Case Report

ISSN 2639-9458

Microbiology & Infectious Diseases

Naso-Oral Irrigation with Electrolyzed Saline Solution Reduced COVID-19 Antigen Levels: Case Report

Kembu Nakamoto MD, PhD[1]*, Hiroshi Hashiyada MD[1], Toshiyuki Fujii MD, PhD[1], Kazuki Motoyama MD[1], Kazuya Yoshida MD, PhD[1], Sadahiro Kawamoto MD[2] and Yuko Kawamura MD, PhD[2]

[1]*Divisions of General Thoracic Surgery Shunan Memorial Hospital, Kudamatsu, Yamaguchi, Japan.*

[2]*Respiratory Medicine Shunan Memorial Hospital, Kudamatsu, Yamaguchi, Japan.*

***Correspondence:**

Dr K Nakamoto, Divisions of General Thoracic Surgery Shunan Memorial Hospital, 1-10-1 Ikunoya-minami, Kudamatsu, 744-0033 Yamaguchi, Japan, Tel: +81833-45-3330, Fax: +81833-45-3331.

Received: 22 June 2021; **Accepted:** 26 August 2021

Citation: Nakamoto K, Hashiyada H, Fujii T, et al. Naso-Oral Irrigation with Electrolyzed Saline Solution Reduced COVID-19 Antigen Levels: Case Report. Microbiol Infect Dis. 2021; 5(4): 1-5.

ABSTRACT

Rationale: *Super acidic (pH<2.7) electrolyzed saline (ES) is a non-toxic and all-purpose disinfectant for viruses, bacteria and fungi. The effect of gargling ES was investigated in COVID-19.*

Patients and Methods: *Three patients with/without pneumonia were admitted since June 8, 2021. Treatment strategies followed to the Japanese Guidelines for Acute Respiratory Distress Syndrome 2016 with modifications for remote treatment. ES gargling were used to decontaminate the primary infection site. Each patient gargled a glass of ES on the day of admission (day 1), and then gargled half a glass of ES 3 times a day for the following 3 days.*

Results: *Gargling ES resulted in a prompt (within a week) reduction in salivary SARS-CoV-2 antigen levels, and all 3 patients recovered and were released from quarantine within 2 weeks.*

Conclusions: *Non-specific virucidal activity of ES was reconfirmed in COVID-19. ES gargling will suppress disease progression and transmission of COVID-19.*

Introduction

Electrolyzed saline (ES) is a non-toxic and all-purpose disinfectant, which kills viruses; bacteria, except spore-forming bacteria; and fungi [1,2]. The US Food and Drug Administration (FDA) approved ES as a high-level disinfectant in October 2002 [3]. We have used ES as a disinfectant and sterilizer against the biocontamination of residential spaces, medical equipment, skin, mucosae, and the closed pleural/abdominal cavity since 1993 [1]. We routinely instruct patients to gargle ES as an oral hygiene procedure for preoperative preparation and flu-related pharyngitis [4]. Gargling ES promptly reduced SARS-CoV-2 antigen (Ag) levels in 3 patients. The effects of ES gargling in these 3 patients are discussed.

Patients and Methods

The institutional review board of our hospital granted ethical approval for this study (IRB approval #2602, SMH, March 24, 2015; #02-02, SMH, Nov. 11, 2020; #03-05, SMH, May 25, 2021). Informed consent was obtained from each patient.

Three patients from the regional COVID-19 monitoring center have been admitted to our hospital since June 8, 2021, which has been designated as an official hospital for COVID-19 treatment.

Remote treatment strategies for COVID-19 infection

Treatment strategies generally followed the Japanese Guidelines for Acute Respiratory Distress Syndrome 2016 [5] with modifications.

Prompt decontamination of the primary infection site

ES gargling and the nasal injection of ES solution were used to decontaminate the primary infection site. Each patient gargled a glass of ES and then received bilateral 2-ml nasal injections of ES with a 5-ml syringe on the day of admission (day 1). Each patient then gargled half a glass of ES with/without nasal injections 3 times a day for the following 3 days.

Anti-viral drug therapy

Remdesivir (Veklury□; Gilead Sciences, USA) was administered for 5 days when pneumonia was observed on computed tomography (CT). Favipiravir (Avigan□, FUJIFILM Toyama Chemical Co., Tokyo) was administered when no pneumonia was observed on CT from day 2.

Suppression of pulmonary interstitial edema

Blowing up a rubber balloon was used to induce a positive end-expiratory pressure (PEEP) load and prevent permeability edema. This method was employed as an alternative to mechanical ventilation.

Oxygenation

Minimal oxygen was given to maintain $\%SpO_2$ between 90~95% to reduce production of oxygen radicals, if patients complained of dyspnea.

Online monitoring of disease changes

The patients' symptoms (fever, general fatigue, naso-oral sensory defects, and dyspnea), the percentage oxygen saturation ($\%SpO_2$), blood tests, pneumonic shadows on CT images, and salivary or nasal swab SARS-CoV-2 Ag levels (according to the Lumipulse SARS-CoV-2 Ag test; Lumipulse G1200, FUJIREBIO, Tokyo) were monitored. Symptoms and $\%SpO_2$ levels were monitored every day; chest CT scans were carried out on admission and on days 2, 4, 7, and as needed before discharge; and salivary Ag tests were performed on admission before ES gargling, on day 2 (in the early morning), and on days 7 and 14. The nasal swab Ag test was performed just before discharge.

Custom-made ES preparation

ES quickly loses its disinfective activity. A custom-made ES preparation was used in this study. Aqueous ES solution was produced from a 0.1% salt/tap water mixture using a water electrolysis generator (Oxilyzer Medical C-L, Koken Ltd., Tokyo). Electrolyzed acidic water with a pH of <2.7 was generated at the anode compartment and was collected for immediate use.

Patients' presentations

The patients were a 45 y.o. male, a 72 y.o. male, and a 65 y.o. female. The elderly patients were partners and had received their 2nd COVID-19 vaccinations a week ago, whereas the remaining patient had not received any vaccinations. None of the patients had comorbidities. All of the patients had mild fever and general fatigue. Two patients had mild sensory disturbance. The two male patients had very high (above the measurable limit of 5000 pg/ml) salivary Ag levels on day 1, and exhibited non-segmental diffuse pneumonia and fine interstitial shadows on CT images without respiratory insufficiency on day 2. These two patients received anti-viral drug injections for 5 days from day 4, as it took 2 days to obtain the drugs after the CT-based diagnosis. The Ag levels of the 3 patients decreased overnight after they first gargled ES, and the Ag had completely disappeared by the morning of day 7 (Figure 1). The nasal swab Ag test conducted on day 14 was also negative. The pneumonic shadows in the two male patients gradually faded away (Figure 2). None of the patients required oxygenation during

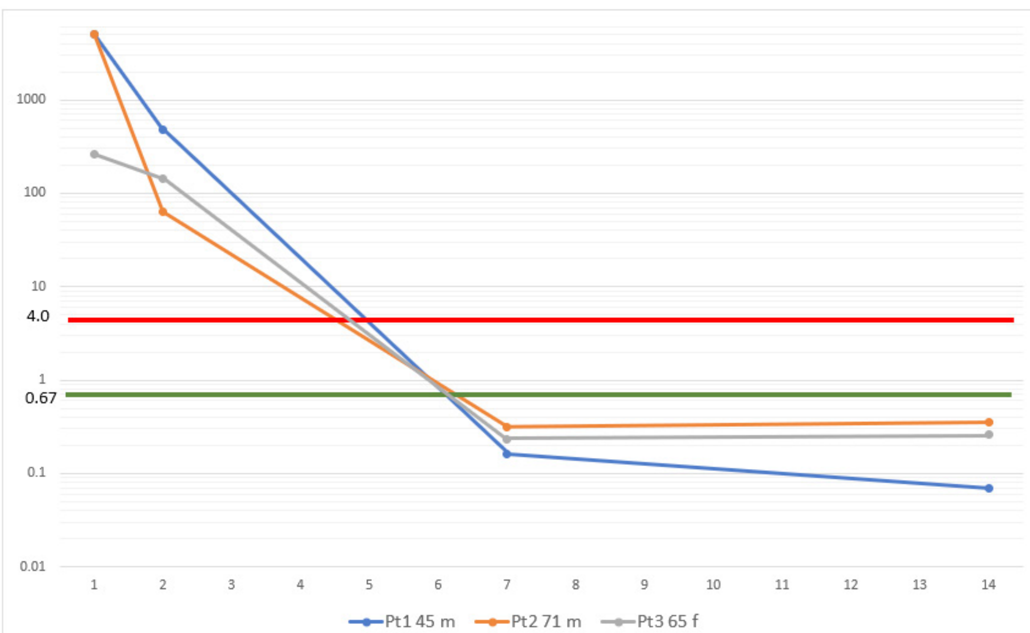

Figure 1: Reduction of salivary SARS-CoV-2 antigen (Ag) levels by gargling electrolyzed saline (ES) (logarithmic graph).

The salivary level of the SARS-CoV-2 Ag was markedly decreased by gargling ES and was reduced on day 7 after admission. Blue line: A 45 y.o. male patient, orange line: A 72 y.o. male patient, gray line: A 65 y.o. female patient; Arrows: ES gargling; Above red line: COVID-19-positive; Below green line: COVID-19-negative; Vertical axis: salivary SARS-CoV-2 Ag level (pg/ml), Horizontal axis: time since admission (days).

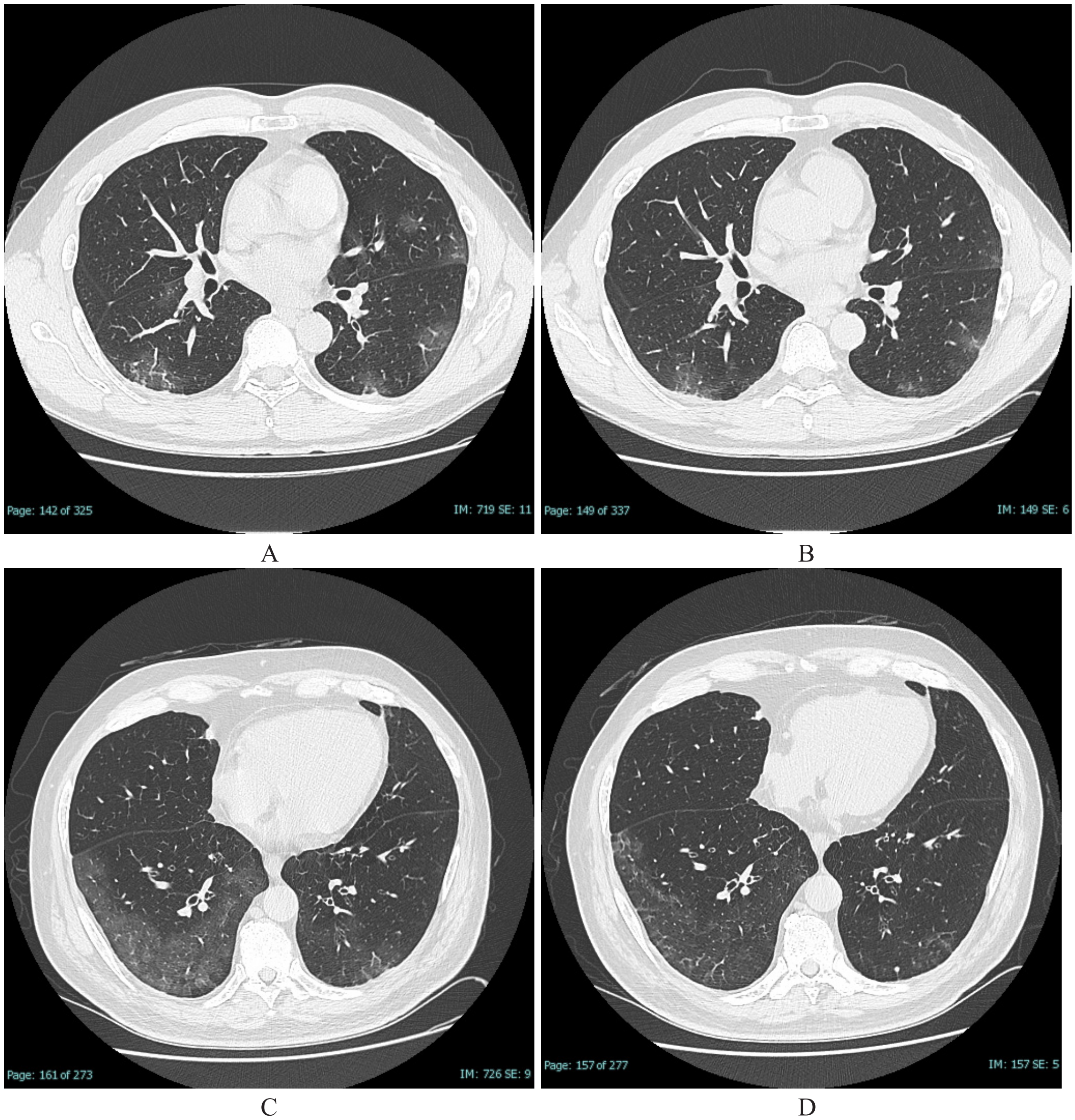

Figure 2: Amelioration of viral pneumonia.

Two male patients exhibited multiple non-segmental diffuse pneumonia with fine interstitial consolidation on computed tomographic (CT) images on day 2. The pneumonic shadows in these patients gradually faded away. A, C: CT performed on admission (day 1); B, D: CT performed on day 10; Top: 45 y.o. male patient; Bottom: 72y.o. male patient.

admission. Our treatment strategy resulted in prompt reductions in SARS-CoV-2 Ag levels, and all 3 patients were discharged on day 14 and returned to normal life.

Discussion

We showed that ES had strong virucidal activity against the SARS-CoV-2 Ag in all 3 of our patients. Local disinfection through gargling ES blocked the progression of the disease. The reason why local control suppressed systemic disease, such as pleural drainage for septic empyema [6], is unclear. The following hypotheses are suggested: **1.** The SARS-CoV-2 Ag has the ability to rapidly proliferate at the primary infection site. **2.** The primary site is the main source of virus particles and/or chemical mediators. **3.** The mechanism responsible for rapid disease progression involves the hematological dissemination of the virus and/or chemical mediators, rather than airway dissemination, which has multiple defense barriers against viruses [7], from an early phase. **4.** The lungs are the first receiver of venous return from the affected site. The clinical features of COVID-19 resemble those of adult respiratory distress syndrome [8], and the main target organ is the pulmonary vascular endothelium [9]. Alveolar capillaries with thin walls in the basement membrane and endothelium are involved in gas exchange in the low-pressure circulatory system [10]. These capillaries are sensitive to cytokine reactions [11]. The multiple simultaneous non-segmental pulmonary lesions seen in the early phase of the infection are due to interstitial permeability edema [8]. **5.** Residual virus in the interstitial spaces is removed by macrophages or other factors in the pulmonary lobules [7,12].

Based on the abovementioned hypothesis, we developed the following treatment strategy against COVID-19: **1.** Immediate local decontamination with ES irrigation reduces the levels of the virus and cytokine producers and blocks the hematological spread of the virus and cytokine reactions. **2.** Appropriate anti-viral drugs should be administered [13]; however, the effects of such drugs were not evaluable in this study. **3.** Inducing PEEP [8] through a simple procedure (blowing up a balloon) is helpful for suppressing pulmonary edema in the reversible phase.

ES is a non-toxic all-purpose disinfectant, which kills viruses, bacteria, and fungi [1,2]. The US FDA approved ES as a high-level disinfectant in October 2002 [3]. ES solution has been our first-choice disinfectant for residential spaces, medical equipment, skin, mucosae, and closed pleural/abdominal cavities since 1993 [4]. ES is a novel disinfectant and has no adverse effects on the human body or the environment because it is immediately converted to water after coming into contact with an organism [3]. The antimicrobial mechanism of ES is based on the effects of hypochlorite and superoxide [2] under a super acidic state (pH 2.2–2.8). A super acidic state conveys hydrolipid affinity on ES solution [4]. Due to its lipid affinity, ES instantly binds to and passes through virus envelopes and bacterial cell walls. Viruses may be more susceptible to ES than bacteria because they lack cell walls and do not form biofilms.

Based on the disinfective activity of ES against bacteria and fungi, it is speculated that the residual SARS-CoV-2 Ag detected in saliva on day 2 may have been dead virus. Gargling a glass of ES almost completely eradicated oral bacteria and fungi. ES even diluted 5-fold with tap water sterilized bacteria and fungi within a minute, and in practical terms 10 seconds is sufficient to achieve sterilization [1]. We routinely use ES for preoperative oral hygiene. The decontaminating effects of gargling with ES are robust, and appropriate oral hygiene (in terms of microorganism levels) was maintained for a few days. Current pharyngeal antiseptics have not virucidal activity against COVID-19 [14]. Among current disinfectants, ES solution is the only one that can be used for virucidal decontamination of the human body [3]. The broad spectrum virucidal activity of ES was reconfirmed in COVID-19 [3,4].

The process used to produce ES solution is quite simple. Also, the associated production costs are quite low; i.e., it costs approximately 1 US dollar to produce 1000 liters of ES. In addition, ES generators are widely used for hospital sanitation and for rinsing fresh vegetables, seafood, and flowers in Japan; therefore, the immediate mass-volume production of ES solution is feasible [4].

ES has a foul smell as it contains hypochlorite, but this is an indicator of its disinfective activity. ES that was kept in a PET bottle stored in a darkroom retained its activity for over a month. However, protein substances reduce the activity. ES discolors some dyes and metal plates, and rusts some metals.

Conclusions

Non-specific virucidal activity of ES [3,4] was reconfirmed in COVID-19. ES promptly eliminated oronasal SARS-CoV-2 Ag and facilitated early recovery from COVID-19. Gargling ES instantly reduced the risk of the droplet transmission of COVID-19, and COVID-19 patients who gargled ES did not require long-term quarantine.

Acknowledgements

The authors thank Kazuo Nagano, MT; Ayumi Takamitsu, MT; Yasushi Umeda, MT; Takashi Yamanaka, PhC; Tokio Imada, PhC; Mr. Hideyuki Hayashida; and Mr. Kenji Iwata for their assistance with the microbiological examinations, preparation of the ES, and/or administrative work.

References

1. Nakamoto K, Takeshige M, Fujii T, et al. Electrolyzed saline for elimination of bacterial colonization in the empyema space. Surg Infect. 2016; 17: 724-729.
2. Hotta K. Acid electrolyzed saline solution: Its function and medical application. J Jpn Soc Intensive Care Med. 2000; 7: 97-105.
3. https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines-H.pdf
4. Nakamoto K, Kawamoto S, Kawamura Y, et al. Background analysis of community acquired pneumonia: Environmental biocontamination in residential spaces. Microbiol Infect Dis. 2021; 5: 1-6.
5. The committee on Japanese Guidelines for ARDS. ARDS clinical practice guidelines 2016. J Jpn Soc Intensive Care Med. 2017; 24: 57-63.
6. Nakamoto K, Takeshige M, Fujii T, et al. Intrapleural irrigation with electrolyzed saline for acute empyema. Int J Current Med Pharma Research. 2017; 3: 2440-2445.
7. Fulmer JD, Crystal RG. The interrelationships of lung biochemistry, structure, and function. In: Crystal RG eds. The biochemical basis of pulmonary function. New York, Basel: Marcell Dekker, Inc. 1976; 428-429.
8. Petty TL. Adult respiratory distress syndrome. In: Petty TL, eds. Intensive and rehabilitative care 3rd ed. Philadelphia: Lea & Febiger. 1982; 205.
9. Huertas A, Montani D, Savele L, et al. Endothelial cell dysfunction: a major player in SARS-CoV-2 infection (COVID-19)? Eur Respir J. 2020; 56: 2001634.
10. Hardaway RM. Capillary perfusion in health and disease. Mount Kisco, New York: Futura Publishing Co. 1981: 232.
11. Kuhr III C. The cells of the lung and their organelles. In: Crystal RG eds the biochemical basis of pulmonary function. New York, Basel: Marcell Dekker, Inc. 1976; 35-36.
12. Nakamoto k, Maeda M, Taniguchi K, et al. A study on optimal temperature for isolated lung preservation. Ann Thorac Surg. 1992; 53: 101-108.

13. Beigel JH, Tomashek KY, Dodd LE, et al. Remdesivir for the treatment of COVID-19: Final report. N Engl J Med. 2020; 383: 1813-1826.
14. Davidson BL, Tapson VF, Irwin RS, et al. Pharyngeal antiseptics to reduce COVID-19 pneumonia. Am J Med. 2021; 134: 297-298.