



## ARTICLE

Chronic Non-invasive Ventilation for Chronic Obstructive Pulmonary Disease

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## CLINICAL QUESTION

Do patients with COPD and chronic respiratory failure benefit from non-invasive ventilation (NIV)?

## SUMMARY

Chronic obstructive lung disease (COPD) is a common disease with significant associated morbidity and mortality. Non-invasive ventilation is commonly prescribed to COPD patients with hypercapnic respiratory failure. Theoretical benefits of improved respiratory mechanics, improved nocturnal gas exchange, and preservation of hypoxic/hypercapnic sensitivity make this an attractive intervention and worth further investigation.

This Cochrane review was done using a pooled analysis of individual participant data (IPD) when able and meta-analyses otherwise. Randomized controlled trials (RCT) that enrolled patients with COPD and compared NIV to standard therapy were included. Studies were grouped based on indication: stable COPD and COPD post hospitalization for exacerbation. COPD patients were defined by GOLD criteria. Patients in the intervention arm were prescribed NIV for at least 5 hours per day. Certainty of the evidence was graded for primary outcomes and survival for each of the two groups using the GRADE working group criteria.

Twenty-one studies were included. Most of these enrolled patients with stable COPD (17) versus post exacerbation (4). Bi-level pressure support with or without back up rate was used in all but two studies which did not specify mode of ventilation. Mean inspiratory airway pressure (IPAP) and expiratory airway pressure (EPAP) were reported based on indication (stable versus post exacerbation). Mean IPAP ranged between 16-21 cmH<sub>2</sub>O and was higher in the post exacerbation group. Stable COPD study patients were initiated in both inpatient and outpatient settings. Patients enrolled in the post-hospitalization studies were all initiated on NIV as inpatients. At 12 months, actual mean NIV use was 5.5 hours per night in the stable COPD group and 6.8 hours in the post exacerbation group.

Among patients with stable COPD there was a reduction in PaCO<sub>2</sub> at both three and twelve months (mean reduction 4.5 and 3.5mmHg respectively). This evidence was graded high quality. Heterogeneity exploration revealed that this effect was limited to subgroups of patients with high



baseline pCO<sub>2</sub> (> 54 mmHg) and those receiving high IPAP (> 18 cmH<sub>2</sub>O). Evidence for a reduction in all-cause mortality (HR 0.78, 95% CI 0.58-0.97) was graded moderate. All other outcomes, including health related quality of life, exercise capacity, and change in PaO<sub>2</sub>, were equivocal between groups or significant but with low or very low certainty.

In the post COPD exacerbation group there was also a significant improvement in PaCO<sub>2</sub> at three and twelve months compared to control (mean reduction 3 and 3.9 mmHg respectively). This evidence was graded high quality (at 12 months) and moderate quality (at three months). Admission free survival was improved in the NIV group (HR 0.71, 95% CI 0.54–0.94) but certainty of this evidence was graded as low. There was no difference in all-cause mortality, change in oxygen concentration, exacerbations, hospitalizations, or health related quality of life.

In summary:

- NIV was shown to reduce PaCO<sub>2</sub> with high certainty for both stable and post exacerbation COPD patients. However, this effect is limited to patients with high initial PaCO<sub>2</sub> (>54 at sea level) or receiving high IPAP (>18 cm H<sub>2</sub>O).
- NIV was associated with reduced all-cause mortality in the stable group but not in the post exacerbation group.
- Admission free survival was lower amongst post exacerbation COPD patient but there was no change in overall exacerbations or hospitalizations which suggests that time to next hospitalize or death was delayed by NIV.
- NIV improved measures of health related quality of life (HRQL) for patients with stable COPD though the evidence was graded very low certainty. NIV did not provide any such improvement in HRQL for COPD patient post exacerbation.
- The authors' conclusion was that this review supports the use of NIV for all COPD patients with chronic hypercapnic respiratory failure. The role for NIV in the setting of COPD with hypercapnia shortly after exacerbation is not clear.

## GROUP OPINION

This review was discussed among members of the COPD group. The following recommendations were made based in part on this review but it was also noted that several important studies, some of which were not included in this review, need to be considered as well.

Group opinion was that NIV should be considered for all patients with stable COPD (without recent exacerbation) and persistent PaCO<sub>2</sub> > 52 mmHg. The patient should be educated regarding the intended benefits of NIV which include improved mortality, even in the absence of an improved HRQL. NIV should also be considered post exacerbation requiring hospitalization if hypercapnia persists at least two weeks after discharge. Patients in this group should be educated



regarding the potential benefits of improved mortality and reduced rates of COPD readmission. This opinion is stronger than that of the authors of the Cochrane Review and is based in part on a randomized controlled trial that showed decreased time to death and readmission with NIV in this population [1] as well as a more recent meta-analysis that showed decreased rates of readmission and improved mortality with NIV [2].

For all patients, a high intensity strategy should be employed with goal IPAP > 18 cm H<sub>2</sub>O. Higher IPAP settings could also be considered, if tolerated, with a goal of PaCO<sub>2</sub> reduction of at least 20%. EPAP should be titrated to reduce apneas and snoring. If targets cannot be met with pressure targeted modes of NIV more advanced volume targeted home ventilators should be considered. These recommendations are based on this Cochrane Review as well as two prior meta analyses that showed minimal NIV benefit among patients with low IPAP settings [1] and lack of NIV benefit except for a subgroup of patients whose IPAP was increased with goal of PaCO<sub>2</sub> reduction [2].

Patients in both groups should be instructed to use NIV for a minimum of 5 hours per night. Patients should also be screened for sleep disordered breathing prior to initiation of NIV. Shared decision making should be used between provider and patient. It was noted that there are still several questions about NIV use in COPD that remain unresolved and deserve further investigation. This includes optimal ventilator mode (pressure versus volume targeted), optimal PaCO<sub>2</sub> threshold to initiate therapy (there is a discrepancy between ATS and CMS recommendations), and IPAP titration targets.

## References

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