Topical Preparations to Reduce SARS-CoV-2 Aerosolization in Head and Neck Mucosal Surgery

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Abstract

Introduction: The COVID-19 pandemic caused by the SARS-CoV-2 virus has put healthcare workers at risk when exposed to aerosolized viral particles during upper airway mucosal surgery. The objective of this review was to discuss topical preparations that could be utilized preoperatively to help to decrease viral load and potentially reduce the risks of viral transmission.

Methods: PubMed/MEDLINE database review of articles studying topical preparations with virucidal activity against coronaviruses.

Results: Povidone – Iodine (PVP-I) solutions ranging from 0.23% to 7% have been found to demonstrate highly effective virucidal activity against a broad range of viruses including several coronaviruses responsible for recent epidemics: SARS-CoV-1, MERS-CoV.

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Introduction

As the COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 continues to escalate globally, we are faced with developing methods to provide care to our patients while also keeping them, our co-workers, and ourselves safe. Healthcare workers are at increased risk of exposure to the virus, and there is

mounting evidence that otolaryngologists are among the highest at risk. This is likely due to a high viral load of SARS-CoV-2 in the upper aerodigestive tract and because of the direct contact that practitioners have with the mucosa during both diagnostic and therapeutic procedures.[1–3] Once the respiratory mucosa is manipulated, viral particles have the ability to become aerosolized, can become airborne for three or more hours, and may spread to contaminate multiple surfaces in the surrounding area.[4–6] Of particular concern is that even asymptomatic patients may be responsible for viral aerosolization, given its long incubation period (5-7 days), and that these asymptomatic patients may unknowingly place our surgical teams at risk.[1,7–9]

We do, however, still have an obligation to perform urgent and emergent cases for life-threatening situations or diseases, such as cancer, where failure to act will lead to high morbidity. Indeed, it is known that cancer patients are susceptible to infection. Early data from China has shown that among patients with COVID-19, there is an approximately three-fold higher proportion of patients with cancer than the incidence of cancer in the general population.[10] Open, endoscopic and robotic oncologic surgery of the upper airway may expose providers to high levels of viral particles in the respiratory mucosa and saliva.[2,11] Several institutions have generated head and neck specific algorithms to help risk stratify patients and procedures advocating strongly for preoperative SARS-CoV-2 testing and appropriate utilization of personal protective equipment (PPE) in patients undergoing head and neck mucosal surgery.[12,13] There has been very little published, however, regarding whether there exist any topical agents that could be utilized preoperatively to potentially lower the viral load in the upper aerodigestive tract thereby mitigating any risk of viral aerosolization in persons undergoing head and neck mucosal surgery. In this review, we aimed to review the literature discussing topical agents that are safe to use as oral rinses and that may have virucidal activity against SARS-CoV-2.

Methods

We conducted a search of the PubMed/MEDLINE databases for articles relevant to topical agents with virucidal activity against coronaviruses. Search terms included: alcohol, peridex, iodine, chlorhexidine, topical, mouthwash, virus, coronavirus, COVID-19. To focus the search, we concentrated on articles that focused either on in-vitro studies or studies examining their utilization on mucosal surfaces. We supplemented the searches by reviewing references from each relevant manuscript. The selection of data was determined subjectively to be synthesized into this review. Institutional review board approval was not required for this study.

Discussion

Povidone – Iodine

Povidone – Iodine (PVP-I) is a widely used iodine complex carried in a polyvinylpyrrolidone carrier that was developed in the 1950s and is available as a surgical skin prep agent and as a mouthwash.[14] It has demonstrated both antibacterial and antiviral activity in past studies.[14] While studies on virucidal activity of PVP-I have not yet been performed specifically on SARS-CoV-2, there have been numerous in-vitro studies demonstrating its effectiveness against multiple viruses including related coronaviruses. A 1997 study compared PVP-I to other antiseptics in inactivating a broad range of both enveloped and non-enveloped viruses (adeno-, mumps, rota-, polio-, coxsackie-, rhino-, herpes simplex, rubella, measles, influenza and human immunodeficiency viruses) and demonstrated PVP-I to have the broadest spectrum of antiviral activity among agents tested.[15] Kariwa et al. tested several different commercially available PVP-I formulations against SARS-CoV-1 viral samples (responsible for the severe acute respiratory syndrome (SARS) epidemic) and found that the viral infectivity was reduced to below detectable levels within 2 minutes of application.[16] In an industry sponsored study, Eggers et al carried out in-vitro tests of PVP-I solutions (1% to 7.5%) against MERS-CoV (responsible for the Middle East respiratory syndrome (MERS) epidemic) and found that the viral titre reduction of >99.99% within 15 seconds of application.[17] A subsequent study examined a diluted PVP-I (0.23%) formulation against SARS-CoV-1, MERS-CoV, and Influenza A (H1N1) applied for 15 seconds and again found a >99.99% reduction of viral titres.[18] Despite ample in-vitro studies, there are few clinical studies of PVP-I specifically against viruses. Still, in a small prospective Japanese study of school aged children, it was found that cohorts who were encouraged to used PVP-I gargle had significantly

lower rates of absences from school due to the common cold and influenza.[19]

From a safety perspective, it has been tolerated for use in the upper airway as has been demonstrated in numerous human studies. In the oral cavity and oropharynx it has been used safely at a range of doses from 1% to 10% for oropharyngeal infection prophylaxis, mucositis and prevention of ventilator associated pneumonia.[20–24]Commercial over-the-counter oral mouthrinse formulations are typically of 1% PVP-I. Though there is some degree of mucosal absorption, even long term oral utilization has not been shown to cause thyroid dysfunction.[25] It has also been utilized in the sinonasal mucosa at lower concentrations (0.08%) in the treatment of recalcitrant chronic rhinosinusitis without evidence of thyroid dysfunction, olfactory dysfunction or mucociliary clearance changes.[26] Other studies have examined the effect of PVP-I in varying concentrations 0.5% to 5% on the sinonasal mucosa without detrimental effect to the nasal epithelium; however, one recent in-vitro study found that iodine preparations of 5% to 10% demonstrated some degree of ciliotoxicity.[27–30]Fortunately, PVP-I also exhibits the least ototoxicity of topical prep solutions and is safe to use as an ophthalmic prep agent (1% to 5%), which is relevant to head and neck procedure that involve or expose the skull base otologic or orbital apparatuses.[31,32]Unlike alcohol based preparations, it is not flammable which is relevant when using electrocautery in the airway.[33]

Chlorhexidine

Chlorhexidine is a disinfectant and antiseptic that has been in medical use since the 1950s. Oral rinse preparations are commonly used in dentistry to reduce plaque build-up and treat gingivitis, and studies show that it can reduce bacterial counts in saliva after as little as 30 seconds of exposure.[34] There is more limited evidence showing its virucidal effects. In vitro studies in the 1970s first demonstrated activity of chlorhexidine gluconate against herpesvirus strains though not poliovirus or adenovirus.[35] Later studies showed that chlorhexidine tends to have virucidal activity against enveloped viruses, though does not show the same effect against non-enveloped viruses. Bernstein et al showed virucidal activity of chlorhexidine gluconate against the enveloped viruses herpesvirus 1, cytomegalovirus, influenza A, parainfluenza, and hepatitis B after 5 minutes of exposure in vitro, with no activity against poliovirus.[36] Baqui demonstrated this effect against human immunodeficiency virus 1 in vitro as well with two preparations of chlorhexidine as well as Listerine mouthwashes.[37]There are few studies examining chlorhexidine and coronaviruses, and those that do exist examine the effects of chlorhexidine on sterilization of inert surfaces rather than living tissue. These studies do, however, show sensitivity of coronavirus to chlorhexidine though only when used in combination with other compounds such as ethanol or cetrimide.[38] In isolation, chlorhexidine has been found to be less effective against coronaviruses than PVP-I in both in-vitro studies and studies of disinfection of inanimate surfaces.[15,39] Overall, there are limited data demonstrating the activity of chlorhexidine against coronaviruses and it is also associated with high levels of ototoxicity and can be flammable when utilized in commercial preparations that commonly include alcohol.[31,33]

Recommendation

On the basis of this review, the authors believe that the topical application of PVP-I is safe and may help to reduce the viral load, and the potential aerosolization, of SARS-CoV-2. Until confirmatory studies are conducted, our institutional consensus is to dilute commonly available PVP-I (typically 10%) 1:3 with saline to achieve a 2.5% concentration and bulb syringe the solution into the oral/nasal cavity, after intubation, but immediately prior to head and neck procedures that require instrumentation of the upper airway mucosa during the COVID-19 pandemic. We leave the solution in for approximately 1 minute before irrigating with saline and suctioning it out to reduce residual absorption and limit tissue staining. This procedure is applied to both COVID-19 positive adult patients and to patients with unknown status unless they have a contraindication to topical iodine (allergy/anaphylaxis, labile thyroid disease, contact dermatitis, pregnancy/nursing, active radioiodine therapy). This concentration is ten times the lowest PVP-I concentration found to be effective in-vitro to eliminate related coronaviruses but still likely a safe concentration for one-time use based upon past studies described. Due to a paucity of supporting literature, no recommendation can be made for the use of chlorhexidine-based rinses.

Conclusion

Though no topical therapies have been studied to specifically reduce the viral load and potential aerosolization of SARS-CoV-2 during upper airway mucosal surgery, Povidone – Iodine solutions have demonstrated effective virucidal activity against related coronaviruses in numerous studies. They are relatively safe to use in the upper airway, require very brief application times, and may potentially reduce the risk of SARS-CoV-2 aerosolization and transmission during upper airway mucosal surgery.

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