LETTER TO THE EDITOR

Potential Hazards of Neuromuscular Blocking Agents in the Treatment of Acute Respiratory Distress Syndrome. Comment on: "Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome"

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Papazian *et al*. recently reported a lower adjusted mortality with administration of cisatracurium besylate in early acute respiratory distress syndrome (ARDS) [1]. Given the incidence of ARDS (190,000 estimated annual cases in the United States) [2] and the absence of any other effective pharmacotherapy, this trial seems likely to impact the care of thousands of patients annually.

While the mechanisms responsible for the adjusted mortality benefit reported by Papazian *et al.* remain speculative, it is highly likely that lower transpulmonary pressures (TPPs) in the cisatracurium group were responsible for some portion of the reported benefit. This is suggested by the three-fold incidence of pneumothorax in the placebo group compared to the cisatracurium group despite no difference in plateau pressures between the groups. This complication is significant in its own right, and probably serves as a marker for less obvious barotrauma at the alveolar level.

Neuromuscular blocking agents (NBA) such as cisatracurium have a number of drawbacks compared to other methods of reducing TPP. While not demonstrated by Papazian *et al.*, others have shown that NBA can cause persistent muscle weakness for over 72 hours and that even minimal NBA-evoked muscle weakness produces clinically relevant impairment of upper airway and pulmonary function [3-5]. Spontaneous breathing during ventilatory support improves ventilation perfusion matching in patients with ARDS, and data suggest that NBA exacerbate mechanical ventilation-induced diaphragm dysfunction [6]. Given that techniques now exist to measure TPP at the bedside, it is possible to optimize TPP without incurring the detrimental effects of NBA administration [7]. Ventilator strategies tailored to individual patient physiology, rather than across the board NBA administration, ultimately have the greatest potential to minimize ventilator induced lung injury [8]. The unusually high dose of cisatracurium used by Papazian *et al.* (15mg bolus, followed by 37.5mg per hour for 48 hours) may further exacerbate these potential problems [1].

NBA administration has also been associated with post-traumatic stress disorder and psychiatric symptoms in survivors of ARDS [9]. We are particularly concerned that Papazian *et al*.'s study did not describe a method for or discuss the importance of monitoring sedation during neuromuscular blockade, and did not monitor psychiatric outcomes. If there is a significant rise in the numbers of patients treated with NBA as a result of this trial, ensuring adequate sedation and tracking psychiatric outcomes will be increasingly important.

The TPP reductions that likely underlie the benefit shown in Papazian *et al.*'s study can be achieved using sedative agents and monitoring devices that lack the drawbacks of NBA. Given the potential side effects of prolonged NBA administration, their results should be confirmed in a multicenter trial before paralysis becomes standard practice in early ARDS.

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