ORIGINAL ARTICLE

Gargling with 7.5% Sodium Bicarbonate Solution for SARS-CoV-2 Viremia Clearance: Our Institutional Clinical Experience

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ABSTRACT

Background: Gargling had been reported to have some roles in the prevention and treatment of respiratory tract infections. The purpose of this study was to assess the ability of regular gargling using 7.5% sodium bicarbonate to eliminate SARS-CoV-2 in the oropharynx and nasopharynx.

Methodology: This pilot, open-labeled, nonrandomized, parallel single-center study. The effect of 30 seconds, three times per day gargling using 7.5% sodium bicarbonate solution—25 mL on SARS-CoV-2 viral clearance among COVID-19 patients in a dedicated COVID hospital at AIIMS Patna, Bihar, India. We monitored the progress on by days 0, 1, 2, 3, 4, 5, 6, and 7 by observing variables like clinical category, P/F ratio, neutrophil/lymphocyte ratio (NLR), platelet count, ferritin, lactate dehydrogenase (LDH), CRP, procalcitonin, d-dimer, INR, APTT, and sequential organ function assessment (SOFA) score. We have also done repeat reverse transcription-polymerase chain reaction (RT-PCR) testing on day 5 and day 7.

Results: A total of 10 patients (7 males and 3 females) were included in our study after confirmed COVID positivity. The age range was from 30 to 61 years. Based on clinical severity and P/F ratio, 7 patients were included in the milder group as their ratio was more than 200 and the rest 3 patients were included in the moderate group as P/F ratio was less than 200. Two respondents had comorbidities, which were non-Hodgkin's lymphoma and ovarian carcinoma. Viral clearance was achieved at day 7 in 3 of 10 patients. However, the analysis of using 7.5% sodium bicarbonate 25 mL gargle statistically showed nonsignificant p-value for all of our studied variables. However, the PCR results were negative on 24 hour apart, i.e., on day 5 and day 7.

Conclusions: This is only a preliminary study which showed that gargling with 7.5% sodium bicarbonate may not be effective in achieving early SARS-CoV-2 viral clearance among mild COVID-19 patients. However, still larger studies are required to ascertain the benefit of gargling for different stages of COVID-19 patients with keeping in mind the important variables suggestive of viremia clearance.

Keywords: 7.5% sodium bicarbonate, COVID-19, Gargling.

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-23901

INTRODUCTION

Even after 1 year of the Corona Virus Disease-19 (COVID-19) pandemic, no drug has been found that has an established role in the management of COVID-19. The world is still fighting with the multiple peaks across the globe. The invention of vaccines has created new hopes but its efficacy and role in new mutant species of the virus are still undetermined. Thus, scientists around the world are still in search of medications effective against these virus. The main reservoirs for droplet transmission are the nasopharynx and oropharynx as these areas have a very high viral load, which is responsible for pulmonary disease progression.1

The role of gargle solution with virucidal properties may prove to be an effective modality for interrupting the COVID-19 disease progression.2 The presence of two negative real-time reverse transcription-polymerase chain reaction (RT-PCR) results collected from the samples of the upper respiratory tract, at ≥24-hour intervals, is defined as viral clearance.3 The effects of pH on coronaviruses and to determine whether a pH-dependent conformational change in the peplomeric glycoprotein might play a role in virus-induced cell fusion and/or penetration have already been described in the literature. The studies have mentioned that there is more reduction in the viral entry if alkaline conditions are retained in the host cells, i.e., pH >7, while under acidified conditions (pH <7), there is more viral load inside the host cells.4 The coronavirus was found to be quite stable at pH 6.0 and 37°C (half-life, approximately 24 hours) but was rapidly and irreversibly inactivated by brief treatment at pH 8.0 and 37°C (half-life, approximately 30 minutes).5 Sodium bicarbonate seems to be the preferable way to increase the pH of baking soda, and it has been used to save many lives during the Spanish Flu pandemic in 1918.6 It was

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How to cite this article: Kumar N, Kumar A, Mahto M, Singh PK. Gargling with 7.5% Sodium Bicarbonate Solution for SARS-CoV-2 Viremia Clearance: Our Institutional Clinical Experience. Indian J Crit Care Med 2021;25(7):791-794.

Source of support: Nil

Conflict of interest: None
thought that a lysosomotropic agent like sodium bicarbonate that has been reported to be involved in the neutralization of acidosis could be a safer and easily available option for possible prophylactic and therapeutic interventions against SARS-CoV-2 replication and pathogenesis. However, there is no literature to date that studied the effect of sodium bicarbonate gargle in COVID-19. Therefore, we performed this pilot study to observe the effect of gargling with 7.5% sodium bicarbonate solution for viral clearance among COVID-19 patients.

**Material and Methods**

**Study Design**

This was a nonrandomized, open-labeled, single-center pilot study.

**Sample Size and Population**

The median time from diagnosis to negative conversion was found to be 14.5 days in asymptomatic and 18 days in symptomatic patients if the disease follows the natural course. We assumed a negative conversion in at least 50% of the cases after 7 days, and by keeping the power of the study to be 80% and the alpha error of 0.05, the estimated sample size came to be 11 in each arm. Therefore, we took 10 patients in a single group for this single-armed pilot study.

**Inclusion Criteria**

- All admitted adult patients with age more than 18 years.
- Mild and moderate cases of COVID-19 pneumonia.
- Positive RT-PCR report at the time of admission.

**Exclusion Criteria**

- Refusal to participate.
- Any abnormal radiological images and respiratory symptoms at the time of admission.
- Any severe cases of COVID-19.
- Any reinfected cases with SARS-CoV-2.

After fulfilling the inclusion criteria and properly explaining the details of doing gargling as per our study protocol, patients received 25 mL of 7.5% sodium bicarbonate gargle. We have not done any masking or stratification. All study group patients were instructed to do gargle for 6 days by taking 20 mL of solution, then extend the head backward, and perform gargle for at least 30 seconds, three times per day. After performing the gargle, all patients were instructed to fill the chart showing frequency of gargling, and if any symptoms were present, it should be entered into the chart. The clinical condition and laboratory evaluation were monitored using inflammatory markers like ferritin, lactate dehydrogenase (LDH), procalcitonin, and d-dimer from day 0 up to day 7. On the 5th day and 7th day after the study, we obtained nasopharyngeal and oropharyngeal samples using RT-PCR from the DNA/RNA Extraction Kit supplied by (Indian Council of Medical research) ICMR, New Delhi, at our institute. They are specific for detecting the E gene and RdRP gene.

Each of our RT-PCR assays was provided with a Ct (cycle threshold) value. The specimens were considered positive if the Ct value for both assays of E gene and RdRP gene was 45.0 or lower, and the specimens were negative when no Ct value was obtained. This pilot study received approval from our Institutional Research and Ethics Committee, AIIMS Patna, Bihar, India.

**Data Analysis**

Statistical analysis was performed using the IBM SPSS Statistics (version 20). For expressing mean ± standard deviation, continuous data were used, and for expressing frequency and percentage, categorical data were applied. To test the variation in inflammatory markers among the groups on different days (day 0 to day 7), analysis of variance (ANOVA) was applied. A p-value of < 0.05 was considered as statistically significant.

**Results**

A total of 10 patients (7 male and 3 females) were included in our study after confirming COVID positivity. The minimum age group was 30 years, and the maximum age was 61 years. The mean ± SD of all studied variables are shown in Table 1. Out of 10 patients, 7 patients were included in the milder group (as their P/F ratio was more than 200) and the rest 3 patients were included in the moderate group (as their P/F ratio was less than 200). Out of 10 patients, 2 patients had comorbidities, which were non-Hodgkin’s lymphoma and ovarian carcinoma, and the rest were normal. When baseline P/F ratio, NLR ratio, platelet count, ferritin, LDH, procalcitonin, d-dimer, and SOFA score were compared with their values on day 1 to day 7 among the groups, a nonsignificant change was noted (Table 1). The viral clearance was achieved at day 7 in 3 of 10 patients.

**Discussion**

The entry of SARS-CoV-2 into a host cell may seem to be pH-dependent; because once a virus fuses with a human cell via S-glycoprotein, its entry inside the cell utilizes a pH-dependent endocytic pathway. The pH-dependent thermolability of coronavirus infectivity is the result of conformational changes in the coronavirus peplomer. At pH 8.0 and 37°C, the E2N (Si) subunit is released from peplomers on virions, and at least one epitope of E2N (Si) is altered during this process. At pH 8.0 and 37°C, the E2c (S2) subunit is attached with the virus envelope and forms aggregates. The conformational changes in E2 (S) provide virus entry and fusion with target cells. So we used 7.5% sodium bicarbonate solution hypothesizing that it may bring a conformational change in peplomer of coronavirus at pH 8.0. A study by Kitamura et al. reported a 24% reduction in the incidence of URTI and influenza in school children after performing gargling with diluted 7% povidone–iodine. We thought of using 7.5% sodium bicarbonate solution for providing gargle for our study group based on its properties being alkaline in taste, odorless; pH of 0.1 molar freshly prepared aqueous solution is 8.3 at 25°C and pH of the saturated solution is around 8 to 9 and nontoxic. The study by Uhm et al. has shown that without intervention, the median time from diagnosis to viral clearance was approximately 2 weeks for asymptomatic patients. However, this current study showed a high viral clearance.
rate for 1% PVP-I and essential oils gargles as early as 4 days after intervention (equivalent to 5–6 days after diagnosis). A study by Wölfel et al.\(^{11}\) concluded that on the 4th day of the clinical phase, the pharyngeal viral shedding is highest, suggesting active viral replication. An early stage of COVID-19 is highly infectious, so viral clearance at this stage is very critical. In our study, 7.5% sodium bicarbonate gargle seems to be ineffective in modifying the disease course as indicated by the insignificant change in inflammatory markers and SOFA score. The viral clearance indicated by repeat RT-PCR was also found in only 30% of the cases at day 7. Therefore, the RT-PCR negativity also seems to be unaffected by the use of sodium bicarbonate gargle.

**Limitations**

There were several limiting factors. First, the sample size used for this study was very small. The second limitation was the daily filling of gargling details (like the number, duration, and method) by patients themselves, raising the chances of observation bias. Third, we do not compare the results with other gargle solutions (like chlorhexidine, povidone–iodine, or essential oils formula). Lastly, we have not compared the baseline Ct value with subsequent Ct values.

**Conclusion**

The result of this pilot study concluded that gargling with 7.5% sodium bicarbonate 25 mL solution may not be effective in achieving early SARS-CoV-2 viral clearance among mild COVID-19 patients. Few more randomized controlled studies are needed using a larger sample size for knowing the benefits of gargling with sodium bicarbonate for halting the COVID-19 disease progression.

**Informed Consent**

We have obtained all appropriate patient consent forms from patient relative.

**Author Contributions**

We verify and confirm that each author contributed to every stage of this manuscript equally.

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