ASIA PACIFIC CENTER FOR EVIDENCE BASED HEALTHCARE

Is high-flow nasal cannula oxygenation more effective than noninvasive ventilation or conventional oxygen therapy in treating acute hypoxemic respiratory failure in COVID-19 patients?

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This rapid review summarizes the available evidence on the effectiveness and safety of noninvasive respiratory support modalities in treating COVID-19 patients with acute hypoxemic respiratory failure. This may change as new evidence emerges.

KEY FINDINGS

Very low-quality evidence suggests lower mortality (five observational studies) but higher failure rate of respiratory support (two observational studies) in COVID-19 patients given high-flow nasal cannula (HFNC) oxygen compared with noninvasive ventilation (NIV) and conventional oxygenation therapy. Randomized controlled trials are urgently needed in this area.

- Respiratory failure accounts for about half of deaths in patients with COVID-19 infection.
- High-flow nasal cannula (HFNC) oxygen therapy reduces the need for escalating respiratory support and improves patient comfort compared with conventional oxygen therapy among those with acute respiratory failure.
- Mortality was consistently lower in COVID-19 patients who received HFNC rather than NIV or conventional oxygen therapy (COT) across 5 very low-quality retrospective observational studies from China.
- Several international guidelines recommend the use of HFNC oxygen therapy in COVID-19 patients who develop acute hypoxemic respiratory failure. However, local guidelines from the Philippine Society for Microbiology and Infectious Diseases (PSMID) and the Philippine College of Chest Physicians (PCCP) recommend against HFNC due to risks of transmission and paucity of direct evidence for efficacy.
- Additional infection control precautions, i.e. wearing a surgical mask over the cannula, and locating in a negative pressure room, are recommended whenever using HFNC or NIV.
- There are at least two ongoing trials due to complete by the second quarter of 2021 comparing HFNC oxygenation with NIV or COT in COVID-19 patients.

RESULTS

We found 6 observational studies of COVID-19 patients from China which reported the use of noninvasive respiratory support, treatment failure, and mortality (Liao 2020, Luo 2020, Wang K 2020, Wang Y 2020, Yang 2020, Zhou 2020) (**Table 1**). These studies provide at most low-quality evidence owing to their retrospective nature, small sample sizes, and significant confounding. Caution is needed in interpreting the results, and causality cannot be concluded. Randomized controlled trials (RCTs) are urgently needed in this area.

Although failure of initial respiratory support was higher among patients on HFNC compared with NIV in two observational studies (Wang K 2020, Wang Y 2020), we cannot conclude about the superiority of HFNC or NIV because of methodological limitations and potentially unequal groups at baseline. Limited evidence for mortality come from 5 observational studies (Liao 2020, Luo 2020, Wang Y 2020, Yang 2020, Zhou 2020). Characteristics of patients who received HFNC, NIV or COT were not explicitly described, and so we are unable to determine if both groups were comparable. Rates of death were consistently lower in patients given HFNC therapy compared with those on NIV or COT across all 5 studies.

Table 1. Characteristics of studies included

Study	Design	Location	Population (n)	Age	Sex	Any comorbidity (most common)	Initial Respiratory Support (n)			Outcomes of interest reported
							HFNC	NIV	COT	
Wang Y	Case series	Wuhan city, China (single center)	COVID-19 patients, severe and critically ill (n = 344)	64 years (IQR 52-72)	F: 48%	NR (Hypertension: 41%)	35	34	-	Mortality Ventilatory support (noninvasive / invasive)
Wang K	Case series	Chonqing province, China (multicenter)	2019-nCoV pneumonia with severe acute respiratory failure (n = 27)	65 years (SD 56-75)	F: 59%	NR (Hypertension: 18%, Diabetes: 18%, Chronic heart disease: 18%)	17	9	-	Rescue therapy (NIV, intubation) HFNC success
Liao	Case series	Sichuan province, China (multicenter)	COVID-19 confirmed patients, severe (n = 81[a])	50 years (IQR 39-65)	F: 37%	53.1% (Diabetes: 22%)	31	22	79	Clinical recovery Mortality
Luo	Case series	Wuhan city, China (single center)	COVID-19 patients (n = 403)	56 years (IQR 39-68)	F: 52%	43.4% (Hypertension: 28%)	106	56	-	Mortality
Yang	Case series	Wuhan city, China (single center)	SARS-CoV-2 pneumonia, critically ill (n = 52)	59 years (SD 13.3)	F: 33%	40% (Diabetes: 17%)	33	29	-	Mortality
Zhou	Case series	Wuhan city, China (single center)	COVID-19 confirmed patients (n = 191)	56 years (IQR 46-67)	F: 38%	48% (Hypertension: 30%)	41	26	-	Mortality

[a] 30 patients (37%) developed acute respiratory distress syndrome (ARDS)
Legend: *F*: female, *IQR*: interquartile range for age in median, *NR*: not reported, *SD*: standard deviation for age in mean

We found no studies reporting on the risk of transmission of the SARS-CoV-2 infection to health care workers or other patients from, nor development of nosocomial pneumonia in COVID-19 patients on HFNC oxygen.

There are at least two ongoing trials (one RCT in the United Kingdom, one prospective cohort in China) comparing HFNC oxygenation with NIV or COT in COVID-19 patients (**Appendix A**).

CONCLUSIONS

Very low-quality evidence suggests reduced mortality (5 retrospective studies) but higher failure rates of initial respiratory support (2 retrospective studies) in COVID-19 patients given HFNC oxygenation compared with NIV and COT. Further studies, RCTs in particular, are urgently needed in this area.

Guidelines recommend added infection control precautions, i.e. wearing a surgical mask over the cannula, and admitting the patient in a negative pressure room, whenever using HFNC or NIV due to increased risk of aerosolization.

Declaration of Conflicts of Interest

We have no relevant conflicts to disclose.

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APPENDIX A
Ongoing Clinical Trials

Study	Population / Setting	Intervention	Outcomes	Status
In adult patients with known or suspected COVID-19, does the use of Continuous Positive Airway Pressure (CPAP) or high-flow nasal oxygen (HFNO), compared with standard care reduce mortality or need for tracheal intubation? ISRCTN16912075 Adaptive pragmatic open-label multicenter RCT	Known or suspected SARS-CoV-2 infection with respiratory failure United Kingdom	Arm 1: Continuous positive airway pressure (CPAP), administered according to local protocol/guidelines. Administration will be left to clinical discretion. Arm 2: High flow nasal oxygen (HFNO) will be administered according to local protocol/guidelines. Administration will be left to clinical discretion. Arm 3: Standard care. Standard oxygen therapy according to local protocol/guidelines.	Composite outcome comprising tracheal intubation or mortality within 30 days Secondary: 1. Intubation rate 2. Time to intubation 3. Time to death (mortality), obtained from hospital record or other source 4. Mortality in critical care (level 2/3) 5. Mortality during hospital stay 6. Mortality at 30 days, obtained from hospital record or other source 7. Length of stay in critical care (level 2/3) 8. Length of stay in hospital	Recruiting Trial end date: May 5, 2021
Sequential Oxygen Therapy Strategy for Patients With COVID-19 NCT04312100 Prospective cohort	COVID-19 diagnosed by RT-PCR Ages 18-75 years Zhengzhou, Henan, China	Mild cases with conventional oxygen therapy Moderate/Severe cases with nasal high flow oxygen inhalation Moderate/Severe cases with non-invasive positive pressure ventilation	Incidence of respiratory failure 28-day mortality rate	Recruiting Estimated completion date: February 2021