Acute respiratory distress syndrome (ARDS) is a lethal syndrome characterized by hypoxemia, bilateral infiltrates and diffuse alveolar damage. Patients presenting with ARDS often require intubation and mechanical ventilation for hypoxic respiratory failure. Standard therapy includes low tidal volumes coupled with lower plateau pressures, which reduce mortality and increase ventilator-free days when compared to higher tidal volumes and plateau pressures. However, volumes set by clinicians do not always correspond to the true volume delivered because of patient-ventilator dysynchrony, which can occur despite the use of adequate analgesics and sedatives. Patients may develop breath stacking, leading to higher tidal volumes and increased pressures delivered to the alveolus. Thus, clinicians sometimes consider the use of neuromuscular blocking agents (NMBA) to increase chest wall compliance and minimize work of breathing and patient-ventilator dysynchrony. This review examines the risks and benefits of using NMBA for selected patients with ARDS.

**Rationale**

Breath stacking and patient-ventilator dysynchrony both may contribute to ventilator-induced lung injury. Light et al published the first report of NMBA effects in ARDS, demonstrating that pancuronium boluses diminished hypoxia and cerebral damage, as well as lowered inspiratory pressures and the subsequent risk of pneumothorax. However, several studies that followed demonstrated disparate outcomes, and the benefits of NMBA remained unclear. These uncertainties were addressed by three prospective randomized trials examining the effect of 48 hours of cisatracurium infusion in patients with early, severe ARDS (defined in two of the studies as a PaO2/Fio2 ratio less than 150) who were receiving mechanical ventilation. In the first two trials, patients treated with cisatracurium had an improved PaO2/Fio2 ratio and reduced levels of proinflammatory cytokines (Table 2), which delineates how they are metabolized.

The non-depolarizing paralytic agents differ in their duration of action (short-, intermediate-, and long-acting) as well. Vecuronium, rocuronium, atracurium, and cisatracurium are intermediate-acting drugs. With organ dysfunction, plasma concentrations of vecuronium and rocuronium may be increased, since both are hepatically metabolized and then renally excreted. Vecuronium’s active metabolite is 50% as active as its parent drug and has been associated with prolonged blockade after discontinuation because of decreased renal clearance. Comparatively, rocuronium’s metabolite is 5% to 10% as active as its parent compound, making its accumulation less of a concern. Both agents possess few or no cardiovascular effects. Atracurium and cisatracurium undergo elimination via ester hydrolysis and Hofmann elimination. Therefore, they are preferred for use in critically ill patients with multisystem organ failure. However, laudanosine, a neuroexcitatory metabolite of atracurium, can accumulate in organ dysfunction and may precipitate seizures. Atracurium and cisatracurium have minimal cardiovascular effects, but histamine release is associated with higher doses of atracurium. Pancuronium is a long-acting NMBA affected by renal and hepatic impairment with an active metabolite that is one-third to one-half as active as its parent drug. It also has glycotoxic effects, including an increase in heart rate of 10 or more beats per minute (in more than 90% of intensive care unit [ICU] patients).

**NMBA Selection**

Limited evidence supports the use of a single agent over another. The 2002 neuromuscular blockade guidelines published in Critical Care Medicine indicate that cisatracurium or atracurium are favored when there is evidence of hepatic or renal dysfunction and pancuronium should be avoided if glycotoxic effects are of concern. Subsequent surveys have found the decision-making process in NMBA choice is based on clinician experience and preference rather than on patient-related factors. These surveys preceded the French studies establishing the promising results of cisatracurium. Few trials have directly compared aminosteroids with benzylisoquinoliniums. One prospective, multicenter randomized trial compared recovery times in cisatracurium and vecuronium, and showed a significant reduction in recovery time to 70% response to train-of-four (TOF) for cisatracurium (68 min vs. 367 min, \( P = 0.02 \)). In another analysis of prospective trials in which the primary outcome under investigation was prolongation weakness, approximately

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**Clinical Spotlight**

**Neuromuscular Blockers in ARDS: Choice, Dosing and Monitoring**

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