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Mini Review

Nasal Irrigation in the COVID-19 Era

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Abstract

Rapid spread of SARS-CoV-2 to the community leading to the COVID-19 disease has undoubtedly changed individuals' lives and attitudes and has threatened healthcare systems globally. SARS-CoV-2 attaches and initiates its lifecycle in the nasopharyngeal mucosa via infected droplet inhalation which leads to high viral loads and increased disease transmission and severity. Other than preventive vaccination, additional measures to mitigate both the transmission and progression of SARS-CoV-2 are currently sought. Nasal irrigation can prevent early transmission, minimize viral shedding and disease severity, and limit complications by mechanical washing-out of infectious particles present in the nasal cavities. Several publications have now proposed that both isotonic (0.9% NaCl) and hypertonic (>0.9% NaCl) solutions can be utilized for nasal lavage in COVID-19 patients. Considering that nasal irrigations are safe and easy to use, this nonpharmacological remedy could be adopted by the public, patients and healthcare workers in early disease stages. In this review, the use of nasal rinsing as an adjunctive prophylactic measure to defend against SARS-CoV-2 is summarized and advocated.

Keywords: Nasal irrigation; Isotonic solution; Hypertonic solution; SARS-CoV-2; COVID-19; Viral load reduction

Mini Review

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which causes coronavirus disease-2019 (COVID-19), has brought us against an unprecedented global health crisis with the death toll increasing dramatically each passing day. Since the first outbreak in Wuhan, there have been more than 217 million confirmed cases of COVID-19, including more than 4.5 million deaths according to WHO (https://covid19.who.int/). The disease develops initially as a respiratory infection. Nasal, conjunctival and oral mucosa are entry portals of SARS-CoV-2 as the infection is mainly transmitted by exposure to infected respiratory droplets. The nasal epithelium and nasopharyngeal mucosa are also sites of replication of SARS-CoV-2 with nasal swabs presenting higher viral load compared to throat swabs [1]. The high transmission rate, the multiple SARS-CoV-2 variants and the lack of targeted treatments to combat the pandemic apart from available vaccines, render the addition of extra preventive measures of paramount importance.

Nasal Irrigation (NI) is a well-established practice that has been used for centuries to clean the airways. It facilitates physical drainage of thick mucus, allergens, infective debris and inflammatory mediators while enhancing hydration of the nasal mucosa lining and mucociliary function [2]. Both isotonic (0.9% NaCl) and hypertonic (>0.9% NaCl) solutions are used for nasal douching, with hypertonic solutions yielding more beneficial effects improving nasal symptoms such as nasal congestion, sneezing, nasal itching and rhinorrhea [3]. Recent in vitro studies suggest that solutions rich in chloride ions, e.g., hypertonic solutions with high NaCl strength, may exert anti-viral effects. In these studies, the influx of Cl^- ions generated by NaCl was found to block replication of HSV-1, RSV, MHV68, and CV-B3 viruses in the Vero cell line. More importantly, HCoV-229E (human coronavirus 229E) was significantly inhibited from concentrations of 30mM NaCl and above [4]. Similar results were obtained by Machado [5] who showed that 260 mM NaCl (corresponding to 1.5% NaCl) inhibit 100% SARS-CoV-2 replication in the same cells. Inhibition of virus replication was attributed to an intracellular mechanism and not due to the interaction of SARS-CoV-2 spike protein with its human receptor ACE2 that is indispensable for viral infection. Finally, a third in vitro study showed that the proliferation of yeast on the surface of a facepiece may strongly be reduced when this is coated with hypertonic saline. The authors proposed that this unspecific inhibitory salt effect could protect mask carriers efficiently from SARS-CoV-2 infections [6]. Preclinical studies supporting use of hypertonic solutions for SARS-CoV-2 inhibition can be found in Table 1.

Given the high viral titers detected in the upper respiratory tract of asymptomatic and symptomatic individuals [1], and in agreement with the preclinical data mentioned above, use of NI

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Table 1: Preclinical studies supporting use of hypertonic solutions for SARS-CoV-2 inhibition.

Experimental model	Assays and analyses	Proposed hypothesis	Key Results	Conclusion(s)	Reference
HeLa, 3T3, A549, HuH-7.5, Huh-7 cells infected with herpes simplex virus-1, murine gamma herpesvirus 68, respiratory syncytial virus, influenza A virus, human coronavirus 229E, coxsackie B3 viruses	Assays: Virus replication assays, cell viability assays Statistical analysis: Unpaired two-tailed t-test. p values <0.05 are statistically significant.	Increasing availability of NaCl may show antiviral activity against a broad range of viral infections.	HCoV-229E was significantly inhibited from a concentration of 30mM NaCl and above present in the cells' medium ($p < 0.01$). Viral inhibition by NaCl was also observed for HSV-1, RSV, MHV68, HCoV-229E, CV-B3 viruses in the presence of NaCl. The influx of Cl^- (not Ca^+) ions is essential for the inhibition of viral replication by NaCl.	Epithelial, fibroblast and hepatic cells have enhanced antiviral activity in the presence of increasing concentrations of NaCl. Replication of RNA (human coronavirus 229E, respiratory syncytial virus, influenza A virus, coxsackie virus B3) and DNA (herpes simplex virus-1, murine gamma herpesvirus 68) viruses was inhibited in a dose-dependent manner.	[4]
Vero CCl-81 cells infected with SARS-CoV-2	Assays: Cell viability, cell death quantification, cytopathic effects (CPE) assays Statistical analysis: Unpaired two-tailed t-test, one-way ANOVA. p values <0.05 are statistically significant.	The ability of HTS saline solution to inhibit virus replication in vitro.	260 mM NaCl (1.5% NaCl) inhibited 100% SARS-CoV-2 replication in Vero cells. Virus replication inhibition was due to an intracellular mechanism and not due to the dissociation between spike SARS-CoV-2 protein and its human receptor ACE2. NaCl depolarized the plasma membrane supposedly associated with the inhibition of the SARS-CoV-2 life cycle.	HTS inhibited SARS-CoV-2 virus replication by more than 90% in Vero cells due to perturbation in one or several steps of the virus intracellular cycle.	[5]
Yeast Saccharomyces cerevisiae suspended in HTS environment	Assays: Growth inhibition assays Statistical analysis: Two-sided t-test	HTS-coated filtering facepiece might strongly reduce the numbers of infectious particles on its surface.	Proliferation was inhibited in a concentration-dependent manner, i.e., above 50 g/L, yeast cell proliferation was completely blocked. At a NaCl concentration of 100 g/L, decomposition of the original inoculated organisms was observed in the suspension mix.	HTS inhibited cell proliferation in a dose-dependent manner in yeast which is a unicellular organism comprising a defending cell wall in contrast to viruses. Considering COVID-19, this unspecific salt effect may enforce the protection of filtering facepiece leading to a possible protective effect of humans from viral particles.	[6]

Abbreviations: ACE2: Angiotensin Converting Enzyme 2; COVID-19: Corona Virus Disease 19; CPE: Cytopathic Effect; HCoV: Human Corona Virus; HTS: Hypertonic Solution; NaCl: Sodium Chloride; SARS-CoV-2: Severe Acute Respiratory Syndrome Corona Virus.

as a means to bring down the viral load, reduce transmission, symptoms and duration of illness has been proposed recently in a series of publications. In human samples, Ramalingam and colleagues [7] were the first to show reduced viral shedding as a result of use of hypertonic saline nasal irrigation (HSNI; 2-3% NaCl) combined with standard treatment versus standard treatment alone in the ELVIS (Edinburgh and Lothians Viral Intervention Study) clinical study. The study participants suffered from common cold originating from several viruses including Rhinovirus, coronavirus COV-229E and other strains, Influenza A virus, and Human metapneumovirus. In a follow up study [8] conducted by the same investigators, post-hoc secondary analysis of data from the ELVIS study showed that hypertonic saline nasal irrigation and gargling (HSNIG) reduced the duration of coronavirus upper respiratory tract infection (URTI) by an average of two-and-a-half days. Overall, NI with hypertonic solution reduced illness duration by 22%, use of over-the-counter medication for symptom relief by 36%, and virus spread to the family by 35%. These conclusions suggested that saline rinses can reduce symptom burden and decrease

Table 2. Clinical studies and case reports supporting use of hypertonic or isotonic solutions in patients with COVID-19.

Intervention		Administration	Design and Statistics	Duration	Population/Age	No of patients	Clinical hypothesis	Key Results	Key messages	Reference
Hypertonic solutions	Intervention arm: HTS saline (2%, 2.5%, 3% Cornish sea salt) with nasal irrigation and gargling (HSNIG) Control arm: no intervention	HSNIG arm: as many times as needed (max. 12 times/day) Control arm: no intervention, dealt with disease as they normally did	Pilot, non-blinded, randomized controlled trial (ELVIS study) Statistical analysis: Binomial tests, two-sample t-tests, Mann-Whitney tests. p<0.05 is statistically significant.	14 days	Patients with COV-229E and other URTI. Intervention group: n = 32 (average age=34.6 years), Control group: n = 34 (average age=39.4 years)	66 (Intervention arm: 32, Control arm: 34)	HSNIG may be an effective treatment option for the common cold (URTI infection from Rhinovirus, Coronaviruses COV-229E, COV-OC43, COV-HKU1, COV-NL63, Enterovirus, Influenza A virus, Respiratory syncytial virus, Parainfluenza virus type 3 and Human metapneumovirus).	HSNIG was effective as a treatment of common cold: In the intervention arm, duration of illness was lower by 1.9 days (p = 0.01), over-the-counter medications (OTCM) use by 36% (p = 0.004), transmission within household contacts by 35% (p = 0.006) and viral shedding by ≥0.5 log 10/day (p = 0.04). There was a significant reduction in the duration of runny nose (1.8 days, p = 0.01), blocked nose (2.7 days, p < 0.001), sneezing (1.5 days, p = 0.02), cough (2.4 days, p = 0.003) and hoarseness of voice (1.7 days, p = 0.02). Adverse effects: None mentioned	HSNIG significantly reduced the duration of URTI symptoms, OTCM use and disease transmission within the household.	[7]
	Intervention arm: HTS saline (2%, 2.5%, 3% Cornish sea salt) with nasal irrigation and gargling (HSNIG) Control arm: no intervention	HSNIG arm: as many times as needed (max. 12 times/day) Control arm: no intervention, dealt with disease as they normally did	Post-hoc secondary analysis of ELVIS pilot randomized controlled trial Statistical analysis: As above	14 days	Intervention arm: HCoV 229E = 3, HCoV NL63 = 1, HCoV HKU1 = 3 Control arm: HCoV NL63 = 2, HCoV OC43 = 1, HCoV HKU1 = 5	15 (Intervention arm: 7, Control arm: 8)	HSNIG may be an effective treatment option for COVID-19.	HSNIG effect as a treatment of COVID-19: Patients infected with coronavirus: duration of illness was lower in the intervention arm compared to the control arm (5.6 days, p = 0.054). The difference in the duration of blocked nose was -3.1 days (p = 0.04), cough -3.3 days (p = 0.02) and hoarseness of voice -2.9 days (p = 0.03) in favor of HSNIG. Adverse effects: None mentioned	HSNIG may reduce symptoms and duration of illness in COVID-19 patients.	[8]
	Intervention arm: Nasal rinsing and gargling with hypertonic saline solution	Hypertonic saline nasal rinsing and gargling 5-6 times a day at home	Case report	-	54-year-old moderate smoker, asymptomatic SARS-CoV-2 infected physician (positive nasopharyngeal swab test)	1	Repetitive nasal rinsing and gargling with hypertonic saline could be used for prophylaxis against SARS-CoV-2 infections.	The infected physician remained asymptomatic, and serum immunoglobulin IgG for SARS-CoV-2 tested negative two months after the infection. Adverse effects: Slight, short-lasting, bearable burning sensation in the nose and throat mucous membranes	Repetitive nasal rinsing and gargling with hypertonic saline could be used as an adjunctive inexpensive treatment for SARS-CoV-2 infections.	[10]

	No intervention (Group 1, NI); HTS nasal saline irrigations (NeilMed) (Group 2, HTS); HTS irrigations with ½ teaspoon surfactant (Johnson's Baby Shampoo) (Group 3, HTSS)	NI group: no treatment HTS group: twice daily irrigation with 250cc HTS HTSS group: twice daily irrigation with hypertonic saline with 1% surfactant	Open-label randomized controlled trial Statistical analysis: Kruskal-Wallis test. $p<0.05$ was statistically significant.	21 days	>18-year-old patients diagnosed with SARS-CoV-2	45 (17, 14, 14 in groups 1, 2 and 3, respectively)	Nasal irrigation with HTS saline with or without surfactant may reduce upper respiratory tract symptoms and viral load.	There was a significant difference in median days to symptom resolution for nasal congestion (NI, 14 days; HTS, 5 days; HTSS, 7 days; p=0.04) and headache (NI, 12 days; HTS, 3 days; HTSS, 5 days; p=0.02). There was a trend toward differences between intervention groups and control group for cough (p=0.19), and fatigue (p=0.17). Adverse effects: None mentioned	HTS saline rinses with or without surfactant can reduce symptom burden in COVID-19 patients.	[11]
	Group 1: No intervention; Group 2: Nasal saline irrigation with HTS; Group 3: Nasal saline irrigation with both HTS and nasal steroid spray	Group 1: No treatment Group 2: 10cc HTS to each nostril, twice a day Group 3: 10cc HTS nostril, twice a day and steroid spray 2*2 puffs/each nostril/ Triamcinolone Acetonide 0.055%	Single-center randomized-controlled study Statistical analysis: One-Way ANOVA Test. $p<0.05$ was statistically significant.	30 days	Group 1: 38.5 ± 10.5 years (age range: 16–56) Group 2: 39.2 ± 11.3 years (age range: 18–61) Group 3: 39.2 ± 11.3 years (age range: 18–61) All patients were diagnosed with SARS-CoV-2	150 (50 patients in each group)	Nasal irrigation with HTS and steroid treatment may be successful in the treatment of Post-Viral Olfactory Dysfunction (PVOD) because of COVID-19.	Self-Rating Olfactory Score (SROS) of the group receiving Nasal Saline Triamcinolone Acetonide treatment on the 30th day was significantly higher than in other groups ($p = 0.018$ for Group 1 vs Group 3; $p = 0.033$ for Group 2 vs Group 3). Olfactory Dysfunction Duration (ODD) was significantly reduced in this group compared to other groups ($p = 0.022$ for Group 1 vs Group 3; $p = 0.028$ for Group 2 vs Group 3). Adverse effects: None mentioned	Nasal irrigation with HTS and Triamcinolone Acetonide is successful in olfactory dysfunction treatment due to COVID-19.	[12]

	Study group: Galenic preparation including antibiotics tobramycin 0.45% and lincomycin 0.75% diluted in 5 mL of a solution containing 3% HTS, high-molecular-weight sodium hyaluronate 0.2%, and xylitol 5% Control group: No intervention	Nasal nebulization twice a day	Single-center study Statistical analysis: None mentioned	7-10 days	40 males and 36 females, aged between 31 and 65 years diagnosed with SARS-CoV-2	76 patients	Nebulization with a galenic mixture based on HTS and a series of additional ingredients may shorten the duration of viral shedding in patients with mild COVID-19.	At the end of the treatment, all patients that received the HTS-based galenic preparation were symptomless. The molecular testing, performed on the 10th day, showed that all patients had a negative result. Adverse effects: None mentioned	A galenic preparation with topical antibiotics, HS, HA and xylitol adequately nebulized into the nose by a specific nasal device could shorten the time of viral shedding in patients with COVID-19.	[13]
	Study group: Solution containing hypertonic saline (HS) 3%, high-molecular-weight sodium hyaluronate (HA) 0.2%, and xylitol 5% inhaled via a nasal douche (Rain-wash) connected to an aerosol nebulizer Control group: No intervention	Nasal nebulization twice a day for seven days (7-14 or 14-21)	Single-center study Statistical analysis: None mentioned	2 8 days	80 males and 92 females, aged between 18 and 75 years diagnosed with SARS-CoV-2	172 patients	Nebulization with a galenic mixture based on HTS and a series of additional ingredients may shorten the duration of viral shedding in asymptomatic COVID-19 subjects.	All subjects were positive at the beginning of the study. Seventy-two subjects performed therapy from the 7th to the 14th day and they had a negative result on nasal swab test on the 14th day. Sixty-three subjects performed therapy from the 14th to the 21st day and they had a negative result on nasal swab test on the 21st day. Thirty-seven subjects did not use any medication and were negative on the 28th day. Adverse effects: The treatment was safe and well-tolerated in all treated subjects	A medical device with HS, HA, and xylitol adequately nebulized into the nose by a specific nasal douche could shorten the time of viral shedding in asymptomatic subjects positive to RT-PCR for the RNA of SARS-CoV-2.	[14]

	Solution containing 3% NaCl (HS), high-molecular-weight sodium hyaluronate (HA) and xylitol	As above	Single-center study Statistical analysis: None mentioned	7 days	22 males and 20 females, aged between 22 and 65 years diagnosed with COVID-19	42 patients	Nebulization with a solution containing 3% NaCl, high-molecular-weight sodium hyaluronate and xylitol may shorten the duration of smell impairment in patients with mild COVID-19.	All patients with hyposmia/ hypogeusia improved after treatment and achieved normal sensory function ten days from treatment starting. Cacosmia completely disappeared between 10 and 30 days after the initial administration. All anosmic/ ageusic patients recovered normal smell and taste between 10 and 20 days after treatment; cacosmia resolved between 20 and 40 days after treatment onset. The treatment was safe and well-tolerated in all patients. Adverse effects: No adverse events were reported during treatment	A medical device with HS, HA, and xylitol nebulized into the nose by a specific device could restore smell and taste in a short time and safely in patients with COVID-19.	[15]
Isotonic solutions	Study group: NSNSG treatment Control group: No intervention	Study group: 25 mL NSNSG Control group: No intervention	Single-center study Statistical analysis: Chi-square test, Odds ratio. p<0.05 is statistically significant.	4 days	18 to 80 years, from both sexes, having Ct value 25 or less in RT-PCR test for SARS-CoV-2	129 (Study group: 61, Control group: 68)	NSNSG would wash away virions from mucus suspension and micro aspiration would be prevented.	The normal saline nasal spray and gargle can protect nasal and pharyngeal mucosa from SARS-CoV-2. Adverse effects: None mentioned	NSNSG significantly washes off SARS-CoV-2 from nasal cavity and pharynx and prevents micro aspiration of the virus in lung alveoli and pneumonia.	[9]

Abbreviations:
COVID-19: Corona Virus Disease 19; HA: Sodium Hyaluronate; HS: Hypertonic Saline; HCoV: Human Corona Virus; HSNIG: Hypertonic Solution with Nasal Irrigation and Gargling; HTS: Hypertonic Solution; HTSS: Hypertonic Solution plus Surfactant; NaCl: Sodium Chloride; NI: No Intervention; NSNSG: Normal Saline Nasal Spray and Gargle; OTCM: Over-the-counter Medication; SARS-CoV-2: Severe Acute Respiratory Syndrome Corona Virus; URTI: Upper Respiratory Tract Infections.

viral shedding -including that of coronaviruses- in patients.

A series of additional publications confirmed the results mentioned above further promoting NI as an easily implementable technique to be used for preventing and/or controlling COVID-19 infection. Chatterjee et al [9] performed a clinical trial to investigate if normal saline nasal spray and gargle (NSNSG) can protect nasopharyngeal mucosa from SARS-CoV-2 infection. 129 individuals with laboratory confirmed SARS-CoV-2 were allocated to study and control groups. In the study group, 61 patients received NSNSG for 4 days whereas 68 patients in the control group received no intervention. In 91% of patients of the study group, SARS-CoV-2 severity score was either improved or did not progress compare to the control group. Tolerability with NSNSG was found acceptable in the study group. The authors concluded that NSNSG significantly washes off SARS-CoV-2 from the nasal cavity, pharynx and the lung alveoli preventing micro aspiration and pneumonia [9]. NSNSG with hypertonic solution performed several times a day also helped a 54-year-old asymptomatic SARS-CoV-2 infected physician who was quarantined. The infected physician remained asymptomatic, and serum immunoglobulin IgG for SARS-CoV-2 was tested negative two months after the infection [10].

In non-hospitalized patients with COVID-19, hypertonic saline rinses can reduce symptom burden. An open-label randomized controlled trial evaluated the effect of NI with hypertonic saline or saline with 1% surfactant on upper respiratory symptoms and viral load. Analysis of nasal swabs showed that NI relieved upper respiratory symptoms with nasal congestion and headache resolving a median of 7-9 days earlier in the intervention groups. Additionally, headache was significantly reduced. A trend toward decreased cough and fatigue between groups was also reported [11]. Another study found that when COVID-19 patients performed HSNI supplemented with steroids, the olfactory dysfunction duration was significantly reduced restoring the sense of smell [12].

Duration of viral shedding of SARS-CoV-2 after nebulization with a galenic mixture based on HTS was reduced in two different clinical studies comprising 248 patients with mild or asymptomatic COVID-19. In the first study including 76 patients with mild disease phenotype, a galenic preparation containing hypertonic saline (3%), high-molecular-weight sodium hyaluronate, xylitol and antibiotics was administered twice daily for a period of up to 10 days. At the end of the treatment, all patients were symptomless and had a negative molecular test on the 10th day [13]. In the second study, 172 asymptomatic COVID-19 subjects received the HTS-based preparation mentioned above without antibiotics for 7 days; the patients were negative at the nasal swab testing performed on the 14th or 21st post-treatment day [14]. The same hypertonic solution was additionally administered via nebulization in 42 patients with hyposmia/hypogeusia due to COVID-19. All patients in the study improved after treatment and achieved normal sensory function ten days after treatment initiation. Cacosmia completely disappeared between 10- and 30-days post-treatment [15]. In all cases, the treatment was safe and well-tolerated in all treated subjects. The results from infected patients with mild or no symptoms showed that NI with hypertonic solutions represents

a simple, practically feasible, and globally implementable strategy with important therapeutic value. All research studies supporting use of hypertonic or isotonic solutions in patients with COVID-19 can be found in Table 2.

In agreement with the experimental conclusions reached above, several review studies strongly support use of NI to reduce symptom burden and break the chain of infection. For example, Singh et al [16] drew a parallel between nasal irrigation and hand washing used to contain the spread of the infection. These interventions may be useful in reducing nasopharyngeal viral titers and viral shedding, ultimately leading to COVID-19 transmission reduction. Shetty and co-workers [17] drafted a guide for use of topical solutions for the prophylaxis of healthcare professionals dealing with COVID-19 infected patients. It was noted that irrigation of the nasopharynx and gargle of the oropharynx with hypertonic saline, twice daily before and after patient exposure, could decrease viral attachment and entry into cells. Similar conclusions were reached by a hypothesis paper by Panta and co-workers [18]. Farrell and colleagues [19] postulated that saline irrigations with or without indicated additives are safe to use in the presence of COVID-19 especially for patients who already use these therapies for rhinosinusitis management. Stathis and co-workers [20] compared several commonly used nasal antiseptics and gargles including irrigations with hypertonic solutions. They concluded that hypertonic solution administered as mouth wash and/or NI can be used for reducing the rate of transmission, for reducing viral load very early after infection and for prophylaxis after exposure to SARS-CoV-2. Daily nasal douching and gargling combining hypertonic saline solution with virucidal mucosal therapies such as 0.23% aqueous PVP iodine has also been advised for enhanced protection [21].

Having recognized the potential usefulness of nasal douching in COVID-19 management, this technique is now clinically recommended by different medical associations and committees including the French Association of Pediatric Otorhinolaryngology (AFOP) and French Society of Otorhinolaryngology (SFORL), and ENT Pediatric otolaryngology. It was noted that NI with saline can provide a nonpharmacological technique for treating nasal congestion, especially in infants. The same guideline stresses the importance of extra precautions to be implemented in healthcare settings to avoid contamination of a staff caregiver. Even in the absence of NI, the risk of transmitting the virus within the household members is very high because an infected child has a high risk of contaminating his/her family members [22]. Along the same lines, the recommendations by French Rhinology Association (AFR), French ENT College, French ENT National Union (SNORL), and French National Professional ENT Council (CNPORL) provided the framework to protect healthcare workers against COVID-19 while they continued to provide emergency care helping patients. Hand-washing before and after treatment of patients, washing and disinfecting equipment and soiled surfaces weekly, and discarding all the liquid after each nasal wash are among strict hygiene measures should ideally be taken during treatment [23]. Considering acceptance of such practices by health care professionals, NI with hypertonic saline solutions has also been positively judged and accepted by 43.9% of pharmacists attending the 7th National Hospital and Institution Pharmacists Congress. Analysis of 237 questionnaires using the Turkish COVID-19 Scientific Committee guideline highlighted the use of media tools affecting the attitudes of both the public and health professionals towards use of saline irrigations for prevention and control of the spread of the COVID-19 disease [24].

Conclusively, the aforementioned information in the field of COVID-19 in the last months fully supports the use of NI for management of COVID-19 respiratory tract symptoms and for reduction of disease duration in infected patients. The use of hypertonic solutions could confer added clinical benefit compared to isotonic solutions facilitating nasal decongestion and cleansing simultaneously. NI as a cost-free modality can be globally implemented as a prophylactic and therapeutic strategy posing no side effects or complications in the battle against SARS-CoV-2. Additional clinical and epidemiological studies are indispensable to strengthen the results and the inferred recommendations.

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