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Explore 17 (2021) 127–129

Contents lists available at ScienceDirect

Explore

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

Hypothesis Paper

Do saline water gargling and nasal irrigation confer protection against COVID-19?

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ARTICLE INFO

Article History:
Received 16 July 2020
Revised 28 September 2020
Accepted 29 September 2020

Keywords:
Covid-19
Sars-cov-2
Saltwater gargling
Nasal irrigation
Infection control

ABSTRACT

This report provides a perspective on the relevance of saline water gargling and nasal irrigation to the COVID-19 crisis. While there is limited evidence concerning their curative or preventive role against SARS-CoV-2 infection, previous work on their utility against influenza and recent post-hoc analysis of the Edinburgh and Lothians Viral Intervention Study (ELVIS) provide compelling support to their applicability in the current crisis. Saline water gargling and nasal irrigation represent simple, economical, practically feasible, and globally implementable strategies with therapeutic and prophylactic value. These methods, rooted in the traditional Indian healthcare system, are suitable and reliable in terms of infection control and are relevant examples of harmless interventions. We attempt to derive novel insights into their usefulness, both from theoretical and practical standpoints.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease-2019 (COVID-19), has spread to more than 200 countries, attaining pandemic status. Although many researchers are pursuing key directions for therapy and/or prevention, no acceptable therapy has been found to confer protection. A simple, economical, practically feasible, and globally implementable strategy with therapeutic and prophylactic value is the need of the hour.

1.1. SARS-CoV-2: Infection transmission and localization

SARS-CoV-2 is known to transmit through airborne spread via respiratory droplets and contact transmission via fomites. When a patient coughs out a sufficient number of SARS-CoV-2 viral particles in proximity to a recipient, the emitted particles are likely to gain access to the lower portions of the respiratory epithelia; when fewer particles are coughed out over considerably larger distances, the viruses mainly settle at a location like the throat mucosa.[1] In the upper portions of the respiratory epithelium, nasal cilia may trap and eliminate such pathogens via the muco-ciliary response and other cellular defense pathways. In contrast, the clearance of viruses lodged directly in deeper portions of the respiratory epithelium is challenging due to a lack of competent local defense.[1]

The coronaviruses that cause influenza are mainly localized to the upper respiratory epithelium, but severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) involve the lower respiratory epithelium. On the other hand, SARS-CoV-2 shows a comparatively higher binding capacity to human cells and has acquired the ability to settle in both upper and lower portions, the two important hotspots.[1] Therefore, a differential set of symptoms are observed in COVID-19 patients. Patients with infection localized to the upper respiratory epithelium may experience subtler presentations ranging from alterations in olfaction (anosmia/hyposmia) and taste perception (ageusia/dysgeusia),[2-4] and patients with infection typically localized to the lower respiratory epithelium suffer from disease features like that of pneumonia, necessitating ventilation efforts. Throat mucosa is an important epicenter of viral replication,[1] a feature common to several upper respiratory viruses. Patients either develop cough and/or low-grade fever, or if appropriate immune responses cannot be deployed, may develop pneumonia with or without an intermediate throat stage.[1]

Early clinical evidence by Zou et al. showed that nasal swabs contain a higher viral load of SARS-CoV-2 compared to throat swabs.[5] This pattern is similar to influenza but markedly different from MERS-CoV, which showed higher viral load from throat swabs.[5,6] Recent reverse genetics efforts by Hou et al. using pulmonary epithelial cultures also confirmed a higher distribution of SARS-CoV-2 in proximal portions of the respiratory epithelium.[7] Because the nasal epithelium and nasopharyngeal mucosa are key portals of entry, attachment, localization, and replication of SARS-CoV-2, approaches

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https://doi.org/10.1016/j.explore.2020.09.010
1550-8307/

like saltwater gargling and saline nasal irrigation are likely to have practical value.

Because previous coronavirus infections caused by SARS-CoV or MERS-CoV mainly involved the lower respiratory epithelium and frequently resulted in severe pulmonary complications like pneumonia with a high fatality rate, they were considered medical emergencies, and complementary approaches like saline water gargling and nasal irrigation were not explored. Because the current pandemic is characterized by milder clinical presentations (in ~80–85% cases) with sufficient localization to the upper respiratory epithelium,[7,8] more focus on such easily implementable options is needed.

1.2. Beneficial role of saline water gargling and nasal irrigation

Saltwater gargling is a simple, well-known method that explicitly targets pathogens of the pharyngeal mucosa.[9] The practice of saline nasal irrigation, a popular cleansing technique adapted from traditional Yoga, is more effective against pathogens harbored in the nasal mucosa. In Yogic parlance, saline nasal irrigation is referred to as '*Jala-neti*'.

In woodworkers, who face significant challenges due to the dust accumulated within nasal passages, the use of isotonic saline nasal irrigation resulted in a decreased incidence in sore throats and cold, besides being an effective cleansing practice.[10,11] Nasal irrigation using normal saline (0.9%) and seawater spray (2.3%) were useful in preventing upper respiratory infections in children.[12,13] Saline water gargling and saline nasal irrigation at hypertonic concentrations (1.5–3%) showed protection against the common cold.[14] There is also evidence on the beneficial effect of saline irrigation in chronic inflammatory conditions like rhino-sinusitis,[15,16] which is characterized by the blockage of sinuses. Irrigation may therefore facilitate the clearance of inflammatory exudate.

In vitro evidence by Ramalingam et al. demonstrated that sodium chloride (NaCl) results in a dose-dependent inhibition of replication of a range of DNA and RNA viruses, including the human coronavirus 229E (HCoV-229E).[17] This antiviral effect is mediated through the formation of *hypochlorous acid* (HOCl).[17] HOCl not only accumulates within neutrophils and macrophages but also accumulates within *non-myeloid epithelial cells*.[17] An interesting observation concerning the antiviral effect of NaCl is found in shrimp, which becomes more susceptible to white spot syndrome when water salinity decreases.[18] Another interesting observation comes from human cancer literature; women who possess a GG polymorphism in the promoter of the *MPO* gene (that results in elevated myeloperoxidase production) were shown to have lower cervical cancer incidence, indicative of the innate immune response of cervix epithelial cells against some high-risk strains of human papillomavirus.[19]

Post-hoc analysis[20] of the *Edinburgh and Lothians Viral Intervention Study* (ELVIS)[14] also confirmed the direct beneficial role of hypertonic saline against alpha and beta coronaviruses. This work[20] can be considered the most relevant clinical study suggesting the beneficial effect of gargling and irrigation against SARS-CoV-2 infection. The primary outcome of this study was a reduction in the duration of illness.[20] Recent *in vitro* evidence by Rafael et al. showed that 1.5% NaCl causes 100% inhibition of replication of the SARS-CoV-2 virus,[21] another vital piece of evidence favoring hypertonic saline use.

A study has also shown that even plain water gargling is competent in preventing upper respiratory tract infection, indicating mechanical detachment of viruses as a possible effect of gargling.[22] From a practice point-of-view and logically speaking, the whirling forces caused by gargling movements can undoubtedly contribute to this detachment, thus compromising viral entry. Interestingly, the work of Satomura et al. has shown the additional potential of plain water over povidone-iodine.[22] Although povidone-iodine is an antiseptic with known virucidal properties, it may not be well tolerated as a gargle due to its strong and irritant taste. Also, povidone-iodine may injure pharyngeal mucosa due to its cytotoxic effects, altering microbial flora dynamics thereby, enabling the settling, entry, and invasion of bacterial pathogens and viruses. Therefore, saline water is preferable in contributing to additional infection control over plain water due to the dislodging effect of gargling forces and virucidal effects of NaCl. The fact that gargling is a suitable sampling method for diagnosing mild COVID-19 cases[20] further supports the notion that saline gargling may be beneficial. While few reports in the sinusitis literature doubt the potential of hypertonic saline,[23,24] several pieces of evidence[14,20,21] indicate the reliability of saline gargling and nasal irrigation (preferably at hypertonic concentration) as effective cleansing practices and antiviral strategies.

Managing community transmission is crucial at this time, but there is currently a lack of potential interventions. Elevated SARS-CoV-2 viral load in saliva and nasal secretions[1,8] is strongly connected with community transmission. Because the virus anchors to the upper respiratory epithelium (nasal epithelium and/or throat mucosa),[7] replicates in the throat,[1] and exhibits a broad shedding pattern (before infection and after seroconversion[8]), saline water gargling and nasal irrigation may limit its community spread. In general, these maintenance approaches serve as gatekeepers for oral and nasal portals/passages primarily due to NaCl's broad antiviral effects and cleansing activity associated with gargling and nasal irrigation. Therefore, based on examination of several related pieces of evidence, judicious use of hypertonic saline may reduce SARS-CoV-2 viral load in recovered patients and contribute to breaking the chain of transmission.

1.3. Possible limitations and practice suggestions

Gargling may carry a small risk of swallowing low volumes of hypertonic saline water, and saline nasal irrigation may lead to aspiration. Another possibility during saline nasal irrigation is accidental injury to mucosa due to hot water use. Possible downward displacement of the virus from the upper respiratory to lower respiratory passages, while theoretically possible, is highly unlikely due to the broad-spectrum antiviral effects of NaCl. Disinfection of the irrigation vessel/pot is also vital because unclean vessels may enable lodging of particulate matter that may become a nidus for bacterial infection. However, these limitations are only speculative, and long-term studies have not shown the emergence of any such issues.[10–14] For some beginners, saline nasal irrigation may appear slightly difficult than gargling, but studies have shown this to be a well-tolerated approach.[10,11]

We note that studies by Ramalingam et al. employed an irrigation cup.[14,20] In the traditional practice of nasal irrigation, a vessel with an angulated spout, referred to as the neti-pot, is used, and the practitioner must assume the appropriate head position to allow free passage of water (Fig. 1). Although the above clinical trials[14,20] have shed new light concerning these practices, we firmly believe that using a neti-pot (in place of an irrigation cup) could further improve the antiviral activity. The neti-pot facilitates smooth passage of saline water as a thick column and can significantly contribute to the wetting of nasal passages, increasing the likelihood of toxin clearance and antiviral activity. As the angulated spout of the neti-pot is brought near the nostril-to form a seal with it, a continuum is established, giving the individual a sense of control on the water column.

On the other hand, the turbulent flow of water from an irrigation cup may result in dispensing of higher quantities of water into the nostril due to a lack of control, raising the possibility of aspiration. Although this is not of significant concern because only low volumes may be aspirated in any instance, the use of a vessel with a design closer to a neti-pot, in our opinion, can improve tolerance and commitment among new users. If a neti-pot or a similar vessel is not accessible, an irrigation cup with a chipped spout is reliable.

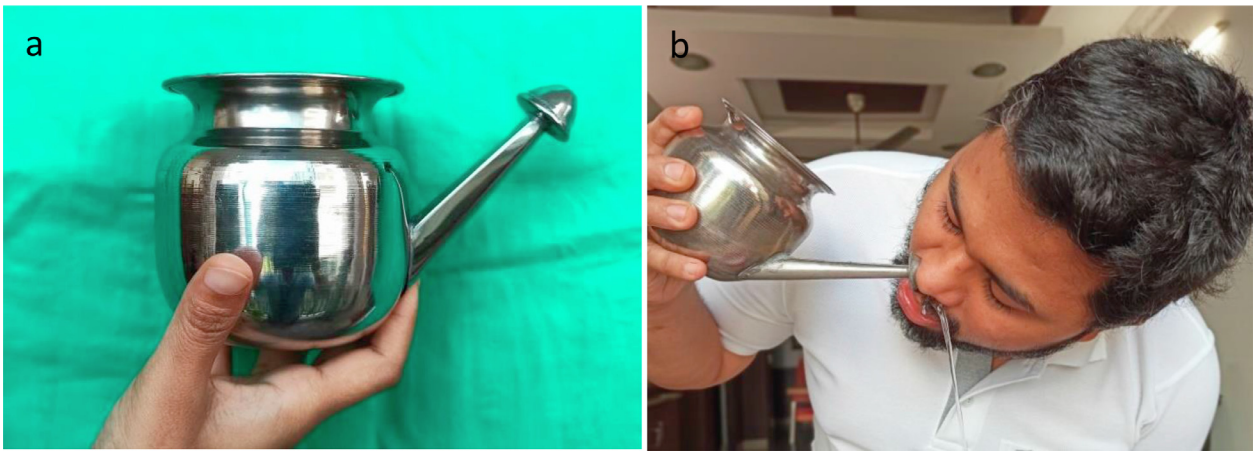

Fig. 1. Saline nasal irrigation or Jala-neti using an appropriate water pot. The neti-pot is a vessel with an angulated spout (panel a) and can contain a sufficient quantity of water for both nostrils. Before initiating the practice, the spout is gently brought close to the nostril to make a perfect seal. A downward and sideward inclination of the head facilitates the easy passage of saline water through the nasal passages due to gravity (panel b). A few moments before the practice, the individual must shift their breathing to the mouth. Following this practice, a lying posture or forward bending postures can be opted to facilitate the evacuation of retained water (Dr. PP is the demonstrator).

2. Concluding remarks

While there is limited clinical evidence concerning the curative or preventive role of saline water gargling and nasal irrigation against SARS-CoV-2 infection, all the previous studies outlined above provide compelling support to their applicability in the current crisis. Additionally, considering risks and benefits, these are undoubtedly harmless approaches and can be attempted fairly easily by most individuals; they do not require new knowledge or training. They can be easily implemented by individuals with mild symptoms, those facing obstacles to physician visits, and especially by those in home quarantine.[5] It must be borne in mind that some individuals often confuse simple influenza for COVID-19 because these tend to be indistinguishable in some cases.[4,5] Negative opinions of saltwater gargling and nasal irrigation[25] prevents use of these measures in the context of an actual viral infection; however, appropriate consideration of these complementary therapies may minimize infection, improve the overall course of the disease, and in the broader context, may even de-link the chain of community transmission. In our opinion, these are suitable options worth considering in the current crisis. We note that due to the lack of conclusive evidence, specific clinical studies are warranted.

Funding source

None declared,

Declaration of Competing Interest

None declared.

Acknowledgement

None declared.

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