Control of Respiratory Drive by Non-invasive Ventilation as an Early Predictor of Success

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To the editor,

Early prediction of failure of non-invasive ventilation (NIV) in patients with de novo acute hypoxemic respiratory failure is crucial to prevent patient self-inflicted lung injury (P-SILI) and avoid delayed intubation. NIV should cope with the elevated respiratory drive to deliver effective yet still protective ventilation. However, drive increases for many different reasons: lung collapse and shunt lead to hypoxia, high dead space and elevated metabolic demand rises the levels of CO_2, lung inflammation and altered mechanics activate chemo- and mechano-receptors, anxiety and subjective discomfort act on the neural respiratory drive amplifying the response to chemical and mechanical stimuli [1]. The clinical study by Tonelli et al. [2] testing the hypothesis that inspiratory effort estimated by esophageal balloon manometry might be an early predictor of NIV failure and worsening lung injury is a valuable addition to the field. Tonelli and coworkers report that lack of reduction in the swing of esophageal pressure (ΔP_{es}) after two hours from start of NIV is an accurate predictor of NIV failure.

According to the study protocol, pressure support (PS) was initially set at 10 cmH_2O and then modified to maintain the expired tidal volume (Vte) <9.5 ml/kg PBW and the respiratory rate <30 bpm. Of note, as a consequence of these per protocol adjustments, PS level at 2 hours was significantly lower in the NIV failure group, while Vte didn't differ [3]. As pointed out by Tuffet et al. [4], the level of assistance during NIV influences the respiratory effort and they suggest a different interpretation of the study results according to which the level of assistance, when properly modulated to decrease respiratory effort, may avoid intubation. Indeed, in the NIV success group, increasing PS allowed to match the ventilation demand of the patient while maintaining protective ventilation, therefore controlling the respiratory

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drive. At the opposite, the respiratory drive remained high despite NIV support in the failure group, halting the increase in PS level to maintain protective Vte. Thus, we may speculate that, if the PS level would have been left unchanged for the first two hours, we would have observed a persistently elevated Vte, presumably higher than the targeted <9.5 ml/kg of PBW, in the failure group vs. lower protective Vte in the other group. The results by Tonelli et al. are consistent with those previously published by Carteaux et al. [5] who reported that a Vte higher than 9.5 ml/kg PBW is independently associated with NIV failure.

Improvement in lung mechanics and unloading of the respiratory muscles by NIV might have contributed to effective control of the respiratory drive in the success group. The correlation between ΔPes and Vte/ΔP_L (i.e., the dynamic lung compliance) at baseline confirms that effort is correlated with severity and that the "mechanical factors" related to the size of the baby lung act as strong determinants of the respiratory drive in this population. Nevertheless, other "non-mechanical" determinants of the respiratory drive must have been at play in the failure group. These factors couldn't be corrected by NIV, and might require specific treatments, such as sedation to treat anxiety and discomfort, etiologic therapy to switch off inflammation, extracorporeal CO_2 removal to decrease the ventilation demand [6]. In this perspective, more precise understanding of the mechanisms of increased respiratory drive in each patient with de novo acute hypoxemic respiratory failure might allow an individualized "physiology-driven" treatment, aimed at avoiding intubation. We think that a multimodal approach for early identification and treatment of the contributing causes of elevated respiratory drive might be key to avoid P-SILI and endotracheal intubation.

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