

# Letter to the Editor

## A link of non-invasive ventilation in chronic hypercapnic COPD patients with pulmonary hypertension. A new index of prognosis?

### *To Editor.*

In the February issue European Review for Medical and Pharmacological Sciences published Parola D et al<sup>1</sup> published an interesting and original article to evaluate the effect of NIV treatment in patients with acute exacerbation of COPD, with or without respiratory acidosis, and its effect in patients with pulmonary hypertension.

This is a non-randomized clinical trial estimating the potential usefulness of NIV in a small cohort of COPD patients with chronic hypercapnia and pulmonary hypertension experiencing disease acute exacerbation. Authors concluded that NIV may serve as a reliable therapeutic tool not only in COPD patients with uncompensated chronic hypercapnia but also in those without respiratory acidosis. They also state that pulmonary hypertension may represent a poor prognostic indicator for treatment responsiveness in patients with COPD experiencing disease deterioration and undergoing a course of NIV.

The study presents with major caveats that pose significant limitations to the scientific rigidity of the data presented and should be addressed cautiously.

Firstly, we consider some major limitations: (1) this is an underpowered non-randomized study that lacks of control arm. Therefore, it is relatively unknown whether COPD patients with compensated respiratory acidosis would have a favorable prognosis by applying only conservative therapeutic means including oxygen support, bronchodilators, diuretics and corticosteroids. (2) Authors have applied cardiac ultrasound to estimate the levels of systolic pulmonary artery pressure. The technique lacks of both sensitivity and specificity to set the diagnosis of pulmonary hypertension since patients with COPD often present with severe hyperinflation that severely hampers the acoustic "window" of the method posing significant technical limitations to its diagnostic reliability. Therefore, the most reliable technique to set the diagnosis of PH especially in this category of patients is right heart catheterization. In addition, the threshold of PASP > 55 mmHg is completely arbitrary. The revised criteria for PH in the Dana point meeting state that patients presenting with PASP > 50 mmHg in the cardiac echo may have PH (mean PAP > 25 mmHg) based on right heart catheterization. (3) While Authors report a statistically significant improvement in both arterial blood gases analysis and 6MWT after NIV application they do not present data regarding days of hospitalization. It is surprising that Authors subjected their patients to 6MWT while on acute exacerbation with respiratory acidosis. Based on the ATS/ERS guidelines for 6MWT two of the relative contraindications of 6MWT is resting tachycardia (> 120 bpm) and elevated systolic/diastolic blood pressure (> 180/120 respectively)<sup>2</sup>. Authors should comment on that. Arterial blood gases values illustrated in Table I lack of FiO<sub>2</sub> data and do not report the stage of disease based on functional criteria.

Secondly, we are rather confused by the study design and the exclusion criteria applied by the Authors. Why did Authors exclude patients with COPD and OSAHS or CHF? This is called selection bias. Since COPD is a systematic disease the majority of these patients present with significant co-morbidities. Did the Authors estimate levels of NT-proBNP to assess potential right heart failure during acute exacerbation?

Thirdly, in addition Authors fail to report causes of acute exacerbations? Based on literature approximately 70-80% of COPD exacerbations are due to respiratory infections. Since increased tracheo-bronchial secretions represent relative contra-indications of NIV Authors should comment on that.

The study does not assess the side effects of NIV application. There was no follow-up for the patients who presented with compensated hypercapnic failure. How long did the effect on ABGs and 6MWT last? Could it be that after a few days without NIV the patients were again hypercapnic? If yes, what is the point of NIV application and why is the original correction so important?

A patient with compensated chronic hypercapnic respiratory failure that is subjected to mechanical ventilation could be at a high risk of developing acidemia once the mechanical ventilation is withdrawn. It would be useful to assess these patients' relapse rate.

Finally, additionally there are some minor limitations: Authors state that the definition of PH is "mean PAP > 25 mmHg with a normal PCWP at rest and PAP > 30 mmHg with exercise". Based on the findings by Kovacs et al<sup>3</sup> the exercise criterion was abandoned in the revised joint PH meeting since it seems that the mean pulmonary arterial pressure ( $P_{pa}^-$ ) is largely age-dependent and unreliable. Therefore, in the proceedings of the Dana Point meeting, the new haemodynamic definition of PH will be a  $P_{pa}^-$  at rest  $\geq$  25 mmHg. This definition, which covers all forms of PH, will be adopted by the revised joint PH guidelines of the European Society of Cardiology and the European Respiratory Society, in which PH will be divided into pre-capillary and post-capillary forms, based on whether mean  $P_{pcw}$  is  $\leq$  15 or  $>$  15 mmHg, respectively<sup>4,5</sup>. There are some spelling errors that should be addressed, i.e. page 188, first paragraph: (1) reported data on this topic; (2) the use of NIV is effective also in patients affected by hypercapnic and hypoxiemic respiratory failure.

We consider that further clinical studies are, therefore, crucial to evaluate clinical impact of niv and relations in chronic hypercapnic COPD patients with pulmonary hypertension.

## References

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