Received: 23 July 2020 | Revised: 13 October 2020 | Accepted: 14 October 2020

DOI: 10.1111/eci.13435

ORIGINAL ARTICLE

WILEY

The value of high-flow nasal cannula oxygen therapy in treating novel coronavirus pneumonia

Xiao-bao Teng[1] | **Ya Shen**[1] | **Ming-feng Han**[1] | **Gang Yang**[2] | **Lei Zha**[2] | **Jing-feng Shi**[1]

[1]Department of Respiratory and Critical Care Medicine, No. 2 People's Hospital of Fuyang City, Fuyang, China

[2]Department of Respiratory and Critical Care Medicine, No. 2 People's Hospital of Wuhu City, Wuhu Anhui, China

Correspondence
Ming-feng Han, Department of Respiratory and Critical Care Medicine,N0. 2 People's Hospital of Fuyang City, No. 1088 of Yinghexi Road, Yingzhou District, Fuyang, Anhui, 236000, China.
Eamil: hanmingf_eng@163.com

Funding information
The second batch of COVID-19 emergency science and technology project in Fuyang city (FK20202802).

Abstract

Objective: This study aimed to investigate the value of high-flow nasal cannula (HNFC) oxygen therapy in treating patients with severe novel coronavirus pneumonia (COVID-19).

Methods: The clinical data of 22 patients with severe COVID-19 were collected. The heart rate (HR), respiratory rate (RR) and oxygenation index (PO_2/FiO_2) at 0, 6, 24 and 72 hours after treatment were compared between the HFNC oxygen therapy group and the conventional oxygen therapy (COT) group. In addition, the white blood cell (WBC) count, lymphocyte (L) count, C-reactive protein (CRP) and procalcitonin (PCT) were compared before and at 72 hours after oxygen therapy treatment.

Results: The differences at 0 hours between the two groups were not statistically significant. Compared with COT group,in the HFNC oxygen therapy group, HR, RR and PaO_2/FiO_2 were better at 6 hours after treatment, PaO_2/FiO_2 was better at 24 and 72 hours. After 72 hours, L and CRP had improved in the HFNC oxygen therapy group compared with the COT group, but the differences in WBC and PCT were not statistically significant. The length of stay in the intensive care unit (ICU) and the total length of hospitalization was shorter in the HFNC oxygen therapy group than in the COT group.

Conclusion: Compared with COT, early application of HFNC oxygen therapy in patients with severe COVID-19 can improve oxygenation and RR, and HFNC oxygen therapy can improve the infection indexes of patients and reduce the length of stay in the ICU of patients. Therefore, it has high clinical application value.

KEYWORDS
coronavirus disease 2019, high nasal flow oxygen therapy, pneumonia

1 | INTRODUCTION

Since December 2019, patients with pneumonia of unknown origin have been admitted to many hospitals in Wuhan. The World Health Organization named this virus novel coronavirus 2019 (COVID-19). The pneumonia caused by this virus is different to community-acquired pneumonia (CAP) and hospital-acquired pneumonia/ventilator-acquired

Xiao-bao Teng and Ya Shen contributed equally to this study.

pneumonia, as it has strong ability to spread from person to person. The COVID-19 Diagnosis and Treatment Plan (trial version 7) [1] states that patients with asymptomatic infection can also be a source of infection. Patients with the severe type of the virus often have varying degrees of hypoxia and dyspnoea, and therefore respiratory support therapy is very important for these patients. High-flow nasal cannula (HFNC) oxygen therapy is a new respiratory support technology that has attracted attention in medical applications in recent years,. It has the advantages of stable oxygen supply performance and constant oxygen output concentration. Moreover, it can maintain the air temperature in the range of 31-37°C and provide gas humidity of up to 100%. Therefore, the technology has the advantages of the common nasal tampon and mask. The positive end-expiratory pressure (PEEP) it produces can increase the functional residual capacity and bring about almost the same partial function as noninvasive ventilation. Compared with the traditional oxygen therapy, it has the advantages of high comfort, good compliance, and an obvious therapeutic effect. Many studies have proved its application value in the treatment of acute respiratory failure.[2,3] Therefore, the application of HFNC oxygen therapy may improve the prognosis of patients with COVID-19. This study was designed to investigate the value of HFNC oxygen therapy in treating patients with severe COVID-19. The study results are reported below.

2 | DATA AND METHODS

2.1 | Subjects

The data of 22 patients diagnosed with severe COVID-19 in Fuyang Second People's Hospital between January 2020 and February 2020 were collected. Of these patients, 12 were randomized assigned to the HFNC oxygen therapy group and 10 were randomized assigned to the conventional oxygen therapy (COT) group. Inclusion criteria: The age of the patients was >18 years; the patients met the diagnostic criteria for patients with severe COVID-19 in the COVID-19 Diagnosis and Treatment Plan (trial version 7).[1] Exclusion criteria: Partial pressure of carbon dioxide ($PaCO_2$) >50 mmhg or previous chronic obstructive pulmonary disease or asthma; acute cardiogenic pulmonary oedema or acute coronary syndrome; Glasgow coma scale <13. Elimination criteria: During the treatment, the patient could not cooperate with and tolerate HFNC oxygen therapy; pneumothorax occurred during the treatment; the patient needed invasive mechanical ventilation during the treatment; the patient could not continue the treatment due to their deterioration during the course of treatment; the patient was unable to participate in the whole trial. In this study, all patients' family expressed their willingness to participate in the trial and provided a signed form giving informed consent. The current study has been approved by the Ethics Committee of our hospital.

2.2 | Research methods

2.2.1 | HFNC oxygen therapy group

After being diagnosed with severe COVID-19 by the COVID-19 treatment expert group of Fuyang Second People's Hospital, the patients were immediately admitted to the intensive care unit (ICU), and HFNC oxygen therapy was applied. The HFNC oxygen therapy machine model was Optiflow PT101AZ (Fisher & Paykel, Auckland, New Zealand). The initial parameters were as follows: temperature was 37°C, flow rate was 50 L/min, and oxygen concentration was 50%. Parameters were adjusted according to blood oxygen saturation level (SpO_2), blood gas and tolerance, maintaining SpO_2 above 93%. The duration of continuous treatment for all patients was more than 72 hours.

2.2.2 | COT group

After being diagnosed with COVID-19 by the treatment expert group and admitted to the ICU, the patients began to inhale oxygen utilizing a nasal catheter or a common mask (including Venturi and oxygen storage mask). The initial oxygen absorption flow was set at 5 L/min, which was adjusted according to the condition of SPO_2, maintaining SpO_2 above 93%. The duration of treatment was more than 72 hours.

2.2.3 | Data collection

One mL of blood was drawn from the radial artery of the patient and analysed using the Philips blood gas analyser (RAPIDPOINT 500, Siemens Healthcare Diagnostics Inc511 Benedict Avenue,Tarrytown,NewYork 10 591 USA). The heart rate (HR), respiratory rate (RR) and oxygenation index (PaO_2/FiO_2) values of all patients were collected at 0, 6, 24 and 72 hours after treatment. Furthermore, 5 mL of fasting venous blood was drawn 1 day before and 3 days after HFNC oxygen therapy and COT application, centrifuged and tested for white blood cell (WBC) count, lymphocyte (L) count, C-reactive protein (CRP) and procalcitonin (PCT) by a blood routine analyser(Sysmex XE2100,Sysmex,Kobe, Japan) and automatic biochemical analyser (Hitachi 7600-020,HITACHI,No. 6-6, Yitinu, Marunouchi, Chiyoda District, Tokyo). In addition to oxygen therapy, all patients were given lopinavir/ritonavir tablets and interferon α as

antiviral treatment for regulation of gastrointestinal flora and protection of organ function, and their vital signs and other symptoms were monitored.

2.3 | Statistical analysis

Statistical analysis was conducted using SPSS16.0 (SPSS Inc Chicago) statistical software. Measurement data were normally distributed and expressed as mean ± standard deviation ($\overline{x}\pm$ SD) and compared utilizing a t test or repeated measures analysis of variance (ANOVA). Count data were expressed as frequency or percentage and compared utilizing a Chi-square test. $P < .05$ was considered statistically significant.

3 | RESULTS

3.1 | Comparison of general information

The differences in age, gender, interval from onset to diagnosis and underlying diseases (hypertension, diabetes, coronary heart disease) between the two groups were not statistically significant ($P > .05$), as shown in Table 1.

3.2 | Comparison of HR, RR and PaO2/FiO2 at each time point between the two groups

The differences in HR, RR and PaO_2/FiO_2 at 0 hours of treatment with the two oxygen therapies between the two groups were not statistically significant. At 6 hours after treatment with the two oxygen therapies, HR, RR and PaO_2/FiO_2 were better in the HFNC oxygen therapy group than in the COT group ($P < .05$). At 24 and 72 hours after treatment, PaO_2/FiO_2 was better in the HFNC oxygen therapy group than in the COT group ($P < .05$), but the differences in HR and RR were not statistically significant ($P > .05$). Repeated measures ANOVA revealed that the differences in HR, RR and PaO_2/FiO_2 at different time points were statistically significant (F = 3774.719, 4484.716, 2399.247, respectively, $P = .000$ for all), and the difference in the improvement of PaO_2/FiO_2 between the two groups was statistically significant (F = 6.201, $P = .022$), but the differences in the improvement of HR and RR were not statistically significant ($P > .05$), as shown in Tables 2, 3 and 4, respectively. At 6, 24 and 72 hours after treatment, RR was lower in the HFNC oxygen therapy group than in the COT group, and PaO_2/FiO_2 was higher in the HFNC oxygen therapy group than in the COT group, as shown in Figures 1 and 2, respectively.

3.3 | Comparison of infection indexes between two groups before and after oxygen therapy

The differences in CRP, PCT, WBC and L before HFNC oxygen therapy and COT treatment between the two groups were not statistically significant ($P > .05$). At 72 hours after treatment, CRP and L in the HFNC oxygen therapy group had improved significantly, the differences between the two groups were statistically significant ($P < .05$ for all), but the differences in PCT and WBC were not statistically significant ($P > .05$ for all), as shown in Table 5.

3.4 | Comparison of length of ICU stay and total length of hospitalization between the two groups

All patients in this study were cured and discharged. The length of ICU stay was 4.00 ± 0.74 days in the HFNC oxygen therapy group and 4.90 ± 1.00 days in the COT group, and the difference was statistically significant ($P = .024$). The total length of hospitalization was 14.67 ± 1.97 days in the HFNC oxygen therapy group and 16.60 ± 2.54 days in the COT group, but the difference was not statistically significant ($P = .058$), as shown in Table 6.

4 | DISCUSSION

We found that the differences at 0 hours between the two groups were not statistically significant. Compared with COT group,in the HFNC oxygen therapy group, HR, RR and PaO_2/FiO_2 were better at 6 hours after treatment, PaO_2/FiO_2 was better at 24 and 72 hours. After 72 hours, L and CRP

TABLE 1 Comparison of general conditions and underlying diseases of patients

Group	Age (years)	Gender (male/female)	Confirmed time (day)	Hypertension (case) (%)	Diabetes (case) (%)	Coronary heart disease (case) (%)
HFNC	56.6 ± 3.0	8/4	7.9 ± 0.7	7(58.3)	3(25)	1 (8.3)
COT	53.5 ± 5.5	7/3	7.8 ± 1.2	4(40)	3(30)	0 (0)
t/χ^2 value	0.519	0.028	0.089	0.733	0.069	0.873
P value	.610	.867	.930	.392	793	.350

TABLE 2 Comparison of HR at each time point between the two groups (beats/minute)

Group	Treatment 0 h	Treatment 6 h	Treatment 24 h	Treatment 72 h
HFNC	91.58 ± 3.64	79.83 ± 1.86	79.83 ± 1.47	78.92 ± 1.36
COT	87.10 ± 2.13	85.50 ± 1.86	78.70 ± 2.92	75.40 ± 3.25
T value	1.007	−2.135	0.365	0.998
P value	.326	.045	.719	.338

TABLE 3 Comparison of RR at each time point between the two groups

Group	Treatment 0 h	Treatment 6 h	Treatment 24 h	Treatment 72 h
HFNC	22.08 ± 0.70	18.75 ± 0.41	18.25 ± 0.46	17.08 ± 0.50
COT	21.60 ± 0.40	20.70 ± 0.26	18.60 ± 0.37	18.10 ± 0.43
T value	0.567	−3.825	−0.573	−1.504
P value	.577	.001	.573	.148

TABLE 4 Comparison of PaO_2/FiO_2 at each time point between the two groups

Group	Treatment 0 h	Treatment 6 h	Treatment 24 h	Treatment 72 h
HFNC	224.25 ± 12.60	269.00 ± 9.901	296.50 ± 6.61	320.92 ± 4.79
COT	216.70 ± 4.62	238.50 ± 7.32	261.60 ± 8.16	286.40 ± 7.29
T value	0.522	2.391	3.363	4.080
P value	.618	.027	.003	.001

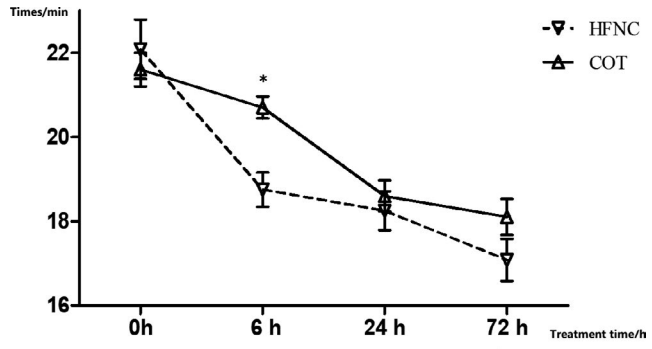

FIGURE 1 RR change trend based on each time point in the two groups

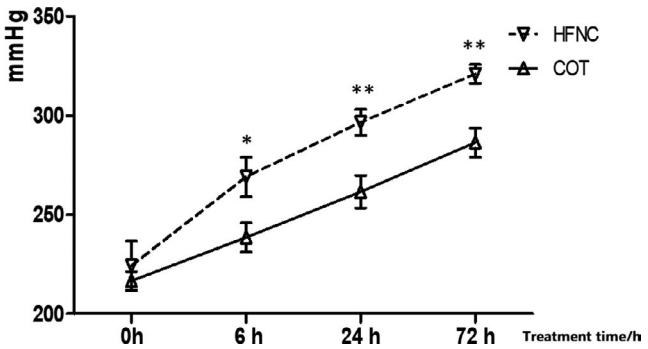

FIGURE 2 PaO_2/FiO_2 change trend based on each time point in the two groups

had improved in the HFNC oxygen therapy group compared with the COT group, but the differences in WBC and PCT were not statistically significant. The length of stay in the intensive care unit (ICU) and the total length of hospitalization was shorter in the HFNC oxygen therapy group than in the COT group. Thus, compared with COT, early application of HFNC oxygen therapy in patients with severe COVID-19 can improve oxygenation and RR, and HFNC oxygen therapy can improve the infection indexes of patients and reduce the length of stay in the ICU of patients. Therefore, it has high clinical application value.

In this study, observation of the indexes of circulatory respiration at different time points in patients with severe COVID-19 after applying different oxygen therapy strategies revealed that compared with the COT group, in the HFNC oxygen therapy group, HR and RR had improved more significantly at 6 hours after treatment, but the differences in HR and RR at 24 and 72 hours after treatment between the two groups were not statistically significant. Moreover, the PaO_2/FiO_2 of the HFNC oxygen therapy group was better than that of the COT group, and the difference was statistically significant. In addition, the RR of the HFNC oxygen therapy group

TABLE 5 Comparison of infection indexes before and after oxygen therapy between two groups

Group	CRP (mg/L)		PCT (ng/mL)		WBC ($\times 10^9$/L)		L ($\times 10^9$/L)	
	Before the application	After the application	Before the application	After the application	Before the application	After the application	Before the application	After the application
HFNC	50.18 ± 13.06	15.20 ± 2.93	0.08 ± 0.02	0.07 ± 0.01	5.34 ± 0.74	6.14 ± 0.95	0.80 ± 0.08	1.17 ± 0.08
COT	49.6 ± 8.00	40.30 ± 11.82	0.07 ± 0.02	0.08 ± 0.02	6.74 ± 1.01	7.10 ± 0.78	0.75 ± 0.13	0.94 ± 0.07
T value	0.037	−2.238	0.434	−0.636	−1.108	−0.734	0.359	2.158
P value	.971	.037	.669	.532	.281	.471	.723	.043

TABLE 6 Comparison of length of ICU stay and total length of hospital stay between the two groups

Group	Length of ICU stay (d)	Total hospital stay (d)
HFNC	4.00 ± 0.74	14.67 ± 1.97
COT	4.90 ± 1.00	16.60 ± 2.54
T value	−2.435	−2.009
P value	.024	.058

was lower than that of the COT group, and the PaO_2/FiO_2 of the HFNC oxygen therapy group was higher than that of the COT group. This is consistent with the results of many foreign studies,[4-6] all of which proved that compared with conventional oxygen therapy, HFNC oxygen therapy is more effective in improving the RR and PaO_2/FiO_2 of patients with acute respiratory failure. By analysing the clinical effect of HFNC oxygen therapy in the treatment of acute hypoxic respiratory failure, Chinese scholars Wang et al [7] found that after HFNC oxygen therapy treatment, RR and PaO_2/FiO_2 had improved significantly, and the improvement in RR and PaO2/FiO2 was more obvious with the prolongation of the treatment time.

The reason for this result is related to the characteristics of HFNC oxygen therapy that are outlined below. Compared with ordinary oxygen therapy devices (nasal catheter, mask), HFNC oxygen therapy has a unique air-oxygen mixing device. This device can mix air and oxygen and output constant gas flow and oxygen concentration, which is not affected by other external factors. In addition, the humidification device and heating pipeline of HFNC oxygen therapy can accurately heat and humidify the gas to the appropriate level for patients, reduces the loss of heat and water in the respiratory tract, and is conducive to the recovery of airway ciliary function, thus promoting the discharge of secretions.[8] Moreover, HFNC oxygen therapy can provide gas flow of up to 60 L/min, which can produce a certain PEEP effect. Furthermore, with the increase in the gas flow rate, PEEP will also increase. A study revealed that for every 10 L/min increase in the gas flow rate, PEEP increased by 0.5-1.0 cm H_2O, and the flow rate of 60 L/min could produce 8.7 cm H_2O of PEEP in the pharyngeal cavity of female patients.[9] This effect could promote the re-expansion of alveoli, increase functional residual capacity, and reduce the respiratory work.[10] In addition, since HFNC oxygen therapy has a high gas flow rate, it has a certain effect of respiratory tract flushing. When the exhaled air containing a low concentration of oxygen in the dead cavity of the nasopharynx anatomy is washed out of the body, the patient will inhale fresh higher concentration oxygen, thereby improving the oxygenation.[11-13]

Some of the patients with COVID-19 had bacterial infection. The COVID-19 Diagnosis and Treatment Plan (trial version 7) [1] states that in the early stage of the virus, the patient's WBC count is normal or decreased, the L count may reduce in the majority of patients, CRP and erythrocyte sedimentation rate increase, and PCT is usually normal. Furthermore, the guidelines state that a progressive decrease in the L count and a progressive increase in CRP are the clinical early warning indexes of severe and critical types of COVID-19. In this study, the data of 22 patients with severe COVID-19 were statistically analysed. Results revealed that in the early stage, L count decreased, CRP increased, and WBC and PCT were within the normal range, which is the same as described in the guidelines. After 72 hours of HFNC oxygen therapy or COT treatment, the above infection indexes were analysed again. CRP and L had improved in both groups, but in the HFNC oxygen therapy group they had improved more significantly. Therefore, HFNC oxygen therapy may be able to help accelerate the recovery of patients with severe COVID-19. Cuq et al [14] studied the heating and humidification functions of HFNC oxygen therapy and found that after inhaling the air with a suitable temperature and humidity, the patient's subjective comfort significantly improved, and the respiratory secretion was more easily discharged; therefore, it could reduce the incidence of lower respiratory tract infection. Moreover, the application of HFNC oxygen therapy could reduce the work of respiratory muscles, improve patients' oxygenation, reduce energy consumption and accelerate the recovery of patients' physical condition; therefore, it was beneficial to the recovery of patients. However, due to the small number of cases and poor representativeness in this study, data from a large sample is needed to verify this conclusion.

In this study, all the patients were cured and met the discharge standard of the COVID-19 Diagnosis and Treatment Plan (trial version 7).[1] Analysis revealed that the length of ICU stay and the total length of hospitalization was shorter in the HFNC oxygen therapy group than in the COT group, and the difference in the length of ICU stay between the two groups was statistically significant. This suggests that the application of HFNC oxygen therapy can reduce the length of ICU stay and the total length of hospitalization. Therefore, as an oxygen therapy strategy widely used in clinics, HFNC oxygen therapy has shown its important role in acute respiratory failure. In this study, we analysed the recovery of each index after the application of HFNC oxygen therapy and compared it with the COT group. The result suggests that HFNC oxygen therapy has good application value in the treatment of patients with severe COVID-19 and should be promoted in clinical diagnosis and treatment. One limitation is that sample size is not calculated. Our limitation is that the sample size is small, and the exclusion of patients who progressed to require intubation and mechanical ventilator support allows for an analysis of the response to high-flow versus conventional oxygen, but does not allow a description or analysis of a crossover from one therapy to another or a progression to noninvasive ventilation or invasive mechanical ventilator support.

ACKNOWLEDGEMENTS

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

CONSENT FOR PUBLICATION

All participants signed a document of informed consent.

ORCID

Ming-feng Han https://orcid.org/0000-0001-8091-2285

REFERENCES

1. National Health Commission, PRC. Diagnosis and treatment protocol for COVID-19 (trial No Seven edition).
2. Frat JP, Thille AW, Mercat A, et al. High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure. *N Engl J Med*. 2015;372(23):2185-2196.
3. Peters SG, Holets SR, Gay PC. High-flow nasal cannula therapy in do-not-intubate patients with hypoxemic respiratory distress. *Respir Care*. 2013;58(4):597.
4. Frat JP, Brugiere B, Ragot S, et al. Sequential application of oxygen therapy via high-flow nasal cannula and noninvasive ventilation in acute respiratory failure: an observational pilot study. *Respir Care*. 2014;60(2):170-178.
5. Schwabbauer N, Berg B, Blumenstock G, Haap M, Hetzel J, Riessen R. Nasal high–flow oxygen therapy in patients with hypoxic respiratory failure: effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). *BMC Anesthesiol*. 2014;14(1):1471-2253.
6. Vargas F, Saint-Leger M, Boyer A, Bui NH, Hilbert G. Physiologic effects of high-flow nasal cannula oxygen in critical care subjects. *Respir Care*. 2015;60:1369-1376.
7. Wang R, Sun B, Li X, et al. Clinical efficacy of transnasal high-flow oxygen therapy in the treatment of acute hypoxic respiratory failure. *Chinese J Tuberculosis Respir*. 2017;2:155-157.
8. Wang L, Xia J, Yang X. Advances in the treatment of adults with transnasal high-flow oxygen humidification. *Chinese J Tuberculosis Respir*. 2016;039(002):153-157.
9. Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. *Aust Crit Care*. 2007;20(4):126–131.
10. Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth*. 2011;107(6):998-1004.
11. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: Mechanisms of action. *Respir Med*. 2009;103(10):1400-1405.
12. Spence CJT, Buchmann NA, Jermy MC. Unsteady flow in the nasal cavity with high flow therapy measured by stereoscopic PIV. *Exp Fluids*. 2012;52(3):569-579.
13. Frizzola M, Miller TL, Rodriguez ME, et al. High-flow nasal cannula: Impact on oxygenation and ventilation in an acute lung injury model. *Pediatr Pulmonol*. 2011;46(1):67-74.
14. Cuquemelle E, Pham T, Papon JF, Louis B, Danin PE, Brochard L. Heated and Humidified High-Flow Oxygen Therapy Reduces Discomfort During Hypoxemic Respiratory Failure. *Respir Care*. 2012;57(10):1571-1577.

How to cite this article: Teng X-B, Shen Y, Han M-F, Yang G, Zha L, Shi J-F. The value of high-flow nasal cannula oxygen therapy in treating novel coronavirus pneumonia. *Eur J Clin Invest*. 2021;51:e13435. https://doi.org/10.1111/eci.13435