Volume-Targeted Versus Pressure-Limited Noninvasive Ventilation in Hypercapnic Respiratory Failure: What Could Be Established in Real Practice?

To the Editor:

We have read with interest the original article titled "Volume-Targeted Versus Pressure-Limited Noninvasive Ventilation in Subjects with Acute Hypercapnic Respiratory Failure: A Multi-Center Randomized, Controlled Trial."¹ In this study, Cao et al¹ used a prospective, randomized controlled trial in the general respiratory wards to establish whether the ventilatory strategy with volume-targeted noninvasive ventilation (VT-NIV) was more effective than pressure-limited NIV (PL-NIV).

We have some remarks on this study for practical implications. First, regarding methodology, we believe patient selection was inadequate, as only subjects with exacerbations of chronic pathologies (eg, COPD, asthma, bronchiectasis, and obstructive sleep apnea syndrome) were randomized into 2 groups of 29 subjects with similar demographics and blood gas analysis (pH, P_{CO_2} , P_{aO_2}/F_{IO_2} , and HCO_3^-). The authors randomized subjects with mild to moderate acute-on-chronic hypercapnic respiratory failure, of which 12% reported previous use of NIV. However, they did not specify the causes or conditions for which these subjects received previous treatment with NIV.

Second, evaluation of key determinants of severity and grading needs to be more precisely defined in three aspects. There is an absence of parameters in the evaluation of acute hypercapnic respiratory failure. The authors did not report on (1) severity of mental status impairment;² (2) HCO_3^- , mmol/L, base excess at 2–6 h and at 12 h after NIV use, without clearly establishing the moment when they reached their compensation; and (3) conventional therapy such as inhaled β_2 -agonists, anticholinergic agents, systemic steroids, and antibiotics, along with the method of delivery, dose, and frequency of treatments in both groups.

The third issue relates to the prolonged use of NIV detailed in the study. The authors reported on duration of NIV – median (IQR) of 6.0 d (4.0–9.5) for PL-NIV versus 9.0 (4.0–13.0) d for VT-NIV. Today, it is known that more than half of patients with

acute hypercapnic respiratory failure treated with NIV resolve within the first 24 h, 80% experience resolution within 48 h, and 92% resolve within 72 h. Patients with initial pH values between 7.30 and 7.35 require fewer days of NIV than those with a pH between 7.21 and 7.25.

In accordance with the guidelines, NIV should be first-line therapy in patients with exacerbations of chronic airway diseases, with pH < 7.35 and P_{CO_2} > 45 mm Hg, until pH is normalized to 7.35–7.45. This prolonged use of NIV could indicate that these subjects had chronic hypercapnia, and therefore the reported NIV results may differ from other patient populations.^{3,4}

Fourth, the authors used inadequate ventilation settings. In the non-intervention group, the authors tried to obtain a V_T of 8–10 mL/kg predicted body weight. They noted variations in the exhaled V_T of approximately 1 mL/kg predicted body weight, with 9.5 mL/kg at the start of the NIV, and 10.3 mL/kg at 6 h. On the other hand, 2 h after the use of NIV, the authors reported an increase in the pressures inspired by the PL-NIV group as shown in Figure 4D, at the moment when a greater decrease of P_{CO_2} in the VT-NIV group was observed. This pressure increase in favor of PL-NIV was maintained for up to 6 h. The maximum inspiratory positive airway pressure target should have been programmed as much as possible during the first hours of PL-NIV.⁵

We believe that these assessments should be taken into account when analyzing these results for proper clinical practical recommendation.

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Volume-Targeted Versus Pressure-Limited in Noninvasive Ventilation in Hypercapnic Respiratory Failure. What Could Be Established in Real Practice?—Reply

In Reply:

We thank Drs Briones Claudett and Esquinas for their interest and for commenting on our work.¹ It is our immense pleasure to response to such comments.

Regarding the methodology, we recruited 58 subjects with mild-to-moderate acute hypercapnic respiratory failure that mainly included COPD, asthma, bronchiectasis, and obstructive sleep apnea syndrome. Despite the small sample size, there were similar demographic and baseline characteristics between the two groups. As noted by Drs Briones Claudett and Esquinas, we included 7 subjects (12%) who had received noninvasive ventilation (NIV) previously, suggesting that in these subjects chronic hypercapnic respiratory failure occurred in the past. However, it is difficult to retrospectively obtain the specific conditions on which the previous NIV treatment was given.

It is of great importance to precisely define the severity of illness. Herein, we defined the eligible subjects as those with arterial pH < 7.35 and ≥ 7.25 with P_{aCO_2} >