Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Oral Oncology 105 (2020) 104724

Contents lists available at ScienceDirect

Oral Oncology

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

Letter to the editor

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

Letter to the Editor

In response to the novel coronavirus SARS-CoV-2, healthcare systems have been challenged to allocate scarce resources while striving to achieve distribution justice to meet the critical needs of the communities they serve. Though there are ongoing randomized trials evaluating the utility of systemic therapies, post-convalescent serum, and vaccine development, these interventions are costly and time intensive. Alternative therapies and preventative measures are needed now, not only to accelerate the flattening of the epidemiologic curve, but also safeguard providers and patients as we re-evaluate tiered surgical responses and operational processes moving forward.

Early investigations in China have suggested that cancer patients harbored a higher risk of infection compared with the overall population and that infected cancer patients, particularly those who received chemotherapy or underwent surgery within a month of infection, were more susceptible to the need for critical care, respiratory support, and mortality [1]. In the viral hotspot of Wuhan, nosocomial spread was suspected in 12% of patients and 29% of health professionals at a tertiary care institution [2], while 63% of the city's infected population were healthcare workers [3]. These findings suggest that not only are patients with malignancy a vulnerable population to increased infection risk, but so too are healthcare providers on the front lines.

As viral load appears highest in the nasopharynx, and high in human saliva, these anatomical areas likely seed the lower airway and serve as one of the main reservoirs for aerosolized transmission and progression of pulmonary disease. Furthermore, viral loads of asymptomatic and symptomatic patients are similar, suggesting the transmission potential of asymptomatic/minimally symptomatic patients [4]. As such, head and neck oncologists and skull base surgeons are among those at highest risk of nosocomial transmission. The first described case, albeit anecdotal, of operative-related spread occurred during endoscopic pituitary surgery in Wuhan, wherein fourteen personnel became infected [5]. There is a pervasive dynamic tension between our responsibility to flatten the curve and our commitment – our Hippocratic oath – to first do no harm, recognizing that delay in cancer treatment will influence disease outcomes. How do we protect ourselves and our patients while trying to equilibrate this tension? In response to this question, there has been a deluge of suggested procedural guidelines to reduce aerosolization and description of appropriate PPE [5]. Among those approaches, povidone-iodine (PVP-I), a widely available, topical broad spectrum antiseptic, has been suggested for nasal and oral application as a perioperative infection control strategy.

The utility and excellent safety profile of both topical nasal and oral solutions of PVP-I has long been recognized, especially at dilute concentrations (e.g. 0.001%). A detailed review of its virucidal activity against a wide range of common viruses, including SARS-CoV and MERS-CoV coronaviruses, is beyond the scope of this article [6]. As a word of caution, *in vitro* studies using 10% and 5% PVP-I have demonstrated cilotoxicity on human respiratory cells [7]. However other investigations demonstrate continued virucidal effects of diluted PVP-I concentrations, without evidence of respiratory cilia toxicity, diminished olfactory function, or changes in mucosal appearance [8]. *In vitro* studies of 0.23% PVP-I mouthwash (1:30 dilution) can inactivate both SARS-CoV and MERSCoV following a 15-second exposure [6]. Though rare, prolonged use of topical 10% PVP-I solution (weeks-months) may increase the risk of iodine toxicity [9]. Allergy, contact sensitivity, and skin reactions are rare [10].

Here we present a novel intervention strategy utilizing topical applications of PVP-I to attenuate nosocomial transmission of COVID-19 surrounding head and neck and skull base oncology care. Given that frontline providers exposed to open and endoscopic upper aerodigestive procedures may serve as vectors of transmission, this protocol identifies healthcare workers as a potential target population for treatment intervention, especially in high-prevalence areas. Given the increased penetration of the nasopharynx with large volume nasal irrigations, we aim to incorporate chronic rhinosinusitis treatment models and propose the following formulations for administration: (1) **Nasal irrigation**: 240 mL of 0.4% PVP-I solution (dilution of 10 mL of commercially available 10% aqueous PVP-I into 240 mL of normal saline with a sinus rinse delivery bottle); and (2) **Oral/oropharyngeal wash**: 10 mL of 0.5% aqueous PVP-I solution (1:20 dilution in sterile or distilled water); in addition to appropriate PPE. Certainly, literature supports the safety of these dosages, and higher concentrations of PVP-I may be well-tolerated without mucociliary toxicity; we recommend lower concentrations out of an abundance of caution. Moreover, though nasal irrigations may yield increased discomfort compared to atomized sprays, this delivery mode decreases the theoretical risk of aerosolizing viral particles. The following outlines a stratified treatment approach:

1. Apply nasal and oral PVP-I every 2–3 h, up to 4×/day **in patients** that:
   a. Have suspected/confirmed SARS-CoV-2 infection
   b. Are undergoing high-risk procedures (e.g. those involving nasal mucosal, oral, pharyngeal, and pulmonary secretions)
   c. Are from COVID-19 hotspots
2. Apply nasal and oral PVP-I prior to and after patient contact (with repeated contact, apply every 2–3 h, up to 4×/day) **in healthcare providers** that:

https://doi.org/10.1016/j.oraloncology.2020.104724
Received 12 April 2020; Accepted 15 April 2020
Available online 16 April 2020

a. Are involved in care of patients with suspected/confirmed SARS-CoV-2 infection
b. Are involved in high-risk procedures of patients in COVID-19 hotspots
c. Lack adequate PPE (e.g. N95, PAPR)

3. Optional nasal and oral application of PVP-I every 2–3 h, up to 4×/day **in patients and/or healthcare providers** in:
a. High-risk procedures in asymptomatic patients
b. COVID-19 hotspots

This strategy benefits from broad availability of materials, excellent safety profile and associated low costs. Given the ease of acquirement of materials, healthcare providers may immediately implement this intervention as a form of "personal protective equipment" to augment current practice recommendations. It is important to acknowledge that there is a potential risk in that prophylactic treatment of healthcare providers could increase susceptibility to SARS-CoV-2 infection by affecting mucociliary function or local immunity. As previously mentioned, and worth restating, we recommend a lower concentration out of an abundance of caution to minimize this untested possibility. Though we describe this protocol in the context of frontline providers caring for head and neck and skull base patients, this strategy may be applied to additional practitioners with occupational exposures. Let us flatten the epidemiologic curve *and* keep our commitment to first do no harm.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

References

[1] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21(3):335–7.
[2] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. Jama 2020.
[3] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) Outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. Jama 2020.
[4] Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 2020;382(12):1177–9.
[5] Vukkadala N, Qian ZJ, Holsinger FC, Patel ZM, Rosenthal E. COVID-19 and the otolaryngologist – preliminary evidence-based review. Laryngoscope 2020.
[6] 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 Therapy 2018;7(2):249–59.
[7] Kim JH, Rimmer J, Mrad N, Ahmadzada S, Harvey RJ. Betadine has a ciliotoxic effect on ciliated human respiratory cells. J Laryngol Otol 2015;129(Suppl 1):S45–50.
[8] 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 Oto-rhino-laryngology Relat Special 2007;69(2):92–9.
[9] Ramaswamykanive H, Nanavati Z, Mackie J, Linderman R, Lavee O. Cardiovascular collapse following povidone-iodine wash. Anaesth Intensive Care 2011;39(1):127–30.
[10] Lachapelle JM. A comparison of the irritant and allergenic properties of antiseptics. Eur J Dermatol: EJD 2014;24(1):3–9.

Leila J. Mady[a], Mark W. Kubik[b], Khalil Baddour[a], Carl H. Snyderman[a], Nicholas R. Rowan[b,*]
[a] *Department of Otolaryngology – Head and Neck Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA*
[b] *Department of Otolaryngology – Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA*
E-mail address: nrowan1@jhmi.edu (N.R. Rowan).

[*] Corresponding author at: Department of Otolaryngology – Head and Neck Surgery, Johns Hopkins University School of Medicine, 601 North Caroline Street, 6th Floor Suite 6164, Baltimore, MD 21287, USA.