critical care perspectives in emergency medicine

High vs. Low-Intensity NIPPV for Acute COPD Exacerbations

Key Article

- *Luo Z, Yichong L, Li W, et al. Effect of high-intensity vs low-intensity noninvasive positive pressure ventilation on the need for endotracheal intubation in patients with an acute exacerbation of chronic obstructive pulmonary disease. JAMA. 2024. Published online September 2024.*

Background

- NIPPV is commonly used in the management of critically ill patients with an acute COPD exacerbation.
- NIPPV for acute COPD exacerbations is associated with decreased rates of intubation and lower in-hospital mortality.
- Low-intensity NIPPV (IPAP < 18 cm H2O) is typically used in clinical practice.
- High-intensity NIPPV (IPAP 20-30 cm H2O) in theory may be more effective at increasing alveolar ventilation and offsetting the extra dead space of the facemask.
- At present, when compared to low-intensity NIPPV, high-intensity NIPPV has been shown to be superior at decreasing inspiratory effort and improving gas exchange, ventilatory function, patient tolerance, and reducing elevated levels of PaCO2.
- However, the effect of high-intensity NIPPV on the need for intubation has not been assessed.

Objective

- To determine whether high-intensity NIPPV could reduce the need for intubation during hospitalization in patients with an acute COPD exacerbation and hypercapnia when compared with low-intensity NIPPV.

Methods

- Investigator-initiated, 2-group, single-blind, multicenter, randomized trial
- 30 general respiratory (non-ICU) wards across China
- Patients
    - Included
        - Adults ≥ 18 years
        - Arterial pH < 7.35 and arterial PaCO2 > 45 mm Hg
        - Persistently elevated PaCO2 > 45 mm Hg after 6 hours of low-intensity NIPPV
    - Excluded
        - Patients < 18 years of age
        - Excessive respiratory secretions or upper airway obstruction
        - Recent oral, facial, or cranial trauma or surgery
        - Recent gastric or esophageal surgery
        - Active upper GIB
        - P:F ratio of < 100
        - Pneumothorax
        - Severe hemodynamic instability

        - Severe metabolic acidosis with pH < 7.20
- Interventions
    - Randomized 1:1
    - High-Intensity NIPPV
        - IPAP initially adjusted in increments or decrements of 1-2 cm H2O to obtain a **Vt of 10-15 ml/kg** of predicted body weight (usually 20-30 cm H2O) and a RR < 25 bpm.
        - Subsequent adjustments based on ABG values to target normocapnia.
    - Low-intensity NIPPV
        - IPAP initially adjusted in increments or decrements of 1-2 cmH2O to a max of 20 cm H2O obtain a **Vt of 6-10 ml/kg** of predicted body weight and a RR < 25 bpm.
        - Subsequent adjustments to IPAP were based on ABG values to achieve a pH of 7.35 or higher.
    - Patients encouraged to use NIPPV continuously for the first 6 hrs after randomization and for at least 10 hrs per day.
    - IPAP and daily use of NIPPV gradually decreased when the target ABG levels reached, and clinical conditions improved.
        - Resolution of COPD exacerbation
        - RR < 25 bpm
        - HR < 110 bpm
        - PaO2 >. 60 mm Hg on an FiO2 less than 40%
- Primary outcome
    - Need for endotracheal intubation.
        - pH < 7.25 with a PaCO2 that increased > 20% compared to baseline.
        - Clinical signs
            - Altered mentation (coma, delirium)
            - Accessory muscle use or thoracoabdominal paradoxical movement
            - Excessive secretions, aspiration, vomiting.
            - UGIB
            - Hemodynamic instability no responsive to IVFs or low-dose pressors
            - Cardiac or respiratory arrest
- Secondary outcomes
    - Endotracheal intubation during hospitalization
    - Endotracheal intubation by day 28
    - NPPV weaning success
    - Mortality (in-hospital, day 28, day 90)
    - ICU admission
    - Hospital DC
    - Hospital LOS
    - Days free of mechanical ventilation
    - Days free of ICU admission
    - Hospital readmission at day 90

Results

- A total of 300 patients were randomized
    - High-intensity NIPPV: 147
    - Low-intensity NIPPV: 153

    - Baseline characteristics were similar between the groups.
        - Mean age: 73 years
        - 68% male
- Ventilator Interventions
    - Mean IPAP at 2 hrs
        - High-intensity NIPPV: 25 cm H2O
        - Low-intensity NIPPV: 17 cm H2O
    - Mean Vt at 2 hrs
        - High-intensity NIPPV: 11 ml/kg PBW
        - Low-intensity NIPPV: 7.7 ml/kg PBW
    - Median daily use
        - High-intensity NIPPV: 20 hrs day 1, 18 hrs day 2, 17 hrs day 3
        - Low-intensity NIPPV: 18 hrs day 1, 17 hrs day 2, 16 hrs day 3
    - Mean PaCO2 levels at 72 hrs
        - High-intensity NIPPV: 53 mm Hg
        - Low-intensity NIPPV: 64 mm Hg
    - More patients in the high-intensity NIPPV group achieved normocapnia compared with low-intensity NIPPV.
- Interim Analysis
    - Primary outcome differed significantly between the groups (9.0%).
    - DSMB terminated the trial early as a result.
- Primary Outcome – Meeting prespecified criteria for endotracheal intubation
    - High-intensity NIPPV: 4.8%
    - Low-intensity NIPPV: 13.7%
- Secondary outcomes
    - Composite of endotracheal intubation or avoiding intubation by crossover to high-intensity NIPPV
        - High-intensity NIPPV: 3.4%
        - Low-intensity NIPPV: 11.1%
        - Of the 21 patients in the low-intensity NIPPV group who met criteria for intubation, 13 (62%) crossed over to the high-intensity NIPPV group. Of these 13, 11 were NOT intubated.
    - All other secondary outcomes did not differ significantly between the two groups.
- Safety Outcomes
    - Abdominal distension occurred more frequently in the high-intensity NIPPV group.
        - No patient requested removal of NIPPV due to distension.
    - No cases of pneumothorax
    - Serious events rare in both groups.

Limitations Identified by Authors

- Study was terminated early – only enrolled half of the target 600 patients.
- Study was non-blinded.
- Trial not powered for mortality.
- Crossover from low-intensity group to high-intensity group.
- All centers within China.

Take Home Point

- High-intensity NIPPV significantly reduced the number of patients who met criteria for intubation in those presenting with an acute COPD exacerbation with hypercapnia despite 6 hours of low-intensity NIPPV.