HFNC vs. NIV for Acute Respiratory Failure

Key Article

- *RENOVATE Investigators. High-flow nasal oxygen vs noninvasive ventilation in patients with acute respiratory failure. The RENOVATE randomized clinical trial. JAMA. 2024. Published online December 10, 2024.*

Background

- Both HFNC and NIV are used to treat patients with acute hypoxemic respiratory failure.
- Patients may not tolerate NIV due to discomfort and high pressures.
- HFNC (compared to low-flow oxygen) improves oxygenation, reduces dead space, improves alveolar recruitment, enhances clearance of secretions, and is heated and humidified.
- HFNC has been shown to:
    - Reduce PaCO2 levels in acute COPD exacerbations.
    - Decrease cardiac preload.
    - Improve signs of respiratory failure in patients with acute heart failure
- HFNC is easier to use and more comfortable compared with NIV.
- However, HFNC may be less effective than NIV in reducing the work of breathing during acute respiratory failure.
- Current guidelines recommend NIV for acute respiratory failure caused by COPD and acute cardiogenic pulmonary edema. However, the evidence for these recommendations is based on comparisons with low-flow O2 and not HFNC.
- At present, there remains uncertainty regarding the effectiveness of HFNC compared to NIV for acute hypoxemic respiratory failure.

Objective

- To evaluate the noninferiority of HFNC compared with NIV and assess potential superiority in reducing rates of intubation and death in 5 patient groups with acute respiratory failure.

Methods

- Multicenter, adaptive, noninferiority, randomized clinical trial.
- 33 hospitals in Brazil
- Patients
    - Included
        - Adults ≥ 18 years
        - Admitted to the ED, ICU, or hospital ward
        - Acute respiratory failure
            - SpO2 < 90% or PaO2 < 60 mm Hg on RA
            - Respiratory effort
                - Accessory muscle use
                - Paradoxical breathing
                - Thoracoabdominal asynchrony

                - Tachypnea: RR > 25 bpm
            - 5 patient groups
                - Nonimmunocompromised with hypoxemia
                - Immunocompromised with hypoxemia
                - COPD exacerbation with respiratory acidosis
                - Acute cardiogenic pulmonary edema
                - Hypoxemic COVID-19 (added later)
        - Excluded
            - Urgent need for intubation
            - Hemodynamic instability
            - Contraindications to NIV
- Interventions
    - Randomized 1:1
        - HFNC
            - Delivered continuously with initial flow at 30 L/min for COPD with acidosis and 45 L/min for the other 4 groups.
            - Titrated gradually to 60 L/min or highest tolerated.
            - FiO2 started at 50% and titrated to maintain SpO2 88%-92% for COPD exacerbation and 92%-98% for the other 4 groups.
            - After 24 hrs, weaning from HFNC could begin if clinical improvement was achieved.
            - NIV rescue therapy was permitted for COPD and ACPE exacerbations at physician discretion.
        - NIV
            - Delivered via FM
            - IPAP
                - For COPD, set 12-16 cm H2O
                - All others, set 12-14 cm H2O
                - Could be titrated to a max of 20 cm H2O
            - EPAP
                - For COPD, set at 4 cm H2O
                - All others, set at 8 cm H2O
                - Could be titrated to a max of 12 cm H20
            - FiO2 titrated to maintain SpO2 88%-92% for COPD and 92%-98% for all others
            - Tidal volume target: 6-9 ml/kg IBW
- Primary outcome
    - Intubation or death at 7 days (predefined criteria were applied)
- Secondary outcomes
    - 28-day mortality
    - 90-day mortality
    - Mechanical-ventilation free days at day 28
    - ICU-free days at day 28
    - ICU LOS within 90 days
    - Vasopressor-free days at day 28
- Statistical Analysis
    - Used Bayesian adaptive statistical methods to assess primary outcome

    - Noninferiority margin established based on absolute effect of 36% for NIV on the rate of intubation.
    - Noninferiority was declared if the posterior probability was higher than 0.992.
    - If noninferiority demonstrated, then superiority was declared if the posterior probability was also higher than 0.992 for an OR < 1.

Results

- A total of 1766 patients were included in the final analysis
    - HFNC: 883 patients
    - NIV: 883 patients
    - At first interim analysis, enrollment stopped in the immunocompromised with hypoxemia patient group for futility; enrollment stopped at the 5th interim analysis for hypoxemic COVID-19 group and at the 6th interim analysis for nonimmunocompromised with hypoxemia and ACPE groups.
- Patient Groups
    - Hypoxemic COVID-19 patients: 882 patients
    - Nonimmunocompromised with hypoxemia: 485 patients
    - Acute cardiogenic pulmonary edema: 272 patients
    - COPD exacerbation with respiratory acidosis: 77 patients
    - Immunocompromised with hypoxemia: 50 patients
    - 40% randomized in the ED or hospital ward
- Primary Outcome
    - HFNC: 39%
    - NIV: 38.1%
    - HFNC noninferior to NIV for nonimmunocompromised with hypoxemia, COPD exacerbation with respiratory acidosis, acute cardiogenic pulmonary edema, and hypoxemic COVID-19
- Primary Outcome in Patient Groups
    - COPD
        - HFNC: 28.6%
        - NIV: 26.2%
    - ACPE
        - HFNC: 10.3%
        - NIV: 21.3%
    - Hypoxemic COVID-19
        - HFNC: 51.3%
        - NIV: 47%
    - Nonimmunocompromised with hypoxemia
        - HFNC: 32.5%
        - NIV: 33.1%
    - Immunocompromised with hypoxemia
        - HFNC: 57.1%
        - NIV: 36.4%
- Secondary Outcomes
    - No difference between the 2 treatment groups for any of the 5 patient groups.
- Adverse Events
    - Incidence of serious adverse events was similar between the groups

Limitations Identified by Authors

- NIV used in 23% of patients in the COPD exacerbation group.
- Post-hoc analysis without borrowing suggested possible harm with use of HFNC in COPD group.
- Enrollment in immunocompromised with hypoxemia group stopped early for futility – small sample size
- NIV was used through a FM

Take Home Point

- HFNC was noninferior to NIV in the rates of intubation or death for patients with acute COPD exacerbation with respiratory acidosis, acute cardiogenic pulmonary edema, hypoxemic COVID-19, and nonimmunocompromised with hypoxemia.