

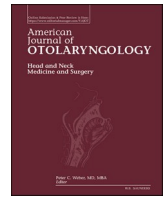


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Tolerability and usability of 0.5% PVP-I gargles and nasal drops in 6692 patients: Observational study[☆]

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ABSTRACT

Objectives:

1. To assess the feasibility and usability of 0.5% PVP-I gargles and nasal drops in patients attending ENT consultations for a period of 5 months as a pre requisite prior to ENT examination.
2. To assess the tolerance of 0.5% PVP-I in these patients for regular use for a period of 8 days.

Study design: Observational study.

Setting: Secondary care ENT Centre.

Methods: All patients attending the hospital for office ENT consultations from 15th April 2020 to 15th September 2020 were included in the study. A total of 6692 office patients were evaluated for feasibility, usability and tolerability of the 0.5% PVP-I gargles and nasal drops.

Results: Overall practicability of using 0.5% PVP-I gargles and nasal drops at office level was assessed in terms of feasibility and usability. Feasibility and usability was considered in terms of the ease of the dispensing method of the 0.5% PVP-I gargles and nasal drops by the health care workers to the patients prior to ENT examination. Tolerance was assessed in terms of altered taste, staining of teeth or nasal skin or irritation in the nose. None reported any serious reactions or adverse effects following use of 0.5% PVP-I.

Conclusion: The study reports the successful feasibility and usability of 0.5% PVP-I gargles and nasal drops and bears the potential to provide benefits in preventing transmission from the patients to the health care workers and vice versa.

Level of evidence: 4.

1. Introduction

SARS-CoV-2, which causes Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China in late December 2019 and was declared as a public health emergency of international concern by the World Health Organization (WHO) on January 30, 2020. The SARS CoV2 virus is transmitted through respiratory droplets via coughing, sneezing and physical contact from contaminated surfaces to the mucosa. Transmission reduction by the minimization of aerosolized virus is of key importance. At present, there is neither any treatment nor vaccine for COVID-19 infection besides preventive measures recommended by the WHO like hand washing and maintaining social distance. Povidone-iodine (PVP-I) is an antiseptic that has primarily been used for the prevention or management of wound infections for more than a century.

Its antibacterial, antiviral, and antifungal properties and its safety have been well-documented. Studies by Eggers et al. [1,2] have demonstrated the in vitro antiviral activity of PVP-I against the coronaviruses that have caused epidemics of SARS (severe acute respiratory syndrome epidemic of 2002–03) and MERS (Middle East respiratory syndrome epidemic of 2012–13) [1,2] Their in-vitro study [1,2] showed that the lowest concentration of PVP-I effective was 0.23%. We have been using PVP-I as gargles and nasal drops in the concentration of 0.5% to compensate for the dilution of the PVP-I in saliva and nasal secretions. It was started as a protective measure for our health care workers in the tough COVID times due to the similarity of SARS CoV and SARS CoV-2 and the virucidal action of PVP-I in SARS CoV. 0.5% PVP-I wasn't commercially available. Hence we prepared it from commercially available 10% PVP-I solution and used it as nasal drops and gargles as a

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pre requisite before otorhinolaryngological office consultations. We report the use of 0.5% PVP-I gargles and nasal drops in 6692 patients (irrespective of the COVID status) attending clinic for otorhinolaryngologic consultations as a prophylactic measure on the oropharyngeal and nasopharyngeal mucosa. In our previous study [3] about the repurposing of the 0.5% PVP-I nasal drops and gargles, we have proposed that protocolled 0.5% PVP-I nasal drops and oral gargles 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 have also proposed the use of 0.5% PVP-I as an irrigation fluid to reduce the viral load in oropharyngeal, nasal cavities, and middle ear and mastoid during surgeries [4]. In this study, we report the feasibility and usability of the dispensing of the nasal drops and gargles as primary end points and tolerance as the secondary end point.

2. Methods and materials

An observational study was carried out on the total number of patients attending Otorhinolaryngology consultations at our Secondary care ENT centre for a period of 5 months from 15th April to 15th September 2020. These patients were dispensed with 0.5% PVP-I gargles and nasal drops 15 min prior to examination. This included patients with or without symptoms of COVID-19 and having procedures in or around the mouth and nose or procedures that transit these areas. The patients with thyroid disease, previous known allergies to PVP-I, children below 5 years, pregnant and lactating women were excluded from the study. A total of 6692 office patients attending ENT consultations at our hospital were evaluated for feasibility, usability and tolerability of the 0.5% PVP-I gargles and nasal drops. Written consent was taken in all the patients for use of 0.5% PVP-I prior to examination. The mean average of otorhinolaryngology consultations done per day is 51.47. Month-wise distribution of the study group is tabulated in Table 1. The initial months of April, May and June had less number of patients due to total shutdown announced in the country due to Covid 19.

Of 6692 patients, a total of 3105 patients were advised and dispensed with 0.5% PVP-I nasal drops to be used 3–4 drops in each nostril 3 times regularly for 8 days and 4321 patients were dispensed 0.5% PVP-I gargles for four times daily usage for 8 days. The feasibility & usability of using 0.5% PVP-I gargles and nasal drops was assessed in all patients as primary end points and tolerance to the gargles and nasal drops in those dispensed for a period of 8 days was evaluated as secondary end point. The study has been approved by the Institutional Ethics committee. The patients and the relatives were explained about PVP-I gargles and nasal drops. All the details of the patients were recorded.

The detailed protocol adopted is as follows

All the patients seeking ENT office based consultations at our Centre from 15th April 2020 to 15th September 2020 were given application of 0.5% PVP-I solution as gargles and nasal drops irrespective of the COVID status. The dispensing of the PVP-I gargles and nasal drops was done by the attendant staff and the patients were examined 15 min after the administration of nasal drops and gargles. Patients were also dispensed 0.5% PVP-I gargles and nasal drops to be used at home regularly for a period of 8 days.

Preparation of 0.5% solution of PVP-I from commercially available Povidone Iodine IP 10% v/w in purified water IP q.s.

Table 1
Monthwise use of 0.5% PVP-I in office patients.

Months of 2020	Number of patients
April	230
May	315
June	990
July	1791
August	1926
September	1440
Total	6692

Use 1 ml of PVP-I in 20 ml of sterile water/purified water.

2.1. Method of application

Disposable paper cups with 10 ml of 0.5% PVP-I solution was administered for gargling and 4–5 drops of 0.5% PVP-I was administered with a disposable plastic dropper into each nostril 15 min prior to examination. The patients were instructed to gargle for minimum of 30 s.

Feasibility and usability was considered in terms of the ease of the dispensing method of the 0.5% PVP-I gargles and nasal drops. Tolerance was assessed in terms of altered taste, staining of teeth or nasal skin or irritation in the nose. The tolerance to the 0.5% PVP-I gargles and nasal drops dispensed was evaluated with the Likert scale (Table 2). In case of any untoward adverse effect, the patients were asked to discontinue the use and to report immediately to the hospital.

3. Results

A total of 6692 patients attending the office based otolaryngological consultations at our hospital were administered 0.5% PVP-I gargles and nasal drops 15 min prior to examination. Feasibility and usability of administration of 0.5% PVP-I gargles and nasal drops in Office patients was evaluated. Out of total of 3105 patients advised and dispensed with 0.5% PVP-I nasal drops for regular use, only 2753 were available for follow up. Out of 4321 patients dispensed with 0.5% PVP-I gargles for daily use, only 3742 patients were available for follow up and for evaluation. The evaluation was done according to Likert scale for tolerance to the 0.5% PVP-I gargles and nasal drops by the attendant staff and was recorded in the forms. 21 patients (0.76%) reported itching sensation in nose on the first day of use of 0.5% PVP-I nasal drops and discontinued its further use. However, none of the patients reported any serious side effects or allergic reaction to 0.5% PVP-I nasal drops and gargles. In all the questions assessed on the Likert Scale, there was favourable response about the use of 0.5% PVP-I gargles and nasal drops, 93.54% No altered taste, 89.36% -No teeth staining, 86.38% -No throat irritation and 92.22% - No nasal skin staining.

The 0.5% PVP-I gargles and nasal drops were used by the Health care workers about three to four times in a day for 5 months. None of them developed any symptoms related to Covid 19 disease.

4. Discussion

The nasal cavity, nasopharynx, oral cavity and oropharynx are the prime areas with high viral load of SARS-CoV-2 with the highest viral loads within the nasopharynx [5]. In vitro studies have demonstrated that the nasal goblet and ciliated cells had the highest expression of ACE2 [6]. It is hence it is of utmost importance to reduce the viral titres so as to reduce the progression and complication of the disease. We have

Table 2
Likert scale.

1. 0.5% PVP –I gargles and nasal drops are easy to prepare	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
2. 0.5% PVP –I gargles and nasal drops are easy to dispense	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
3. 0.5% PVP –I gargles do not cause staining of teeth	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
4. 0.5% PVP –I gargles do not cause throat irritation	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
5. 0.5% PVP –I gargles and nasal drops do not cause altered taste	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
6. 0.5% PVP –I gargles and nasal drops worked effectively for the complaints I had	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
7. 0.5% PVP –I nasal drops do not cause nasal irritation	Agree→Strongly agree	Neutral	Disagree	Strongly disagree
8. 0.5% PVP –I nasal drops do not cause nasal skin staining	Agree→Strongly agree	Neutral	Disagree	Strongly disagree

been regularly using 0.5% PVP-I nasal drops and gargles as a pre requisite prior to ENT examination. It is feasible to prepare and dispense. It has been well tolerated by the patients at the office setup as well as the regular usage at home for 8 days.

Povidone-iodine is considered to have the broadest spectrum of antimicrobial action compared with other common antiseptics such as chlorhexidine, octenidine, polyhexanide [7] showing efficacy against Gram-positive and Gram-negative bacteria, bacteria spores, fungi, protozoa and several viruses. Persistency of effect has also been demonstrated in a study that assessed 1% PVP-I as a preprocedural antibacterial agent in individuals with varying degrees of oral hygiene [8]. Reductions in micro-organism concentrations were found to be sustained for at least 4 h [8]. Furthermore, there is some evidence that PVP-I restores the natural microbial flora following bacterial infection, as observed in the setting of bacterial vaginosis [9].

World Health Organization has included PVP-I in its list of essential medicines as high virucidal activity has been observed against viruses of significant global concern, including hepatitis A and influenza, as well as the Middle-East Respiratory Syndrome and Sudden Acute Respiratory Syndrome coronaviruses. Together with its diverse applications in antimicrobial control, broad accessibility across the globe, and outstanding safety and tolerability profile, PVP-I offers an affordable, potent, and widely available antiseptic option [10].

The active component of PVP-I is iodine. The mechanism of action starts when free iodine is released, which disrupts microbial metabolic pathways, destabilizes structural components of cell membranes, and leads to irreversible damage to pathogens [11].

PVP-I has been used as gargles since many decades. The safety of the PVP-I gargles has been well documented with no irritation or any adverse effects. There has been no change in the gustatory function or staining of the teeth or any effect on thyroid on prolonged use [12–15].

Use of nasal PVP-I is not a new concept. Preoperative nasal decontamination is a routine step to reduce postoperative infectious contamination in patients undergoing orthopedic surgery with no reports of toxicity or adverse events [16]. Repeated administration of PVP-I to the sinonasal mucosa has been described as a safe and effective treatment for chronic sinus disease. This application did not cause any significant effect on mucociliary clearance or olfaction [17,18]. According to these studies, PVP-I did not cause pathological effects on paracellular permeability or cilia beat frequency at concentration of 1.25% [19].

Reduction in the microorganisms for 4 h of use, gives a low risk period during examination after use of 0.5% PVP-I gargles and nasal drops targeting the viral load in oropharynx, oral cavity, nasopharynx. Not only reduces the risk of transmission of the disease to the health care workers but also regular use may reduce the viral titres in the positive patients as well as reduce the overall risk of contracting the disease.

Advantages of the 0.5% PVP-I as a pre requisite for office based ENT examination:

1. Risk free interval for examination after use of 0.5% PVP-I gargles and nasal drops.
2. Easy to prepare and dispense
3. No altered taste
4. No staining of teeth or nasal vestibular skin
5. Not much irritation in the nose or other serious side effects
6. No effect on olfaction or mucociliary function
7. No effect on thyroid function [15]
8. Safe to use

4.1. Limitations

1. Randomised Controlled Trials to be conducted in the future for correlating the in vivo virucidal benefits of 0.5% PVP-I in Covid 19 positive patients.

We propose that no office based ENT examination, office based endoscopic procedures, planned surgical procedures and intubation should be carried out without disinfection by 0.5% PVP-I.

5. Conclusion

Use of 0.5% PVP-I gargles and nasal drops before ENT examination gives a risk free interval for examination, thereby reducing the risk of transfer of infection from patient to health care workers. It is freshly prepared from commercially available 10% PVP-I solution. It is easy to prepare and dispense. It has high feasibility and usability with good tolerance for its use.

CRedit authorship contribution statement

Dr. Mubarak Khan: Concept, study design and manuscript drafting.
Dr. Sapna R. Parab: Study Design, manuscript drafting and editing.

Declaration of competing interest

None.

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