal administration and mouthwash reduced pharyngeal bacterial colonization and subsequent reduction in the incidence of nosocomial pneumonia [19]. Povidone-Iodine-Based Solutions are used as preoperative asepsis preparation in many planned orthopaedic and ophthalmic surgeries for Decolonization of Nasal microbes [9,10].

Considering the antiviral actions of Povidone Iodine at various sites including the extensive use by ophthalmologists for a delicate sensitive special sense organ concerned with vision [10–12], there is absolutely no harm in repurposing 0.5% PVP-I to another two special senses' organ for extrapolating its probable antiviral action against SARS CoV 2. A significant proportion of COVID 19 sufferers are asymptomatic, but shedding these viral particles. And pre-procedure testing for COVID 19 infection, may not be feasible in all patients attending the clinic. Moreover, a false negative test creates a pseudo feeling of security amongst the health care workers. The evidence presented suggests that application of povidone iodine to the nasal and oral mucosa, oropharynx and nasopharynx of patients with COVID-19 may significantly reduce the viral load in these key anatomical areas. This will definitely help to reduce the risk of transmission to health care workers. It also allows a time period to perform procedures at reduced risk. Further reduction of risk of transmission may be achieved by similar application of PVP-I to the HCW providing the care as a form of prophylaxis. We therefore propose that for the duration of the current COVID-19 pandemic. At low concentrations, staining of teeth is minimal and reversible.

We do accept that direct testing and demonstration of the virucidal activity of PVP I against SARS-CoV-2 has not been yet documented. However, the experience gained from the previous studies by Eggers et al. [5,6] showing in vitro virucidal action of PVP-I in SARS COV and MERS [8], we propose to use it for reduction of SAR-CoV-2 viral load in the oral cavity to prevent COVID 19 transmission in the suggested manner. We propose this protocol for disinfection of the oral, oropharyngeal, nasopharyngeal and nasal cavities, similar to the recommended practice of hand sanitisation for transmission reduction. It will potentially prevent the infected patients from passing on the virus and at a portal of virus entry for HCW (potentially protecting them from being infected via the nose/mouth). It is accepted that aerosolised secretions from the lower respiratory tract almost certainly have a part to play in disease transmission and therefore that this proposal forms only part of the strategy to reduce transmission, in addition to the use of personal protective equipment by the health care workers.

We propose that protocolled nasal drops/douching and oropharyngeal wash of PVP-I should be used in current COVID 19 pandemic to limit the spread of SARS – COV-2 from patients to healthcare workers and potentially vice versa. We propose that no office based ENT examination, office based endoscopic procedures, planned surgical procedures and intubation should be carried out without disinfection by PVP-I. Although, we have not estimated the effective reduction in the viral titres of coronavirus 2, but we theoretically presume depending on past studies that the reduction in the titres is possible and can last at least for 20 min in vivo [5,6,8]. The reduction in the titres as well as the length of time for which antisepsis remains has to be researched by various randomised controlled studies. A risk free time of 20 min following the use of PVP-I should be sufficient for examination and short procedures. The question of total iodine exposure seems well within previously recorded safe limits in those without contraindications to its use (history of allergy [20] to PVP, thyroid diseases [21], dermatitis [22] etc.) as only PVP-I is used just before examination. Urgent consideration should be given to the application of PVP-I to patients and HCWs as described above.

The points in favour of the study:

1. Previous studies proving the effectiveness of PVP-I against MERS and SARS CoV
2. The structural similarity of SARS CoV, SARS CoV 2 and MERS
3. 0.5% PVP-I is easy to prepare and is inexpensive
4. PVP-I has been shown to be a safe therapy when used as a mouthwash or taken nasally
5. It is easy to dispense to patients and to health care workers
6. No reported allergies
7. Though not proved, it probably reduces the viral titres of SARS CoV 2

Limitations: Quantitative studies estimating the total reduction of the viral titres of SARS CoV 2 and the time duration for which the antiviral activity lasts.

5. Conclusion

With the considerable past evidence of benefit of the use of PVP-I antiseptic against SARS Cov and MERS in maintenance of oral health prevention and treatment of oropharyngeal infections, we propose the immediate use of PVP-I in healthcare workers and their patients as described to minimise the risk of spread of the disease as an addition to currently recommended PPE used during management of COVID-19 patients. Amidst the deadly menace, we are extrapolating the in vitro efficacy of very economical PVP-I to apply it for in vivo use as there is no harm in considering the potential use of PVP-I in reducing Viral load in oropharyngeal and nasal cavities.

Funding

This study was not financially supported from external sources.

Declaration of competing interest

None.

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