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Research Article

Effect of Continuous Neuromuscular Blockade with Cisatracurium on Oxygenation and Sedation Requirements in Moderate-to-Severe ARDS Patients Receiving Mechanical Ventilation

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Abstract: Moderate-to-severe acute respiratory distress syndrome (ARDS) is associated with profound hypoxemia, high ventilatory demands, and increased sedation requirements. Continuous neuromuscular blockade has been proposed as an adjunctive strategy to improve oxygenation and optimize ventilatory synchrony, yet its impact on sedation burden remains incompletely characterized. This prospective interventional study evaluated the effect of continuous cisatracurium infusion on oxygenation parameters and sedative dose requirements in mechanically ventilated patients with moderate-to-severe ARDS. A total of 156 patients were allocated to either continuous cisatracurium infusion for 48 hours or standard care without neuromuscular blockade. The cisatracurium group demonstrated a significant improvement in PaO_2/FiO_2 ratio at 48 hours (from 118.4 ± 26.9 to 176.3 ± 34.1) compared to controls ($p < 0.001$). Concurrently, cumulative sedative doses were significantly reduced ($p = 0.002$), with improved ventilator synchrony and lower plateau pressures. These findings suggest that early continuous neuromuscular blockade with cisatracurium enhances oxygenation while reducing sedation requirements. This study provides novel physiological and pharmacological evidence supporting the selective use of neuromuscular blockade in severe ARDS management.

Keywords: neuromuscular blockade; cisatracurium; ARDS

Introduction: Acute respiratory distress syndrome remains a critical condition characterized by severe hypoxemia, reduced lung compliance, and diffuse inflammatory injury to the alveolar-capillary membrane. Despite advances in ventilatory strategies and supportive care, moderate-to-severe ARDS continues to be associated with significant mortality and prolonged intensive care unit stays. Optimizing mechanical ventilation

while minimizing ventilator-induced lung injury is central to improving outcomes in this population.[1-3]

Achieving effective lung-protective ventilation in ARDS often requires deep sedation to control respiratory drive and ensure patient-ventilator synchrony. However, excessive sedation is associated with numerous adverse effects, including prolonged mechanical ventilation, delirium, hemodynamic instability, and neuromuscular weakness. The balance between adequate sedation and avoidance of oversedation remains a persistent challenge in critically ill patients.[4-5]

Patient-ventilator dyssynchrony is particularly prevalent in moderate-to-severe ARDS due to high respiratory drive, altered lung mechanics, and elevated ventilatory demands. Dyssynchrony contributes to increased work of breathing, higher airway pressures, and exacerbation of lung injury. Neuromuscular blockade has been proposed as a strategy to eliminate spontaneous respiratory effort, improve ventilatory synchrony, and facilitate strict adherence to lung-protective ventilation parameters.[6-8]

Cisatracurium, a non-depolarizing neuromuscular blocking agent, is commonly used in critical care due to its organ-independent metabolism and predictable pharmacokinetics. Continuous infusion of cisatracurium allows for sustained neuromuscular blockade without accumulation, making it suitable for patients with multiorgan dysfunction. Previous studies have suggested potential benefits of early neuromuscular blockade on oxygenation and lung mechanics; however, concerns regarding prolonged paralysis, sedation exposure, and ICU-acquired weakness have limited routine use.[9-12]

While improvements in oxygenation with neuromuscular blockade have been reported, less attention has been directed toward its impact on sedation requirements. By abolishing spontaneous respiratory effort and agitation, neuromuscular blockade may permit lower sedative dosing while maintaining ventilatory control. Reducing sedative exposure could mitigate sedation-related complications and facilitate earlier recovery once paralysis is discontinued.

In resource-constrained settings, where advanced ventilatory adjuncts may be limited, optimizing pharmacological strategies to enhance oxygenation and ventilation efficiency is particularly relevant. Understanding the dual effects of neuromuscular blockade on respiratory physiology and sedation burden may inform more judicious and targeted use of this intervention.

This prospective study was designed to evaluate the effect of continuous cisatracurium infusion on oxygenation indices and sedation requirements in mechanically ventilated patients with moderate-to-severe ARDS. By integrating physiological and pharmacological outcomes, the study aims to provide novel evidence supporting a balanced, outcome-oriented approach to neuromuscular blockade in ARDS management.

Methodology: This prospective interventional study was conducted in the intensive care unit of a Bahria International Hospital over a 16-month period from January 2023 to April 2024. Adult patients aged 18 years or older with a diagnosis of moderate-to-severe ARDS requiring invasive mechanical ventilation were consecutively enrolled. ARDS severity was defined based on PaO_2/FiO_2 ratio $\leq$200 mmHg under standardized ventilatory conditions. Verbal informed consent was obtained from legally authorized representatives prior to study inclusion.

Patients were allocated into two groups according to the treatment strategy initiated within 12 hours of ARDS diagnosis. The intervention group received continuous

intravenous cisatracurium infusion at a dose of 37.5 mg/hour for 48 hours, with neuromuscular blockade monitored using peripheral nerve stimulation. The control group received standard care without neuromuscular blockade. Both groups were managed with lung-protective ventilation, targeting tidal volumes of 6 mL/kg predicted body weight and plateau pressures below 30 cm H_2O.

Sedation was administered using standardized protocols based on propofol and fentanyl infusions, titrated to achieve targeted sedation depth prior to paralysis and adjusted thereafter according to hemodynamic stability. Daily cumulative sedative doses were recorded. Oxygenation parameters, including PaO_2/FiO_2 ratio, plateau pressure, and static lung compliance, were measured at baseline and at 24 and 48 hours.

Sample size calculation was performed using Epi Info software, assuming a mean difference of 40 mmHg in PaO_2/FiO_2 ratio between groups, with a standard deviation of 80 mmHg, 95% confidence level, and 80% power. The minimum required sample size was calculated as 144 patients; a total of 156 patients were enrolled to account for early mortality and incomplete data.

Inclusion criteria included confirmed moderate-to-severe ARDS, invasive mechanical ventilation, and hemodynamic stability at enrollment. Exclusion criteria comprised pre-existing neuromuscular disease, chronic ventilator dependence, pregnancy, severe hepatic failure, and anticipated death within 24 hours. Statistical analysis included independent t-tests, repeated-measures analysis, and multivariate regression. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Cisatracurium Group (n = 78)	Control Group (n = 78)
Age (years)	54.9 ± 13.7	55.6 ± 14.2
Male (%)	46 (59.0)	48 (61.5)
APACHE II score	24.1 ± 4.8	23.7 ± 5.0
PaO_2/FiO_2 ratio	118.4 ± 26.9	121.1 ± 28.4

This table demonstrates comparable baseline characteristics and disease severity between study groups.

Table 2. Oxygenation and Ventilatory Parameters at 48 Hours

Parameter	Cisatracurium Group	Control Group	p-value
PaO_2/FiO_2 ratio	176.3 ± 34.1	142.7 ± 31.6	<0.001
Plateau pressure (cm H_2O)	25.2 ± 3.6	28.1 ± 4.2	0.002
Static compliance (mL/cm H_2O)	42.6 ± 8.4	35.8 ± 7.9	0.001

This table shows significant improvement in oxygenation and lung mechanics in the cisatracurium group.

Table 3. Sedation Requirements and Clinical Outcomes

Outcome	Cisatracurium Group	Control Group	p-value
Propofol dose (mg/day)	1,120 ± 310	1,460 ± 380	0.002
Fentanyl dose (µg/day)	820 ± 240	1,050 ± 290	0.004
Ventilator days	8.1 ± 3.4	10.6 ± 4.7	0.003
ICU stay (days)	11.2 ± 4.8	14.5 ± 6.1	0.005

This table highlights reduced sedative exposure and improved clinical efficiency in the neuromuscular blockade group.

Discussion: The findings of this prospective study demonstrate that continuous neuromuscular blockade with cisatracurium significantly improves oxygenation and reduces sedation requirements in patients with moderate-to-severe ARDS. The marked increase in PaO_2/FiO_2 ratio observed within 48 hours reflects improved ventilatory synchrony, reduced alveolar overdistension, and more consistent delivery of lung-protective ventilation.[13-14]

Improved oxygenation was accompanied by lower plateau pressures and enhanced static compliance, suggesting a reduction in injurious mechanical forces within the lung. Elimination of spontaneous respiratory effort likely minimized patient-generated transpulmonary pressure swings, thereby reducing ventilator-induced lung injury and facilitating alveolar recruitment.[15-16]

A key novel contribution of this study is the demonstration of significantly reduced sedative requirements in patients receiving continuous neuromuscular blockade. By suppressing agitation and dyssynchrony, cisatracurium allowed for lower doses of propofol and opioids while maintaining ventilatory control. This finding challenges the assumption that neuromuscular blockade necessitates higher sedation exposure and suggests a potential protective effect against sedation-related complications.[17-18]

Reduced ventilator days and shorter ICU stays observed in the cisatracurium group further support the clinical relevance of improved oxygenation and sedation optimization. Prolonged mechanical ventilation is associated with increased risk of infection, muscle weakness, and mortality; therefore, interventions that shorten ventilatory duration may have substantial downstream benefits.[19-20]

Concerns regarding ICU-acquired weakness remain a consideration with neuromuscular blockade; however, the limited duration of cisatracurium infusion and careful patient selection likely mitigated this risk. The use of an agent with organ-independent metabolism further enhanced safety in critically ill patients with multiorgan dysfunction.

The strengths of this study include its prospective design, standardized sedation and ventilation protocols, and integrated assessment of physiological and pharmacological outcomes. Limitations include the single-center setting and lack of long-term neuromuscular follow-up. Future multicenter studies incorporating functional outcomes and longer observation periods are warranted.

Overall, the results support a selective, time-limited application of continuous neuromuscular blockade in carefully chosen patients with severe ARDS. When combined with lung-protective ventilation, cisatracurium appears to offer both physiological and pharmacological advantages that may improve overall critical care outcomes.

Conclusion: Continuous neuromuscular blockade with cisatracurium significantly improves oxygenation while reducing sedation requirements in moderate-to-severe ARDS patients. This study provides novel evidence supporting the balanced use of neuromuscular blockade to optimize ventilation and minimize sedative exposure. The findings address an important clinical gap and inform targeted ARDS management strategies.

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