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Mini Review

Neuromuscular Blockade in Mechanical Ventilated Patient (ARDS)- What to Practice

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Abstract

Asynchrony during mechanical ventilation causes increased mortality and increased ICU length of stay. NMBA avoids asynchrony, might improve oxygenation, improve compliance, and faster weaning of PEEP in ARDS. But also, it has its own set of problems like poor secretion clearance, mucus plugging due to absent cough reflex will cause increased airway pressure and hypoxia, Neuro evaluation difficulty, drying up of cornea, drug interaction. We studied various trials like the Petal trial, Metanalysis in the *BMJ* 2020, Acurasys trial to understand how to use neuromuscular blockers in ARDS and what to be careful of while using them.

Keywords: *Acute Respiratory Distress Syndrome (ARDS); NMBA; PEEP*

Introduction

Acute respiratory distress syndrome (ARDS) is seen in cases of pneumonia, sepsis, aspiration of gastric contents, or severe trauma in intensive care units. Though there are some improvements in the management of ARDS, the mortality rate still seems to remain high at 30 - 40% in most studies. Treatment of ARDS includes judicious fluid management, protective lung ventilation with low tidal volumes and moderate positive end-expiratory pressure, multi-organ support and treating the underlying cause [1]. It has been suggested that the use of Neuromuscular blocking agents during the early course of moderate to severe ARDS in those patients with PaO_2/FIO_2 < 120 mmHg helps to improve oxygenation and reduce patient-ventilator dyssynchrony [2,3].

Why NMBA might help in ARDS?

Asynchrony (ineffective inspiratory effort during the exhalation cycle, double-triggering [breath-stacking], inappropriate cycling, and aborted inspiration, active exhalation causing loss of peep, increased tidal volume due to increased drives) causes increased mortality [4] and increased ICU length of stay. NMBA avoids asynchrony (and resulting biotrauma) and hence may be beneficial. We also know that this might improve oxygenation, improve compliance and faster weaning of PEEP in ARDS [5] and this effect persists beyond 5 days.

What might be a problem?

A study has shown that a decrease in asynchrony index was greater after adjusting ventilator settings than after increasing sedation/analgesia (P < .001) [6]. So then why should we resort to the use of NMBA? Disconnection of ventilator means immediate death if NMBA

is used. Poor secretion clearance and mucus plugging due to absent cough reflex will cause increased airway pressure and hypoxia. Neuro evaluation, drying up of cornea, drug interaction for e.g. with aminoglycosides, and increased duration of immobility are other factors causing a problem.

What is the latest evidence in the use of neuromuscular blockade in ARDS?

1. The petal trial published in the *NEJM* 2019 [7]- an unblinded RCT of 1006 patients from 45 U.S ICU units. Intervention group received - deep sedation with cisatracurium 15 mg stat followed by 37.5 mg/hr (early 48 hour infusion). The Control group received - light sedation (RASS 0 to -1) (however as needed cisatracurium doses could be given, so, 17% of the control group received as needed). Common to both was use of low tidal volume and high peep. Result: There was no significant difference in mortality at 90 days (42.5% (intervention) vs 42.8% (control) Between group difference -0.3% (95% CI-6.4 to 5.0) P value 0.93.

2. Metanalysis in the *BMJ* 2020 [8]- 4 Trials France, 2 trials from China and 1 trial from the U.S (approximately 1450 patients) metanalysis was done. Results: i) Use of NMBA did not reduce 90 day mortality ii) NMBAs may decrease mortality at days 21 - 28, APACHE II scores, and the occurrence of barotrauma and pneumothorax without increasing ICU acquired muscle weakness. iii) Could improve oxygenation after treatment.

What was the case earlier?

The Acurasys trial published in *NEJM* 2010 [9]- A Double-blinded RCT of 340 patients from 20 ICU in France. Intervention group received cisatracurium 15 mg stat followed by 37.5 mg/hr. The Control group received placebo. Common to both was the ARMA trial protocol [10] for ventilation (lower peep than the petal trial) and both arms were deeply sedated. Result: There was a significant improvement in mortality in patients with severe ARDS who were treated with early neuromuscular blocking agents. (Primary outcome: Adjusted 90 day mortality significantly lower in cisatracurium group, Adjusted Hazard ratio 0.68 (95% C.I. 0.48 - 0.98), p = 0.04) (9% Absolute risk reduction).

Why Acurasys and petal were diametrically opposite?

Most importantly almost 50% of patients in the Acurasys trial were proned and only 16% of the patients in rose were proned. Maybe that's the reason that Acurasys trial was a positive trial as both control arms had almost the same mortality. However, what is clear from the petal trial was that continuous neuromuscular blockade was not significantly better than as and when needed doses.

Conclusion

What to do?

For ARDS (with pao_2/fio_2 ratio less than 150) give 48 hours of neuromuscular blockade via continuous infusion if we are proning our patients. If proning is not a part of our care then intermittent paralysis with light sedation could also be enough as per the Petal investigators. Do not use it in status asthmaticus. When doing so, ensure lubricating the eye and eye closure. The "Hoffman" or non-renal or non-hepatic elimination makes atracurium an attractive option in the intensive care unit. Use of peripheral nerve stimulator along with clinical assessment forms good practice points during the use of NMBA.

What to be careful of during the use of NMBA?

Development of acquired weakness, myopathy, pressure ulcers, nerve injuries, and risk of deep venous thrombosis (DVT). In fact, the commonest association of DVT was with the use of NMBA in ICU. The relation between ICU acquired weakness (CIP, CIN, CINM) and NMBA is not very clear. The closest relationship is that of sepsis with CIP with NMBA. The more hypoxic, and the more asynchronous patient may require it more than the moderate hypoxic patient tolerating the ventilator better. Though the petal trial (or the Rose trial) actually failed to demonstrate a benefit there may be a subgroup of ARDS that may benefit. Time will tell!! (till then use it on a patient-to-patient basis).

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