High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure.

AIM:

To compare the use of standard oxygen therapy, nasal high-flow (NHF) oxygen therapy and noninvasive ventilation (NIV) in patients admitted to the intensive care unit (ICU) with acute hypoxemic respiratory failure with respect to intubation rate, mortality and other clinical outcomes.

METHOD:

This 23-center, prospective, randomized trial included patients who had acute hypoxemic respiratory failure without hypercapnia, a ratio of partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) of ≤300 mmHg, a partial pressure of carbon dioxide ($PaCO_2$) ≤45 mmHg and a respiratory rate >25 breaths/minute. All patients were randomized in a 1:1:1 ratio, and oxygen was adjusted to achieve oxygen saturation (SaO_2) of ≥92%. Patients received either standard oxygen therapy via a nonrebreather face mask at ≥10 L/min, NHF oxygen therapy via large-bore nasal prongs (Optiflow™, Fisher & Paykel Healthcare) with heated humidification (MR850™, Fisher & Paykel Healthcare) at a rate of 50 L/min and an initial FiO_2 of 1.0, or NIV via a face mask (Fisher & Paykel Healthcare) connected to an ICU ventilator with pressure support applied in NIV mode. The pressure support level was adjusted with the aim of obtaining an expired tidal volume of 7–10 mL/kg of predicted body weight, with an initial positive end-expiratory pressure (PEEP) of 2–10 cmH_2O; FiO_2 and/or PEEP were adjusted as above. NHF oxygen therapy was applied for at least 2 days and the minimum required duration of NIV was 8 hours/day for 2 days. The primary endpoint was the proportion of patients requiring endotracheal intubation within 28 days after randomization. Secondary outcomes were mortality in the ICU and at 90 days, the number of ventilator-free days from day 1 to day 28, and duration of ICU stay.

RESULTS:

A total of 313 patients were randomized between February 2011 and April 2013; 310 patients were included in the analysis after three patients withdrew consent (94 received standard oxygen therapy, 106 received NHF oxygen therapy and 110 received NIV). For the majority of patients (64%), the cause of acute respiratory failure was community-acquired pneumonia.

Key primary and secondary endpoint data are summarized in the table. Compared with the NHF oxygen therapy group, the hazard ratio (HR) for intubation at day 28 overall was 1.45 (95% confidence interval [CI] 0.83 - 2.55) in the standard oxygen therapy group and 1.65 (95% CI 0.96 - 2.84) in the NIV group. In a subgroup analysis of patients with PaO_2:FiO_2 ≤200 mmHg corresponding values were 2.07 (95% CI 1.09 - 3.94) and 2.57 (1.37- 4.84) in the unadjusted analysis, and 2.14 (95% CI 1.08 - 4.22) and 2.60 (95% CI 1.36 - 4.96) after adjustment for bilateral pulmonary infiltrates, respiratory rate and history of cardiac insufficiency. The unadjusted HR for death at 90 days in the standard versus NHF oxygen therapy group was 2.01 (95% CI 1.01- 3.99; p=0.046) and in the NIV versus NHF group was 2.50 (95% CI 1.31- 4.78; p=0.006). In the adjusted analysis, corresponding values were 2.36 (95% CI 1.18 - 4.70) and 2.33 (1.22 - 4.47).

There was no statistically significant difference between treatment groups in the rate of serious adverse events. At 1 hour after initiation of treatment, patients in the NHF oxygen therapy group had less respiratory discomfort and lower dyspnea scores compared with the other two groups.

Frat J, Thille A, Mercat A, Girault C, Ragot S, Perbet S et al.
N Engl J Med. 2015;372(23):2185-2196.

VARIABLE	STANDARD OXYGEN THERAPY (N=94)	NHF OXYGEN THERAPY (N=106)	NIV (N=110)	P-VALUE*
INTUBATION AT DAY 28 (% PATIENTS)				
Overall	47 (37 - 57)	38 (29 - 47)	50 (41 - 59)	0.18
Patients with PaO_2:FiO_2 ≤200 mmHg	53 (42 - 64)	35 (26 - 46)	58 (47 - 68)	0.009
VENTILATOR-FREE DAYS, n				
Overall	22±10	24±8	19±12	0.02
Patients with PaO_2:FiO_2 ≤200 mmHg	21±10	24±8	18±12	<0.001
MORTALITY, % PATIENTS				
In ICU	19 (12 - 28)	11 (6 - 9)	25 (17 - 33)	0.047
At 90 days	23 (16 - 33)	12 (7 - 20)	28 (21 - 37)	0.02

*For the three-group comparison.
Values are % patients (95% confidence intervals) or mean ± standard deviation.
FiO_2, fraction of inspired oxygen; ICU, intensive care unit; NHF, nasal high flow; NIV, noninvasive ventilation; PaO_2, partial pressure of arterial oxygen.

CONCLUSION:

There was no statistically significant difference between standard oxygen therapy, NHF oxygen therapy and NIV for the primary endpoint (intubation at 28 days). However, NHF oxygen therapy recipients with baseline PaO_2:FiO_2 ≤200 mmHg had a significantly lower 28-day intubation rate compared with the other two groups. In addition, all NHF oxygen therapy recipients had a significantly lower 90-day mortality rate.

KEY POINTS:

- There is no difference in the 28-day intubation rate in patients with acute hypoxemic respiratory failure treated with standard oxygen therapy, NHF oxygen therapy or NIV.
- Acute hypoxemic respiratory failure patients who have a baseline PaO_2:FiO_2 of ≤200 mmHg have a significantly lower 28-day intubation rate when treated with NHF oxygen therapy compared with standard oxygen therapy or NIV.
- In patients with acute hypoxemic respiratory failure, treatment with NHF oxygen therapy is associated with significant reduction in 90-day mortality compared with standard oxygen therapy or NIV.

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