Original Article

Role of Sodium Bicarbonate as Adjuvant Treatment of Nonsevere Computed Tomography-identified COVID-19 Pneumonia: A Preliminary Report

Mohammad Khairy El-Badrawy, Abdelbaset Mohamed Saleh, Adel El-Badrawy[1], Tamer Ali El-Hadidy, Mohamed Abd Ellatif[2], Rehab Ahmad Elmorsey, Ahmed A. Shokeir[3]

Departments of Chest Medicine, [1]Radiology and [2]Medical Biochemistry, Faculty of Medicine, Mansoura University, [3]Urology and Nephrology Center, Mansoura University, Mansoura, Egypt

Abstract

Background: Coronaviruses are classified as pH dependent. Alkaline media induced by sodium bicarbonate (SB) could impede viral entry into cells. We aimed to study the possible role of SB as an adjuvant treatment of nonsevere COVID-19 pneumonia. **Methods:** The study included 182 adults with confirmed nonsevere COVID-19 and chest computed tomography (CT) pneumonia; 127 assigned as study received conventional treatment plus adjuvant SB inhalation and nasal drops, as well as 55 assigned as control treated by conventional treatment only. Clinical and radiological assessments using chest CT score specific for COVID-19 were done at days 0 and 30. **Results:** Both the groups were comparable regarding demographic, clinical, and radiological characteristics. Clinical recovery was reported in 43/127 (33.9%) and 10/55 (18.2%) of the study and control groups, respectively ($P = 0.03$). The mean ± standard deviation time to clinical improvement was 3.31 ± 0.99 and 9.79 ± 6.29 days for the study and control groups, respectively ($P < 0.001$). The median of the total chest CT score was reduced from 10 (4–15) to 3 (0–19) in the study group ($P = 0.000$) and from 13 (2–15) to 11 (2–19) in the control group ($P = 0.53$) on days 0 and 30, respectively. **Conclusions:** SB could be a possible adjuvant therapy for selected patients with nonsevere COVID-19 pneumonia.

Keywords: Chest computed tomography, COVID-19, pneumonia, sodium bicarbonate

Introduction

Since December 2019, when China reported the first cluster of cases with a novel coronavirus COVID-19, the disease has been rapidly transmitted to almost all countries worldwide.[1,2] Owing to the absence of definitive treatment options of COVID-19, investigating alternative adjuvant treatments is appropriate until production of a specific effective medication. The suggestion that sodium bicarbonate (SB) could help to restrain coronavirus 2 (SARS-CoV-2) infection is based upon its anti-influenza properties and its widespread use during the "Spanish flu" pandemic of 1918. SB solution 8.4% is sterile, with a pH >8.6, nonpyrogenic, and is used for the treatment of metabolic acidosis. Bronchoalveolar lavage with SB 8.4% is inhibitory to bacteria, fungi, and tuberculosis in cultures.[3-5] SB is also a disinfectant against feline calicivirus and coxsackievirus.[6,7]

The severity of COVID-19 in adults is clinically classified into mild, moderate, severe, and critical disease according to the WHO interim guidelines published on May 2020.[8,9] The location of care as recommended by the WHO depends on the epidemiologic scenario and should be either at a designated COVID-19 health facility, community facility, or where not possible, at home.[10]

In the present study, we aimed at investigating the role of SB 8.4% as adjuvant therapy in the treatment of patients with moderate clinical stage and moderate radiological chest

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Address for correspondence: Dr. Rehab Ahmad Elmorsey, Department of Chest Medicine, Faculty of Medicine, Mansoura University, Algamhoria Street, Mansoura 35516, Egypt.
E-mail: rehabahmed435@yahoo.com

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computed tomography (CT) score who could be treated at home on the one hand and have objective radiological parameters for follow-up measurement on the other hand.

Methods

Setting

The study was approved by the local ethics committee of Mansoura Faculty of Medicine and registered and modified in the ClinicalTrials.gov (NCT 04374591). The protocol of the study was revised, modified, and approved by the Committee of COVID-19 Research of the Egyptian Ministry of Higher Education and Scientific Research and the Egyptian Ministry of Health (ID14-2020/17). All participants signed fully informed consent.

Patients

Study group, inclusion/exclusion criteria

Between April 15 and August 31, 2020, 442 consecutive patients suspected as COVID-19 presented to the respiratory evaluation zone and outpatient clinic of our university. A total of 301 patients were confirmed as having COVID-19 by reverse transcription–polymerase chain reaction (RT-PCR) and all were subjected to chest CT, out of which 129 patients were excluded because they had mild clinical disease with no CT criteria of pneumonia. Forty-one more patients were excluded since they had severe or critical clinical stage.

Only 131 adult patients (>18 years) defined according to the WHO as moderate disease with CT manifestations of pneumonia and stable clinical condition with oxygen saturation (SpO_2) >90% on room air, respiratory rate <30 breaths/min, and no respiratory distress were enrolled and labeled as a study group. This group was treated by conventional protocol plus adjuvant SB inhalation and nasal drops. Four patients discontinued treatment after 48 h because of bad taste of SB. A total of 127 patients, who completed the treatment and were followed up for 30 days, were eligible for analysis and assigned as a study group. A flowchart of the study group is given in Figure 1.

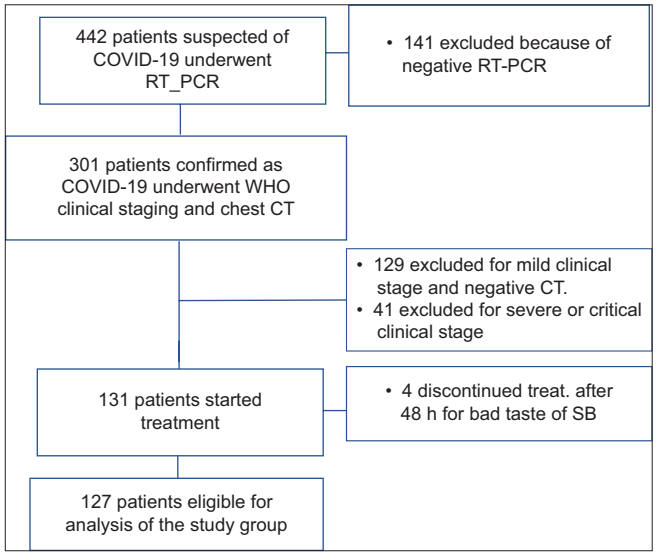

Figure 1: Flow chart of the study group

Control group

A control group of 55 patients were selected among 126 patients who were treated with the conventional protocol without adjuvant SB. The control group was selected to be matched with the study group regarding the demographic, clinical, laboratory, and radiological variables. Inclusion and exclusion criteria were similar in the study and control groups. Both the groups were treated during the same period by two teams of authors.

Treatment

Standard treatment

It is adopted according to the protocol of the Egyptian Ministry of Health[11,12] relative to the clinical stage. Patients who showed deterioration were admitted to a designated COVID-19 isolation hospital and were treated with remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 days), methylprednisolone, O_2 supplementation, and noninvasive and invasive mechanical ventilation as appropriate.

Adjuvant sodium bicarbonate treatment

Inhalation of SB 8.4% via an electric nebulizer (5 ml every 4 h) starting at 7:00–23:00 h every day for 30 days together with instillation of SB 8.4% drops four times daily (three drops for each nostril) was offered to all patients in the study group.[3,4]

All patients were treated at home and were admitted to the hospital if they showed deterioration or no clinical improvement. Home isolation was done according to the European Center for Disease Prevention and Control.[13] For patients isolated in the hospital, clinicians adopted the appropriate personal protective measures as defined by our local infection control.

Chest computed tomography protocol

All patients underwent nonenhanced multidetector computed tomography (MDCT) chest examination using MDCT scanners: SOMATOM go.Now (Siemens Healthineers Henkestraβε. 127, 91052 Erlangen, Germany) on days 0 and 30. Standard CT was performed with the patient in supine position during end-inspiration. The imaging parameters used were as follows: 120 kVp; 100–200 mAs; 3 mm slice thickness; 1 mm section reconstruction; collimation, 0.625 mm; and pitch, 0.75–1.5. The images were viewed on both mediastinal (window width, 350 HU; level, 40 HU) and lung (window width, 1600 HU; level, -600 HU) windows by an expert radiologist who was blinded to the treatment protocol.

Image analysis

CT images for each patient were assessed for the following abnormalities: ground-glass opacity (GGO), consolidation, nodules, number of lung lobe affection, interlobular septal thickening, and pleural effusion. In cases of GGO and consolidation, the severity of the lung involvement was

evaluated according to Bernheim *et al*.,[14] with each of the five lung lobes assessed and scored for the degree of involvement and classified as: score 0, no involvement (0% affected); 1, minimal (1%–25%); 2, mild (26%–50%); 3, moderate (51%–75%); and 4, severe (76%–100%). A total severity score was obtained by summing the five lobe scores, with a range between 0 and 20. A score of 1–5 was graded as "minima," 6–10 as "mild," 11–15 as "moderate," and 16–20 as "severe."

Outcome measures

Besides training of the patient himself, an educated member of the family was assigned and trained on how to take care of the treatment regimen. After the initial visit, physical clinical assessment was carried out at 7 and 30 days, and within this duration, the treating doctors were assigned to do follow-up by daily telephone calls with the patient and his family member to be sure that the patient is compliant to the treatment. The assessor was not blinded to the treatment regimen. Patients were instructed to come to hospital in case of clinical deterioration or any difficulties.

Outcomes were assessed after 30 days of start of treatment by comparing pre- and posttreatment clinical, laboratory, and radiological parameters. For clinical assessment, a score of cough from 0 to 5,[15] a score of expectoration from 0 to 4,[16] and a score of dyspnea from 0 to 4[17] were used before start and on day 30 after treatment. Clinical recovery was defined as no fever, zero scores of cough, expectoration, and dyspnea as well as disappearance of all other clinical symptoms for at least 3 days. Clinical improvement was stated as reporting of better feeling of the patient with persistence of some mild symptoms. Clinical deterioration was referred to as worsening of the clinical condition to severe, critical disease or death.

Laboratory data included C-reactive protein (CRP) and full and differential blood count. Radiological data included the score and grade of chest CT score according to Bernheim *et al*.[14]

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) when normally distributed and as median and range (min–max) when nonnormally distributed. Categorical variables were presented as frequency and percentage. Statistical analysis was done by independent and paired sample Student's *t*, Chi-square, Fisher's exact, Mann–Whitney, and Wilcoxon tests as appropriate with $P < 0.05$ considered statistically significant.

Results

Clinical and laboratory results

Of all 182 patients of the study and control groups, the mean ± SD of age was 49.5 ± 13.2 years and male-to-female ratio was 96/86. Smokers represented 29.7%, rural versus urban residence was 95/87, and high versus low socioeconomic status was 93/89. Of the total number of patients, 84 (46.2%) had a history of contact with index case and the median (range) number of days before examination was 6.[2-12]

Both the groups were comparable regarding all demographic, clinical, laboratory, and radiological characteristics, as shown in Table 1. Of all patients, clinical presentation was dyspnea in 100%, fever in 98.4%, cough in 95.6%, expectoration in 39.6%, and cyanosis in 1.1%. Other nonspecific symptoms such as sore throat and generalized bone aches were reported in 50.5% and 99.5%, respectively. Diarrhea was reported in 50% and anosmia in 49.5%. Both the groups were comparable regarding the frequency of the types of symptoms and the severity of the disease including cough, expectoration, and dyspnea scores, together with the degree of fever, respiratory rate, and $SpO_{2\%}$ on room air [Table 1]. The frequency of all types of comorbidities such as hypertension, diabetes millets, ischemic heart disease, chronic obstructive pulmonary disease, and bronchial asthma was comparable in the study and control groups [Table 1]. Manifestations of chest CT were also comparable in both the groups and included ground-glass opacity in 47%, consolidation in 50%, and nodular lesions in 3% [Table 1].

After 30 days from start of treatment, clinical recovery was reported in 53 (29.1%) patients. A total of 117 (64.3%) improved, while 6 (3.3%) deteriorated to severe or critical disease and 6 (3.3%) patients died [Table 2]. The frequency of clinical recovery of the disease after 30 days of start of treatment was in favor of the study group 43/127 (33.9%) versus 10/55 (18.2%) ($P = 0.03$) [Table 2]. Moreover, the duration to clinical improvement defined as patient "feeling better" with no fever and disappearance or improvement of symptoms, was significantly shorter in the study group (3.31 ± 0.99 vs. 9.79 ± 6.29 days, $P < 0.001$) [Table 2].

Before start of treatment, both the groups were well comparable regarding total count of white blood cells (WBCs), percentage of lymphocytes, and level of CRP [Table 1]. Comparison between pre- and posttreatment laboratory parameters of all patients showed a significant increase in the total count of WBCs, significant increase in the percentage of lymphocytes with significant decrease in the CRP after treatment. The study group showed significantly lower count of WBCs, higher percentage of lymphocytes, and lower values of CRP compared to the control group after treatment [Table 2].

Radiological results

Radiological score

Radiological scores of both the groups were comparable before start of treatment, except the score of the right upper lobe which was significantly higher in the control group. In the study group, the total score of CT was dramatically reduced from a median (min–max) of 10 (4–15) at day 0–3 (0–19) at day 30, $P = 0.000$. In the control group, the total score of CT decreased from 13 (2–15) at baseline to 11 (2–19) on the 30th day, a difference of no significant value ($P = 0.53$) [Table 3].

Table 1: Demographics and baseline characteristics

Variable	All patients (*n*=182)	Study group (*n*=127)	Control group (*n*=55)	*P*
Number of patients				
Age (years), mean±SD	49.53±13.22	49.30±78.21	50.05±14.12	3.10
Sex, *n* (male/female)	96/86	67/60	29/26	1.0
Smoking, *n* (%)	54 (29.7)	38 (29.9)	16 (29.1)	0.91
History of contact with index cases, *n* (%)	84 (46.2)	55 (43.3)	29 (52.7)	0.24
Residence, *n* (%)				0.11
Rural	95 (52.2)	62 (48.8)	33 (60)	
Urban	87 (47.8)	56 (51.2)	22 (40)	
Socioeconomic status, *n* (%)				
High	93 (51.1)	70 (55.1)	23 (41.8)	0.07
Low	89 (48.9)	57 (44.9)	32 (58.2)	
Days before examination, median (range)	6 (2-12)	6 (2-9)	5 (2-12)	0.32
Clinical presentation, *n* (%)				
Fever	179 (98.4)	126 (99.2)	53 (96.4)	0.17
Sore throat	92 (50.5)	64 (50.4)	28 (50.9)	0.95
Generalized bone aches	181 (99.5)	126 (99.2)	55 (100)	0.51
Cough	174 (95.6)	119 (93.7)	55 (100)	0.052
Expectoration	72 (39.6)	53 (41.7)	19 (34.5)	0.023
Shortness of breath	182 (100)	127 (100)	55 (100)	
Cyanosis	2 (1.1)	2 (1.6)	0	0.35
Diarrhea	91 (50.0)	65 (51.2)	26 (47.3)	0.63
Anosmia	90 (49.5)	64 (50.4)	26 (47.3)	0.7
Crepitation	4 (2.2)	3 (2.4)	1 (1.8)	0.82
Severity of the disease				
Cough score, median (range)	2 (0-3)	2 (0-3)	2 (1-3)	0.26
Expectoration score, median (range)	0 (0-2)	0 (0-2)	0 (0-2)	0.56
Dyspnea score, median (range)	2 (1-3)	2 (1-3)	3 (1-3)	0.52
Temperature (ºC), mean±SD	38.32±0.045	38.3±0.57	38.29±0.68	0.59
Respiratory rate (breaths/min), mean±SD	24.9±1.1	24.8±1.8	25±2.6	0.70
SpO_2, percentage on room air, mean±SD	90.5±2.1	90.4±0.9	90.6±1.3	0.16
Comorbidity, *n* (%)				
Hypertension	69 (37.9)	48 (37.8)	21 (38.2)	0.96
Diabetes	31 (17.0)	21 (16.5)	10 (18.2)	0.79
Ischemic heart disease	12 (6.6)	10 (7.9)	2 (/3.6)	0.29
COPD	5 (2.7)	2 (1.6)	3 (5.5)	0.14
Bronchial asthma	10 (5.5)	7 (5.5)	3 (5.5)	0.99
Laboratory results				
Total WBC count/µl, mean±SD	5331±2146	5177±2116	5688±2190	0.14
Percentage of lymphocytes, mean±SD	24±7.7	25±8.3	23±5.9	0.15
CRP (mg/L), median (range)	50.4±30.4	50.7±27.8	49.7±36.0	0.83
Manifestations of chest CT, *n* (%)				
Ground-glass opacity	180 (98.9)	126 (99.2)	54 (98.2)	0.54
Consolidation	50 (27.5)	35 (27.6)	15 (27.3)	0.97
Airway wall thickening and dilatation	90 (49.5)	62 (48.8)	28 (50.9)	0.80
Nodules	21 (11.5)	15 (11.8)	6 (10.9)	0.86
Interlobular septal thickening	41 (22.5)	28 (22)	13 (23.6)	0.81

SD: Standard deviation, WBC: White blood cell, CRP: C-reactive protein, CT: Computed tomography, COPD: Chronic obstructive pulmonary disease, SpO_2: Oxygen saturation

The detailed scores of each of the five lobes of both the groups at baseline and end of the study are shown in Table 3. Notably, in the study group, comparison between the CT scores on days 0 and 30 showed a significant reduction of disease in all the five lobes. On the other hand, these comparisons showed no significant change in the control group. Comparisons between total and differential scores at the end of the study were in favor of the study group.

Radiological grade

Radiological grades were comparable in both the groups before start of the treatment. At the end of the study, the study group showed significantly better results regarding recovery and

Table 2: Summary of clinical and laboratory results

Variable	All patients (*n*=182)	Study (*n*=127)	Control (*n*=55)	*P*
Clinical response after 30 days, *n* (%)				
Recovered	53 (29.1)	43 (33.9)	10 (18.2)	0.03
Improved	117 (64.3)	77 (60.6)	40 (72.7)	3.72
Deteriorated	6 (3.3)	4 (3.1)	2 (3.6)	0.79
Death	6 (3.3)	3 (2.4)	3 (5.5)	0.28
Duration to clinical improvement (days), mean±SD, median (range)	5.23±4.6, 4 (2-30)	3.31±0.99, 3 (2-6)	9.79±6.288, 7 (3-30)	<0.001
Laboratory results				
Total WBC count/µl, mean±SD	8124±4938	6699±1784	11414±7648	<0.001
Percentage of lymphocytes, mean±SD	30±11.4	35±8.8	19±8.4	<0.001
CRP (mg/L), mean±SD, median (range)	13.3±18.1, 6 (0-111)	10.7±16.0, 5 (0-111)	19.3±21.3, 12 (0-100)	0.003

SD: Standard deviation, WBC: White blood cell, CRP: C-reactive protein

Table 3: Chest computed tomography score in both groups before and after treatment

CT score, median (range)	Study before	Study after	Control before	Control after	P1	P2	P3	P4
Right upper lobe	1 (0-4)	0 (0-4)	2 (0-4)	2 (0-4)	0.003	0.000	0.855	0.000
Right middle lobe	2 (0-4)	1 (0-3)	2 (0-4)	2 (0-4)	0.414	0.000	0.582	0.000
Right lower lobe	3 (0-4)	1 (0-4)	3 (0-4)	3 (0-4)	0.791	0.000	0.172	0.000
Left upper lobe	2 (0-4)	0 (0-4)	2 (0-4)	2 (0-4)	0.257	0.000	0.374	0.000
Left lower lobe	3 (0-4)	1 (0-4)	3 (0-4)	3 (0-4)	0.977	0.000	0.755	0.000
Total score	10 (4-15)	3 (0-19)	13 (2-15)	11 (2-19)	0.201	0.000	0.527	0.000

P1=Study before versus control before, P2=Study before versus study after, P3=Control before versus control after, P4=Study after versus control after, CT: Computed tomography

Table 4: Grades of chest computed tomography in both groups before and after treatment

Chest CT grade	All patients (*n*=182), *n* (%)	Study (*n*=127), *n* (%)	Control (*n*=55), *n* (%)	*P*
Before treatment				
No involvement	0	0	0	0.75
Minimal	39 (21.4)	26 (20.5)	13 (23.6)	
Mild	60 (33)	44 (34.6)	16 (29.1)	
Moderate	83 (45.6)	57 (44.9)	26 (47.3)	
Severe	0	0	0	
After treatment				
No involvement	35 (19.2)	35 (27.6)	0	0.000
Minimal	64 (35.2)	56 (44.1)	8 (14.5)	
Mild	37 (20.3)	23 (18.1)	14 (25.5)	
Moderate	30 (16.5)	8 (6.3)	22 (40)	
Severe	16 (8.8)	5 (3.9)	11 (20)	

CT: Computed tomography

downgrading of CT in the study group. There was a dramatic reduction of the number of cases with moderate grade in the study group from 57 (44.9%) before treatment to 8 (6.3%) after treatment, while there was a marginal decrease of the number of patients with moderate grade in the control group from 26 (47.3%) before treatment to only 22 (40%) after treatment. On the other hand, the number of patients who deteriorated and showed severe radiological grade after treatment was significantly less in the study group (5 patients, 3.9%) compared with those of the control group (11 patients, 20%) [Table 4].

Examples of chest CT on days 0 and 30 are shown in Figure 2a-d for the study group and Figure 3a and b for the control group.

Discussion

The present study is the first one in the literature that addresses the possible role of SB as an adjuvant nontoxic tool for enhancing both clinical and radiological recoveries of nonsevere COVID-19 pneumonia that could be given safely at home. The outcomes were measured by the use of objective parameters of different clinical and radiological scores before and after treatment.

The present study included cases with moderate clinical and radiological manifestations of COVID-19 pneumonia. Mild cases without pneumonia were excluded from the analysis because of the absence of objective radiological parameters to prove the cause–effect relationship with SB. The vast majority

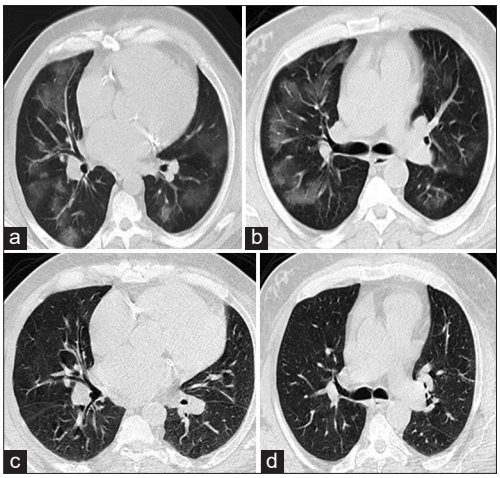

Figure 2: 65-year-old man with coronavirus disease 2019 (COVID-19) in the study group. Initial chest multi-detector computed tomography (MDCT) scan (a and b) shows multiple bilateral pulmonary ground glass opacities. Follow-up chest MDCT scan after 28 days (c and d) shows disappearance of previous bilateral ground glass opacities.

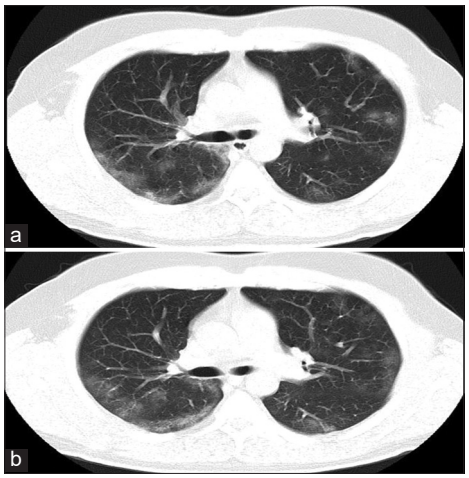

Figure 3: A55-year old man with coronavirus disease (COVID-19) in the control group. Initial chest multidetector computed tomography (MDCT) scan (a) shows multiple bilateral pulmonary ground glass opacities. Follow up chest MDCT scan after 30 days (b) shows stable disease with no detected significant changes as regards bilateral ground glass opacities.

of mild cases will improve with the use of supportive measures only. Therefore, the objective proof of the effect of SB in mild cases will need a huge number of cases which could be a subject of future study. Notably, all the mild cases excluded from the study group were treated by adjuvant SB and all of them were cured completely within few days. On the other hand, severe and critical clinical and radiological cases were also excluded from the study because they were not suitable for home treatment as proposed by the protocol of the present study. Nevertheless, the impact of SB on severe cases of COVID-19 pneumonia could also be a subject for further studies.

Rhinoviruses and coronaviruses are classified as pH-dependent viruses. Studies have shown that alkaline media impede viral entry into cells,[18,19] with low pH essential for the release of the individual viral ribonucleoproteins.[20-23]

To access the cell, the virus has to fuse to the plasma membrane at low pH, which happens through the use of endosomal compartments of the endocytic pathway. Once the virus enters the cell, it utilizes the cell's machinery, and the faster the pH drop, the more rapid the fusion of the virus.[18,19] It was found that coronavirus fusion with the cell membrane was stable at 37°C at a pH 6 (half-life 24 h); conversely, at 37°C at pH 8 (half-life 30 min), the virus was inactivated irreversibly. This is due to the conformational changes in the coronavirus peplomer that are responsible for the pH dependency of the virus.[24]

Drug delivery by aerosol inhalation is a well-established procedure in the treatment of pulmonary diseases. It is widely accepted that the main mechanisms affecting aerosol transport and deposition in the human lung include inertial impaction, gravitational sedimentation, and Brownian diffusion and, to a lesser extent, turbulent flows, interception, and electrostatic precipitation according to the particle size released with electric nebulizer. Particle size between 1 and 5 μm in size is deposited in the airways down to the alveoli. Particles size of more than 5 μm is deposited in the upper airways and at airway bifurcations by inertial impaction. Coronavirus affects the respiratory cells from the upper airways to the alveoli. Deposition of SB particles into the airways may block entry of coronaviruses into the respiratory cells.[25]

One study showed that oral rinse of SB caused a significant increase in salivary pH and prevented overgrowth of aciduric bacteria.[26] SB in a concentration of 7.5–8.4 was shown to be safe for human body with no considerable side effects.[3,4]

Chest CT is a useful tool of evaluation of chest condition before and during the course of follow-up of treatment. The CT score of Bernheim *et al*.[14] used in the present study is an objective tool for measurement of the response to treatment. Obviously, the use of SB has resulted in a better recovery and radiological improvement in the study compared to the control group after 1 month of start of treatment.

A noteworthy observation is the discrepancy between clinical recovery defined as complete disappearance of all clinical signs and symptoms and complete radiological recovery defined as zero score.[14] In the present study of all 182 patients, 53 (29.1%) showed clinical recovery, while 35 (19.2%) showed complete radiological recovery.

In a report of 72,314 cases of COVID-19 from a Chinese center for disease control and prevention, 81% had mild and moderate disease, 41% had severe disease, and 5% became critically ill with organ failure.[27] In the present study, 43% of the study group were excluded because of mild disease and the other 14% were excluded because of severe or critical disease. We included only those patients with nonsevere laboratory-confirmed COVID-19 pneumonia who could be treated at home.

Zheng *et al*.[28] compared the biochemical indices and lymphocyte subpopulation between 103 COVID-19-infected patients and 22 non-COVID-19 pneumonia cases. They classified the COVID-19 cases according to severity as severe, nonsevere, mild, and asymptomatic infected. The authors showed that the number of lymphocytes and platelets was significantly decreased while the level of CRP significantly increased in both severe and nonsevere COVID-19 patients in comparison with non-COVID-19-infected pneumonia patients. All patients in the present study are nonsevere symptomatic CT-identified COVID-19 pneumonia. Comparison between pre- and posttreatment laboratory parameters of all patients showed a significant increase in the total number of WBCs, and the percentage of lymphocytes, while a significant decrease in the level of CRP was detected as well. These findings matched with the results of previous similar studies.[27,28]

According to the protocol of treatment and follow-up of the Egyptian Ministry of Health, posttreatment RT-PCR is not a routine test. Therefore, time to negative RT-PCR after treatment was not analyzed in this study. The release of patients from isolation was based upon the WHO clinical criteria for releasing COVID-19 from isolation that require patients' symptoms to have been resolved for at least 3 days before release from isolation, with a minimum time in isolation of 13 days since symptom onset.[8]

Most patients with COVID-19 present with pneumonia, therefore, chest CT could be a rapid screening test in the emergency department.[29,30] Two studies in China suggested a central role of chest CT with a sensitivity of 98%[31] and 97%.[32] Gietema *et al*.[29] investigated the diagnostic accuracy of CT scanning in detecting COVID-19 in a population with suspected COVID-19 presenting at the emergency department using repeated RT-PCR testing as a reference standard in a prospective manner. The authors concluded that the sensitivity of chest CT is high, particularly in severely ill patients, but with moderate specificity, which could be explained by false-negative RT-PCR test and/or other respiratory viruses, such as influenza, H1N1, and Middle East respiratory syndrome.

In one study, of 888 patients with chest CT pneumonia, GGO was found in 46%, consolidation in 50%, and other findings including reticular/thickened interlobular septa in 1% and nodular lesions in 3%.[32] Similarly, GGO and consolidation represented the vast majority of CT findings among our cases.

Notably, all persons in the study group who were in contact with index cases at home received nasal and oral drops of SB and none of them developed clinical manifestations of COVID-19 during the study duration. Nevertheless, these observations were not included in the present manuscript because of the absence of objective parameters to prove the cause–effect relationship between taking SB and prophylaxis against COVID-19. However, this issue is an interesting subject for further research.

One of the limitations is the exclusion of severe and critical cases, but this cohort of patients could be included in future studies. Although the study is prospective and controlled, it is nonrandomized. The sample size is relatively small, and the study lacks long-term follow-up. Because of some logistic difficulties during this urgent period and overcrowdedness of hospitals, the laboratory data are limited. The assessors of the clinical conditions were not blinded to the treatment protocol, but this limitation was avoided during radiological assessment that was done by an expert radiologist blinded to the type of treatment.

Conclusions

Inhaled SB (8.4%) together with nasal drops could be a possible adjuvant therapy for patients with nonsevere COVID-19 pneumonia. Further randomized controlled trials are required to consolidate these preliminary observations.

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Conflicts of interest

There are no conflicts of interest.

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