

CASE REPORT

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Sequential application with NIV and high-flow nasal cannula oxygen therapy in the treatment of critically ill patient with severe COVID-19: A case report

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ABSTRACT

Introduction: To summarize the experiences of sequential application with noninvasive (NIV) and high-flow nasal cannula oxygen (HFNCO) therapy in the treatment for critically ill patient with severe COVID-19.

Case Report: In a mixed Intensive Care Unit, a medical university affiliated hospital in Guizhou Province, China, sequential application with NIV and HFNCO was used in the treatment for a COVID-19 patient with severe acute respiratory distress syndrome (ARDS), and the vital signs and laboratory results were dynamically monitored. A female patient with severe COVID-19 and severe acute respiratory failure was completely recovered from the disease by sequential application with NIV mechanical ventilation and HFNCO therapy. **Conclusion:** From our limited experience of the case report, NIV and HFNCO could cautiously be used in severe patient with ARDS in condition of close and dynamic monitoring.

Keywords: Case report, COVID-19, High-flow nasal cannula oxygen, Noninvasive, Novel coronavirus

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INTRODUCTION

In December 2019, some unexplained pneumonia cases had been successively reported in Wuhan, Hubei Province, China [1–3]. In January 7, 2020, specialists from Chinese Center for Disease Control and Prevention (CDC) identified this novel coronavirus and named it severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, previously known as 2019-nCoV) [4]. The disease infected by SARS-CoV-2 was termed coronavirus disease 2019 (COVID-19). COVID-19 was seen to rapidly spread throughout China.

Among COVID-19 patients, about 16% of them were severe illness, who are the main source of death [5]. Domestic data showed that mortality of severe COVID-19 patients was about 8–29% [6, 7]. The most important reason resulting in multiple organ dysfunction syndrome (MODS) or even death in COVID-19 is that acute respiratory distress syndrome (ARDS) happened, which was diagnosed by tachypnea with respiratory frequency of ≥ 30 beats per minute (bpm), arterial oxygen pressure/fraction of inspiration O_2 (P/F) < 300 mmHg [with positive end-expiratory pressure (PEEP) of ≥ 5 cmH $_2$ O], with infiltrates in bilateral lung which was unexplained

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by cardiogenic pulmonary edema or other lung diseases [8]. In severe ARDS (with P/F <100 mmHg), the typical management comprises invasive mechanical ventilation, among which consists of small tidal volume, plateau pressure control, prone positioning, etc. [9]. But it is still uncertain that NIV is efficacious in ARDS treatment, especially in severe ones. Accordingly, whether NIV and/or combined with high-flow nasal cannula oxygen therapy (HFNCO) is effective in COVID-19 patient with severe ARDS also remains to be clinically observed. Here we reported a successful sequential application with NIV and HFNCO in a critically ill patient with severe COVID-19. The main clinical characteristics and the treatment practice of our patient were as below.

CASE REPORT

General information

A 61-year-old Chinese woman began to have cough and diarrhea in January 28. She contacted with her younger sister five days ago who returned from Wuhan, China, in January 24, 2020. The patient at baseline was healthy and did not take any medications. One day later, the woman developed fever with a body temperature of 37.8 °C. At the same time, there were pains in the joints of her extremities, with no chest tightness, shortness of breath, and no difficulty in breathing. She went to the hospital in January 30, and a computed tomography (CT) scan showed bilateral infiltrates in the lungs that suggested an infectious process (Figure 1A). She was hospitalized. She does not smoke tobacco and does not consume alcohol. In her past medical history, she was healthy and unaffected.

A physical examination showed a fever with body temperature of 38.6 °C, respiratory rate of 19 bpm and noninvasive blood pressure (NBP) of 153/74 mmHg. She was oriented and cooperative. Her mental status was conscious and her neurological examination was normal. Moist rales were located at middle-lower fields of the right lung. Peripheral blood analysis showed that the white blood cell count (WBC) was $5.42 \times 10^9/L$, with absolute neutrophil count of $4.05 \times 10^9/L$ and absolute lymphocyte count of $0.88 \times 10^9/L$, with hemoglobin (HB) of 13 g/dL and platelet count (PLT) of $171 \times 10^9/L$. C-reactive protein (CRP) was of 14.5 mg/L. Serum urea nitrogen and creatinine levels were normal.

Because of suspicion for contagious disease of COVID-19, she was admitted to the Department of Infectious Disease of our hospital and given antiviral drugs, piperacillin/tazobactam with levofloxacin and oxygen therapy. At the same time, her sputum and throat swabs were collected to test the COVID-19 nucleic acids by reverse transcription-polymerase chain reaction (RT-PCR). In February 2, she was informed that the nucleic acids were positive and was diagnosed with COVID-19 and was isolated. Then Lianhua Qingwen granules were

added to her treatment for antivirus. After three days her condition was severely deteriorated. She felt shortness of breath, obvious dyspnea, and poor oxygenation. She had tachypnea with maximal respiratory rate of about 50 bpm. Arterial blood gas analysis showed that pressure of arterial oxygen tension (PaO₂) was only of 53.4 mmHg with fraction of inspired oxygen (FiO₂) of 60%. Lung CT scan showed that extensiveness of bilateral infiltrates was seen, indicating illness being worsened (Figure 1B). Then she was immediately transferred to the intensive care unit.

Immediate examinations on ICU admission showed a pulse oxygen saturation of 70%, a body temperature of 37.1 °C, NBP of 136/81 mmHg, a maximal respiratory rate of 45–50 bpm, and she was conscious and cooperative. Arterial blood gas analysis revealed a pH of 7.58, PaCO₂ of 43 mmHg, PaO₂ of 58 mmHg (FiO₂ 0.6), and bicarbonate (HCO₃⁻) of 40.3 mmol/L. Biochemical results consisted of serum albumin of 31.3 g/L, proalbumin of 160 mg/L, potassium of 2.676 mmol/L, sodium of 133.5 mmol/L, creatine kinase of 30.47 U/L, creatine kinase-myocardial band (MB) of 16 U/L, brain natriuretic peptide (BNP) of 282.7 ng/L, and procalcitonin (PCT) of 0.03 µg/L, CRP of 33.12 mg/L, interleukin-6 (IL-6) of 20.29 pg/mL. Liver and renal functions were normal.

The main diagnosis at ICU admission included: (1) Critical illness with COVID-19; (2) Severe acute respiratory distress syndrome.

Patient and Public Involvement: It is only a case report which was involved the management experience of severe COVID-19 patient.

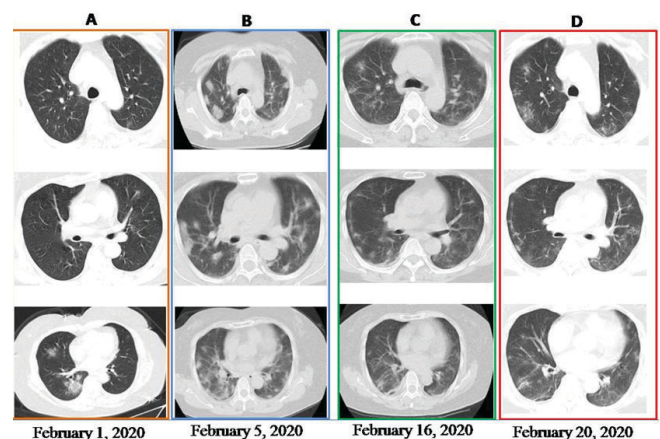


Figure 1: Evolution of lung CT scan imaging. (A) Lung CT shows ground-glass opacity in low field of right lung; (B) Pulmonary lesions are enlarged and distributed at multi-lobes of bilateral lungs; and (C) and (D) Lung lesions are gradually absorbed.

General managements

The patient was given comprehensive treatments, including antiviral therapy (oral abidol, 200 mg three times daily; lopinavir and ritonavir tablets, two tablets, twice daily; and aerosol inhalation of recombinant

human interferon, five million units, twice daily); methylprednisolone (40 mg, twice daily), antibiotics (moxifloxacin 0.4 daily). We also gave the patient intravenous Xuebijing injection, a compound preparation of Chinese herb, consisting of safflower, red peony, chuanxiong, Danshen and angelica, and ulinastatin to depress inflammatory storm, etc. Other general treatment included enteral nutrition and vitamin supplements, maintaining water electrolyte and acid-base balance and psychotherapy, etc.

Respiratory therapy

Our patient was diagnosed with COVID-19 and severe ARDS, and she had indication of intermittent mandatory ventilation (IMV), but we tried to give her NIV first, as she was conscious and cooperative. Parameters and mode of NIV (PHILIPS Respironics V60, Respironics California, Inc, USA) were set as follows: mode of S/T, with respiratory rate (RR) of 16–18 bpm (according to patient's spontaneous RR), inspiratory pressure (IPAP) 8–15 cmH₂O, expiratory pressure (EPAP) 6–10 cmH₂O, pressure support (PS) 8 cmH₂O. Her vital signs, specially the RR, respiratory distress, and the oxygen saturation were closely monitored during NIV period. After 2–3 hours of NIV, her respiratory symptoms were gradually improved.

After having been treated for three days, her respiratory symptoms began to alleviate, and oxygenation improved with PaO₂/FiO₂ from about 90 mmHg (FiO₂ 0.6) to 125 mmHg, and respiratory rate decreased from more than 45 to 22 and 30 bpm. With the patient's condition being improved, we gradually reduced the ventilator parameters, with FiO₂ from 60% to 45%, IPAP from 15 to 10 cmH₂O, EPAP from 10 to 7 cmH₂O, adapting to

the patient's needs anyway. In order to improve patient comfort and keep the patient calm as much as possible, we gave continuously intravenous injection of low-dosage of dexmedetomidine, during which the patient did not show any significant respiratory depression or decreased oxygenation. When the respiratory status of the patient was improved to the level where she could be endured by nasal catheter oxygen for about 5–8 minutes but was not powerful enough to be completely weaned from NIV, we gradually substituted NIV with HFNC. Lung CT scan of our patient was dynamically monitored, which demonstrated that her lung lesions were absorbed obviously (Figure 1C and D). Six days after HFNC treatment, our patient was successfully transferred to complete nasal catheter oxygen therapy, and all symptoms including chest tightness and respiratory distress disappeared except for mild shortness of breath during exercise.

Treatment outcomes

During ICU management, the antiviral, antibacterial/fungus infection therapy, and xuebijing/ulinastatin-use lasted for 13 days, glucocorticoid use for 9 days. For acute respiratory failure, NIV and HFNC had been used for four days and five days, respectively. After 13 days of ICU treatment, she was successfully transferred out of ICU, followed by another four days of comprehensive treatment in general ward, where she was accepted nucleic acid test of novel coronavirus for four times, each time separated by 24 hours, and all the results of nucleic acid test were negative. She was discharged on February 24th. Main clinical process of the COVID-19 patient was summarized in Table 1.

Table 1: Main clinical process of the reported case infected by SARS-CoV-2 in Guiyang, Guizhou Province, China

Course	Date	Clinical major events
Day 1	January 24, 2020	Contacted with her young sister from Wuhan, Hubei Province
Day 5	January 28, 2020	Began cough without sputum, with diarrhea
Day 6	January 29, 2020	Extremity joint pain with fever
Day 7	January 30, 2020	Lung infection was seen in chest CT scan, hospitalized
Day 10	February 2, 2020	Nucleic acid of COVID-19 was positive, antiviral treatment was given
Day 13	February 5, 2020	Aggravation of disease, CT scan showed the enlargement of pulmonary lesions
Day 15	February 7, 2020	The patient was transferred to ICU because of illness deterioration and ARDS. Noninvasive MV, antiviral + antibacterial treatment were given
Day 17	February 9, 2020	An attempt to try HFNC, but failed
Day 18	February 11, 2020	Successful transition from NIV to HFNC, began rehabilitation exercise
Day 23	February 15, 2020	Chest CT reexamination showed that the infectious lesion was obviously absorbed
Day 24	February 16, 2020	Strengthen exercise for lung function, weaning from HFNC and switched to usual oxygen therapy
Day 26	February 18, 2020	Chest CT indicated that infectious lesion were almost absorbed
Day 28	February 20, 2020	Successful transferred out of ICU
Day 32	February 24, 2020	Discharged

CT: computed tomography; COVID-19: coronavirus disease 2019; HFNC: high-flow nasal cannula oxygen therapy; ICU: Intensive Care Unit; ARDS: acute respiratory distress syndrome.

DISCUSSION

According to clinical data from China, the proportion of critically ill patients reached more than 20%, and the mortality rate caused by COVID-19 was about 8–29%, [6, 7]. During her treatment, our patient's condition worsened, with respiratory rate of more than 40 bpm, obvious respiratory distress syndrome, P/F less than 100 mmHg, rapid deterioration of lesions in bilateral lung, and the need of mechanical ventilation, which all confirmed that she was a critically ill COVID-19 patient [10–13]. Moreover our patient also met the Berlin criteria of severe ARDS [14].

At admission of ICU, one of the most important problems of our patient requiring to be solved at once was the severe hypoxemia, which was mainly responsible for multiple organ failure (MOF) and even for the death in ARDS [5], so improving her oxygenation condition was the most urgent task on hand. As she suffered from so severe hypoxemia that it is difficult to improve with routine oxygen therapy, the patient had the indication of mechanical ventilation [15].

In spite of severe hypoxemia and a little bite agitation, our patient was conscious and cooperative, so we gave her NIV mechanical ventilation at first [16, 17]. With about 2 hours of close observation, though RR was not seen obviously declined, the patient's oxygenation was gradually improved and her respiratory distress was attenuated, which indicated NIV was effective. Clinical observations suggested that correct application of NIV could be able to avoid endotracheal intubation and reduce the related complications of endotracheal intubation, such as ventilator associated pneumonia (VAP) [18]. So generally, NIV application should be considered whenever its indication existed in the field of management for critically ill patient. It is noted that NIV is more effective for hypercapnia than hypoxemia, such as in chronic obstructive pulmonary diseases [19]. Our patient was successfully managed with NIV, but the efficaciousness of NIV is variable in primary causes of hypoxemia.

High-flow nasal cannula oxygen is another commonly used technique to ameliorate acute respiratory failure in critical setting. High-flow nasal cannulas deliver a high humidified air/oxygen gas flow (up to 60–70 L/min) via a nasal cannula. One of the main advantages of HFNCO is the ability to deliver a very high flow of humidified gas, exceeding the peak inspiratory flow with a constant oxygen fraction, which can insure patient comfort [20]. Meta-analysis results by Huang et al. and by Monro-Somerville et al. shown that HFNCO owned a similar effectiveness in improving respiratory failure in adult critically ill patient extubation [21], and application of HFNCO was associated with improved comfort and dyspnea scores in critical patient [22]. In our report, we strangely observed that in day 3 of the patient's ICU management, the patient showed respiratory fatigue and obvious inspiratory effort when we attempted to treat her

using HFNCO instead of NIV, in spite of a relative high level of flow rate of 70 L/min being applied in HFNCO [23], but these manifestations quickly disappeared once the patient was switched to NIV again. We are very careful to think that the patient's condition was not well enough to accept HFNCO. Considering that HFNCO might be more convenient and more comfortable than NIV because of no need of mask, so we closely monitored the patient's improvement of respiratory condition at all times and be ready to change to HFNCO at any time. At day 4 of treatment in ICU, the patient was successfully transferred from NIV to HFNCO, and oxygenation and other symptoms all smoothly improved. After five days of HFNCO, the patient was transitioned to the usual oxygen therapy and started to get out of bed intermittently, indicating our patient recovered from severe illness and a de-escalation of therapy was accordingly applied.

From the experience of the patient, we think some points should be emphasized and cautions should be taken into account as well whenever NIV is used for severe COVID-19 pneumonia. First of all, indications and timing of NIV have to be grasped well, which is closely associated with the efficacy of NIV. Second, close monitoring for changes of vital signs are pivotal, especially of respiratory rate, breathing effort, oxygenation, consciousness, blood pressure, and heart rate. Generally, within 2 hours from the start of NIV, if patient's conditions are kept stable or even improved, NIV could be continued, otherwise, the therapeutic strategy should be decisively switched to endotracheal intubation and invasive mechanical ventilation [24]. Finally, some published data demonstrated that NIV and HFNCO are equally effective for some kinds of patients [25, 26], but for severe COVID-19 patient like ours, NIV might offer much more respiratory support than HFNCO dose, suggesting NIV rather than HFNCO be applied in severe stage of the disease. Once the conditions of patient are improved to a level at which patient could wean from NIV for a short time but is unable to completely accept usual oxygen therapy, it is the timing of HFNCO application.

Some shortcomings existed in our case report. First, it is an individual experience and could not stand for general populations of ARDS resulted from other reasons. More importantly, COVID-19 is newly recognized disease, of which many characteristics remain to be elucidated. Domestic pathological data from autopsy showed that COVID-19 is a little different from SARS and H7N9 [27], indicating some special therapeutic protocols have to be explored for COVID-19, including respiratory therapy.

CONCLUSION

Briefly, sequential application with NIV and HFNCO is expected to be effective for severe COVID-19 with close observation.

ABBREVIATIONS

NIV: noninvasive mechanical ventilation; COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; IMV: invasive mechanical ventilation; HFNC: high-flow nasal cannula oxygen therapy; ARF: acute respiratory failure; ICU: Intensive Care Unit; CDC: Center for Disease Control and Disease Control and Prevention; NBP: noninvasive blood pressure; WBC: white blood cell count; HB: hemoglobin; PLT: platelet count; CRP: C-reactive protein; CT: computed tomography; MB: creatine kinase-myocardial band; BNP: brain natriuretic peptide; PCT: procalcitonin; IL-6: interleukin-6; RR: respiratory rate; IPAP: inspiratory pressure; EPAP: expiratory pressure; PS: pressure support; MOF: multiple organ failure; ARDS: acute respiratory distress syndrome; SARS: severe acute respiratory syndrome.

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Author Contributions

Bo Liu – Conception of the work, Acquisition of data, Analysis of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Guarantor of Submission

The corresponding author is the guarantor of submission.

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Consent Statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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