The Role of Neuromuscular Blockade in Acute Respiratory Distress Syndrome

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Learning Objectives

- Identify the subset of Acute Respiratory Distress Syndrome (ARDS) patients who may benefit from neuromuscular blockade
- Discuss complications related to neuromuscular blockade

Neuromuscular blocking agents (NMBA)

- Non-depolarizing
  - Competitively antagonize acetylcholine receptors
  - Bind to the receptor and do not allow depolarization to occur
- Examples:
  - Vecuronium
  - Rocuronium
  - Cisatracurium

When to use?

SCCM / ASHP Clinical Practice Guidelines

NMBAs should be used to manage ventilation only when all other means have been tried without success

- Optimal sedation?
- Maximal sedation?
- Sedation that makes us comfortable?

Am J Health-Syst Pharm 2001;59:179-95.

Practical approach

- Pressure control with PIP > 50 cm water
  - I time > 1.5 sec
  - SaO_2 < 90% on > 50% FiO_2
- PaO_2 / FiO_2 < 150
- Ventilator dyssynchrony
  - PIP > 50 cm water
  - Spontaneous respiratory rate > 30

University of Cincinnati Hospital, 1998.

NMBAs in early ARDS

- Multicenter, double-blind trial
- Onset of ARDS within 48 hours
- Inclusion criteria:
  - PaO_2 / FiO_2 less than 150
  - PEEP of 5 cm water
  - Tidal volume 6-8 mL/kg
  - Bilateral infiltrates consistent with edema
- 339 patients randomized to 48 hours of:
  - Cisatracurium – set rate of 37.5 mg/hr
  - Placebo

Papazian L, et al. *NEJM* 2010;363:1107-16.

NMBAs in early ARDS

Outcome	Cisatracurium	Placebo	RR (95% CI)	p-value
28 day mortality	42/177 (23.7%)	54/162 (33.3%)	0.71 (0.51 - 1)	0.05
Vent-free days				
Day 1 – 28	10.6 ± 9.7	8.5 ± 9.4		0.04
Day 1 – 90	53.1 ± 35.8	44.6 ± 37.5		0.03
Days outside the ICU				
Day 1 – 28	6.9 ± 8.2	5.7 ± 7.8		0.16
Day 1 – 90	47.7 ± 33.5	39.5 ± 35.6		0.03
Barotrauma	9/177 (5.1%)	19/162 (11.7%)	0.43 (0.2 – 0.93)	0.03
Pneumothorax	7/177 (4%)	19/162 (11.7%)	0.34 (0.15 – 0.78)	0.01

Papazian L, et al. *NEJM* 2010;363:1107-16.

NMBAs in early ARDS

- NMBAs beneficial:
  - Higher probability of survival higher in the group with a PaO_2 / FiO_2 less than 120
  - Higher probability of breathing without assistance at 90 days

Papazian L, et al. *NEJM* 2010;363:1107-16.

NMBAs in early ARDS

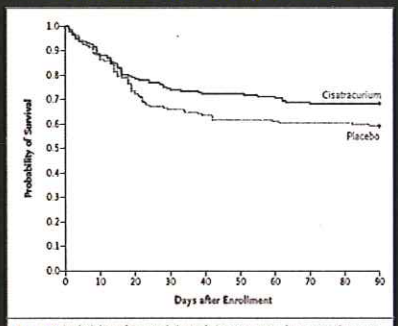

Figure 2. Probability of Survival through Day 90, According to Study Group.

From NEJM, Papazian L, et al. Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome 2010;363:1107-16.
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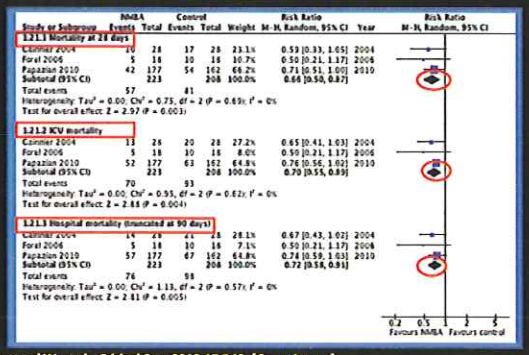
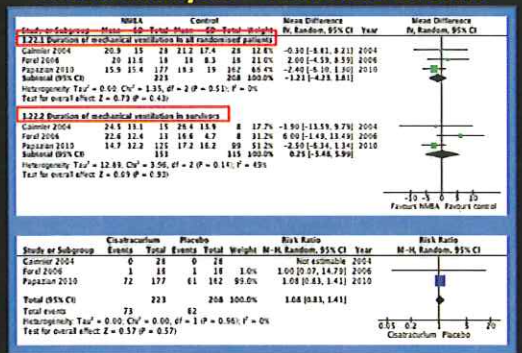
Meta-analysis - Survival



Alhazzani W, et al. *Critical Care* 2013;17:R43. [Open Access]

Meta-analysis – Adverse events



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NMBA Complications

- Prolonged recovery
- Nerve compression
- Venous thromboembolism
- Pressure ulcers
- Corneal ulcerations
- Cardiovascular
  - Tachycardia
  - Hypotension

Prolonged ICU weakness

- Pre-existing conditions
- Steroid myopathy
- Hyperglycemia
- Acute myopathy of critical illness
- Critical illness polyneuropathy
- Disuse atrophy

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NMBA related weakness

- Prolonged recovery from NMBAs
  - Drug / metabolite accumulation
- Acute Quadriplegic Myopathy Syndrome
  - Acute paresis
  - Myonecrosis
  - Abnormal electromyelogram
  - Reduced compound motor action potential

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Prevention of NMBA related weakness

- Intermittent administration
- Lower dosages
- Minimize exposure
  - Drug holidays
- Clinical monitoring
  - Train of four

Learning Assessment Question

Which of the following subsets of patients with ARDS may benefit from neuromuscular blockade?

a. Refractory hypoxemia
b. Ventilator dyssynchrony
c. Increased work of breathing
d. All of the above

Conclusion

- Utilization of neuromuscular blockade may be beneficial in ARDS patients
  - Early therapy (< 48 hours of onset)
  - $PaO_2 / FiO_2 < 120$
  - Ventilator dyssynchrony
- Factors to consider:
  - Adequate sedation and pain control
  - Optimize ventilator settings
  - Minimize total time and dosage of NMBAs
  - Clinical monitoring