HOSPITAL PRACTICE
https://doi.org/10.1080/21548331.2020.1778908

Taylor & Francis
Taylor & Francis Group

CLINICAL FEATURE
EDITORIAL



# Acidified sodium chlorite solution: A potential prophylaxis to mitigate impact of multiple exposures to COVID-19 in frontline health-care providers

Meghana S. Karnik-Henry

Scientific Affairs, Lundbeck, Deerfield, IL, USA

**ABSTRACT**

Limited availability of personal protective equipment is endangering first-line health-care providers treating patients with presumed or confirmed COVID-19 infections. This editorial has multiple objectives in regard to this reality: First, to raise awareness of the need for safe and effective prophylaxis to protect health-care providers with insufficient personal protective equipment from repeated exposures to COVID-19. Second, to summarize the scientific evidence in support of solutions of acidified sodium chlorite (ASC) and its daughter compounds, chlorous acid and chlorine dioxide, as potential targets for said prophylactic use. Third, to propose a regimented protocol using commercially available solutions of ASC having sufficient concentrations of chlorine dioxide for virucidal activity to support safe and effective prophylactic use. And fourth, to raise awareness of and compare other potential prophylactic options currently under investigation.

**ARTICLE HISTORY**
Received 15 May 2020
Accepted 3 June 2020

**KEYWORDS**
COVID-19 prophylaxis; personal protective equipment (PPE); acidified sodium chlorite solution; chlorine dioxide solution; chlorous acid solution

## Introduction

Among essential workers selflessly serving during the coronavirus disease 2019 (COVID-19) pandemic are health-care providers (HCPs). That frontline HCPs are caring for contagious patients with inadequate personal protective equipment (PPE) is well known. Many HCPs have resorted to handmade masks to address this need. Unfortunately, the effectiveness of such masks as PPE is uncertain [1].

COVID-19, like other coronaviruses, is an enveloped, positive-sense RNA virus [2]. It is thought to be highly contagious with human-to-human transmission occurring through respiratory droplets expelled during coughing or sneezing from an infected individual that are then breathed in by the next host [3]. In the early stages of infection, patients experience symptoms of the upper respiratory tract. For those who experience a mild infection, the illness does not progress [3]. For others, illness can progress to a more serious lower respiratory infection, potentially turning fatal [3].

Although not conclusive, some evidence suggests that higher viral load may be associated with more severe clinical outcomes for patients infected with COVID-19 [4]. Similar findings suggesting that high viral load in the nasal passages may be an indicator of severe illness were obtained from analyses of patients infected with SARS-CoV, a distinct coronavirus, during the 2003 global outbreak [5].

Taken together, the lack of adequate and readily available PPE for first-line HCPs, the manner in which COVID-19 is transmitted, and the potential impact of viral load on patient outcome all indicate a need for prophylaxis targeting the upper respiratory tract to mitigate the impact of multiple exposures to the virus.

A safe prophylaxis consisting of a mouth rinse that can be administered to effectively cleanse the back of the throat in combination with a solution administered nasally to cleanse the nasal and nasopharyngeal passages may successfully target the tissues of the upper respiratory tract likely associated with initial infection [6].

Due to their microbicidal properties and their tolerability as cleansers of these same tissues, solutions of acidified sodium chlorite may be appropriate for such prophylactic use.

Acidified sodium chlorite is used as an antiseptic in the industrial setting for food processing and water purification [7]. It has been evaluated or used more recently in over-the-counter oral or nasal cleansing solutions [8–10].

Acidified sodium chlorite (ASC) solution, or sodium chlorite ($NaClO_2$) in aqueous solution with acid ($H^+$), forms semi-stable chlorous acid ($HClO_2$). Chlorous acid degrades to chlorine dioxide ($ClO_2$), which, over time, further degrades to chlorite ($ClO_2^-$) and ultimately, chloride ($Cl^-$) [7]. Exposure to light and higher temperatures accelerates the degradation process [11]. Chlorous acid and $ClO_2$ are thought to be responsible for the microbicidal action of ASC [7].

## Microbicidal properties of $HClO_2$ and $ClO_2$

$HClO_2$ has demonstrated potent virucidal activity *in vitro* with <4 µg/ml of $HClO_2$ effectively inactivating enveloped viruses at a pH consistent with the range observed in human nasal mucosa [12,13]. $HClO_2$ also seems to have limited cytocidal effects at greater than effective virucidal concentrations, suggesting its potential as a strong and safe disinfectant when present at low concentrations [12].

**CONTACT** Meghana S.Karnik-Henry mkhe@lundbeck.comScientific Affairs, Lundbeck, 6 Parkway North, Deerfield, , IL 60015, USA

$ClO_2$ has also demonstrated virucidal properties *in vitro*, including against coronaviruses, with a 0.004% (wt/vol %) solution of $ClO_2$ effectively inactivating 100% of SARS-CoV in wastewater after exposure for 5 minutes, and inactivating 94.4% of the virus after exposure of 1 minute [14].

Additionally, $ClO_2$ gas derived from ASC has been shown to have potent virucidal properties *in vivo*, specifically against influenza A viral infection in mice [15]. Mouth rinse studies of $ClO_2$ solutions derived from ASC have demonstrated antibacterial and antifungal properties when used in people. These solutions have ranged from 0.003% to 0.016% (wt/vol %) $ClO_2$ [9,10]. A study of 0.14% ASC solution ($ClO_2$ percentage not specified) demonstrated effective antibacterial action on saliva for up to 5 hours after single administration when patients rinsed with solution for 1 minute before expectorating [8]. Adverse events in the above studies were minor, if any, with taste disturbance being the most frequent [9].

Published findings on the use of ASC/$ClO_2$intranasal solutions in humans are not available at this time. However, tolerability data-on-file (2017) shared by Sinox Pharma, Inc. show that a 0.008% (wt/vol %) $ClO_2$ solution derived from ASC is nonirritating when administered as an intranasal cleanser to individuals with sub-clinical or clinical sinusitis.

## Safety and tolerability

It is important to note that consuming solutions of ASC or $ClO_2$, particularly those containing high concentrations of either compound, is inadvisable and may cause serious harm [16].

In 2000, the World Health Organization (WHO) published the International Programme on Chemical Safety (IPCS) derived recommendation of a tolerable daily intake of 0.03 mg of chlorite by kg weight, per day. Based on the IPCS recommendation, the WHO set a quality guideline value of 0.7 mg/L for chlorite in drinking-water [7].

In a study of adult male and female African Green monkeys, a daily dose of 9 mg/kg of $ClO_2$ ingested through drinking water seemed to strongly inhibit thyroid synthesis [17].

However, more recent evaluations in animals and humans demonstrate that exposure to low concentrations of ASC or $ClO_2$ (≤0.2% and <0.02%, respectively) such as those found to be effective in human mouth rinse studies are well tolerated [8–10,18].

Further evaluation of both safety and effectiveness when such solutions are employed for prophylactic use in humans to mitigate the effects of multiple exposures of COVID-19 is strongly advised.

## ASC/$ClO_2$ PPE suggested protocol

### *Interventions*

The protocol proposed here (Table 1) is for use in the hospital setting by HCPs treating patients presumed to be infected with COVID-19.

As preparations of $ClO_2$ solution derived from ASC for use in the mouth and nose are commercially available, two such products are suggested for use in this protocol.

**Table 1.** Proposed prophylactic protocol for nasopharyngeal and oropharyngeal cleansing when anticipating treatment of patients presumed or confirmed to have COVID-19.

| | Nasopharyngeal and Nasal Cavity Cleansing (Snoot!™) | Oropharyngeal and Oral Cavity Cleansing (DioxiRinse™) |
|---|---|---|
| **Preparation** | (1) Follow package instructions to 'Mix Snoot!' (Sinox Pharma, Inc.) prior to first shift in relevant health-care setting<br>(2) Let prepared solution stand ≥10 minutes prior to first use | (1) Follow the package instructions to mix DioxiRinse (Frontier Pharmaceutical, Inc.), mixing a total of 15-20 ml of solution for immediate use.<br>(2) Let prepared solution stand for between 30 and 45 seconds prior to use |
| **Administration** | Follow package instruction for 'Use Snoot!' Briefly:<br>(1) Spray solution into each nostril while inhaling and holding opposing nostril closed (each spray from the included spray bottle delivers ~0.1 ml solution)<br>(2) Gently blow nose after 1 minute<br>(3) Expectorate any solution drained into the throat<br>(4) Spray solution a second time into each nostril while inhaling and holding opposing nostril closed<br>(5) Gently blow nose after 1 minute<br>(6) Expectorate any solution drained into the throat<br>(7) Discard solution after 12 hours | (1) Gargle as far into back of throat as possible for 30 seconds<br>(2) Rinse oral cavity for 5–10 more seconds<br>(3) Expectorate |
| **Repetition** | Every 3 hours, up to 4 times a shift in 12 hours, including first use immediately prior to start of shift | |
| **On Maximal Use** | Because nasal cleansing with a $ClO_2$ solution will be coupled with use of an oral rinse, also a $ClO_2$ solution, the maximum recommended use of either product should not exceed 4 administrations within a 24-hour period. | |
| **Special Considerations** | If irritation occurs at later uses relative to earlier ones in a 12-hour period, discard remaining solution and remix fresh solution as directed; strength of solution increases over time, not exceeding 75 ppm $ClO_2$ at 12 hours. | – |

The first is Snoot™ (Sinox Pharma, Inc.) at the 'Original' strength. This formulation yields between 60 parts per million (ppm) and 75 ppm (~0.01% wt/vol) $ClO_2$ over the course of 12 hours, the usage period suggested here. According to data-on-file shared by Sinox Pharma, Inc., this formulation may cause nasal discomfort in some individuals but is unlikely to cause inflammation.

The second recommended product is DioxiRinse™ (Frontier Pharmaceutical, Inc.) to be used at the 'Standard Strength' yielding a concentration of ~40 ppm (0.006% wt/vol) $ClO_2$.

Use will entail daily preparation of solutions for cleansing of the mouth, throat, and nasal passages of participants. Once daily preparation is advised for nasal cleansing. Preparation immediately prior to each use is advised for oral cleansing. Both products should demonstrate virucidal activity and be well tolerated at these strengths/concentrations.

### *Contraindications*

Individuals with allergies to any of the ingredients in either product including but not limited to cinnamon and mint along with individuals experiencing thyroid dysfunction or poor tolerance to either product should be excluded.

### *Pre-administration*

HCPs should be offered the interventions described here as supplemental PPE and should provide their freely given consent to participate in the prospective evaluation of this protocol, with no risk to their professional standing should they refuse to participate.

### *Exceptions to protocol*

In the event that an HCP has direct exposure to expelled particles from a cough or sneeze of an individual with presumed COVID-19, immediate cleansing using both products is suggested, even if the recommended maximum use of 4 times in a 12-hour period is exceeded. However, >6 administrations in a 24-hour period are strongly discouraged.

### *Reporting*

Participants should report any adverse events experienced to their hospital administrators for immediate recording and reporting.

## Discussion

The lack of sufficient PPE to protect first-line HCPs from infection has elevated the need to identify a safe and effective prophylaxis to mitigate the impact of multiple exposures to this virus. Only one of several potential solutions to this problem has been presented here.

Other proposed options for prophylaxis include a protocol detailing the use of a highly diluted form of povidone-iodine (PVP-I) solution as a mouth rinse and nasal spray [19], and the administration of nitric oxide gas to HCPs at the start and end of their shifts [20].

Each potential prophylactic avenue is associated with benefits and challenges (Table 2).

However, none of the challenges posed for any of these options are insurmountable. And HCPs can only benefit from having multiple effective options to choose from. Indeed, the three described here may be too few.

**Table 2.** Benefits and challenges of potential prophylactic interventions to mitigate the impact of HCP exposure to COVID-19 virus.

| Potential Prophylaxis | Benefits | Challenges |
|---|---|---|
| **ASC/ Chlorine Dioxide Solution** | • Uses two readily available commercial products<br>• Each product has been found to be safe and tolerable when used individually<br>• Easy to prepare and administer | • Suggested use of 4 times per shift may be untenable for overextended HCPs with little time to spare between patients for personal care<br>• Lack of tolerability to the nasal cleanser may preclude use by some individuals<br>• The two products have not previously been evaluated for safety when used in tandem or for this specific purpose |
| **PVP-I Solution** | • Readily available and comparatively affordable active ingredient component of solution<br>• Easy to prepare, store, and administer | • Suggested use of 4 times per shift may be untenable for overextended HCPs with little time to spare between patients for personal care<br>• Use may result in temporary staining of nasal and oral tissues<br>• Solution has not previously been evaluated for safety when used as both an oral rinse and a nasal spray, or when used for this specific purpose |
| **Nitric Oxide Gas** | • Compelling administration frequency | • Exposure to nitric oxide gas can prove toxic if not carefully monitored and controlled<br>• Will require expensive, specialized equipment to administer |

## Acknowledgments

The author would like to thank Jack Skeels of Sinox Pharma, Inc. and Valerie Alliger-Bograd of Frontier Pharmaceutical, Inc. for providing valuable information on safety, chemical composition and degradation, and use of Snoot!™ and DioxiRinse™. The author would also like to thank Michael B. Henry, PhD, Ann Hartry, PhD, and Joan Cannon, PharmD, MBA for their thoughtful suggestions and editorial review of this manuscript.

## Declaration of interest

The author is an employee of Lundbeck. The author has no affiliation or financial involvement with any organization or entity with a financial interest in the subject matter or materials discussed in this manuscript, including employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

## ORCID

Meghana S. Karnik-Henry http://orcid.org/0000-0002-2981-7837

## References


1. Wilson AM, Abney SE, King MF, et al. COVID-19 and non-traditional mask use: How do various materials compare in reducing the infection risk for mask wearers? J Hosp Infect. 2020. [Epub ahead of print 2020 Jun 2]. DOI:10.1016/j.jhin.2020.05.036.
2. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 2015;1282:1–23.
3. Cascella M, Rajnik M, Cuomo A, et al. Features, evaluation and treatment coronavirus (COVID-19). InStatpearls [internet] 2020 Mar 8. StatPearls Publishing.
4. Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. Lancet Infect Dis. 2020 Jan;20(6):656–657
5. Hung IF, Cheng VC, Wu AK, et al. Viral loads in clinical specimens and SARS manifestations. Emerg Infect Dis. 2004 Sep;10(9):1550.
6. Sungnak W, Huang N, Bécavin C, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nat Med. 2020;26:681–687.
7. Autrup H, Calow P, Dekant W., Scientific Committee on Health and Environmental Risks opinion on: Environmental impact and effect on antimicrobial resistance of four substances used for the removal of microbial surface contamination of poultry carcasses, 2008.
8. Fernandes-Naglik L, Downes J, Shirlaw P, et al. The clinical and microbiological effects of a novel acidified sodium chlorite mouthrinse on oral bacterial mucosal infections. Oral Dis. 2001 Sep;7 (5):276–280.
9. Grootveld M, Silwood C, Gill D, et al. Evidence for the microbicidal activity of a chlorine dioxide-containing oral rinse formulation in vivo. J Clin Dent. 2001;12(3):67–70.
10. Mohammad AR, Giannini PJ, Preshaw PM, et al. Clinical and microbiological efficacy of chlorine dioxide in the management of chronic atrophic candidiasis: an open study. Int Dent J. 2004 Jun;54(3):154–158.
11. Taylor JB, Wohlers DW. Toxicological profile for chlorine dioxide and chlorite. Washington, DC: U.S. Environmental Protection Agency; 2004.
12. Goda H, Ikeda K, Nishide M, et al. Characterization of virucidal activities of chlorous acid. Jpn J Infect Dis. 2018;JJID–2018;71 (5):333-337.
13. England RJ, Homer JJ, Knight LC, et al. Nasal pH measurement: a reliable and repeatable parameter. Clin Otolaryngol Alli Sci. 1999 Feb;24(1):67–68.
14. Wang XW, Li JS, Jin M, et al. Study on the resistance of severe acute respiratory syndrome-associated coronavirus. J Virol Methods. 2005 Jun 1;126(1–2):171–177.
15. Ogata N, Shibata T. Protective effect of low-concentration chlorine dioxide gas against influenza A virus infection. J Gen Virol. 2008 Jan 1;89(1):60–67.
16. FDA Consumer Update, 2019: https://www.fda.gov/consumers/consumer-updates/danger-dont-drink-miracle-mineral-solution-or-similar-products
17. Bercz JP, Jones L, Garner L, et al. Subchronic toxicity of chlorine dioxide and related compounds in drinking water in the nonhuman primate. Environ Health Perspect. 1982 Dec;46:47–55.
18. Ma JW, Huang BS, Hsu CW, et al. Efficacy and safety evaluation of a chlorine dioxide solution. Int J Environ Res Public Health. 2017 Mar;14(3):329.
19. Kirk-Bayley J, Combes J, Sunkaraneni V, et al., The use of povidone iodine nasal spray and mouthwash during the current COVID-19 pandemic may reduce cross infection and protect healthcare workers; 2020 Mar 28. Available at SSRN: http://dx.doi.10.2139/ssrn.3563092
20. Healy M How a discovery that brought us Viagra could help those battling the coronavirus. Los Angeles Times [Internet]. 2020 April 5 cited 2020 Apr 10. Available from: https://www.latimes.com/science/story/2020-04-05/viagra-discovery-could-treat-coronavirus-patients