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Intermittent and Continuous Infusion Administration of Non-Depolarizing Neuromuscular Blocking Agents (NMBAs)

Indications:

- ARDS with ventilator dysynchrony
- Sedated with RASS goal -5 achieved prior to initiation of paralysis

Non-Depolarizing NMBA Mechanism of Action:

- Competitively inhibits acetylcholine from binding to the receptors and prevents neural transmission at the myoneural junction without producing depolarization

Agent	Bolus Dosing*	Onset	Duration	Elimination	Adverse Effects / Clinical Considerations
Atracurium	0.4-0.5 mg/kg (round to nearest 50 mg)	3-5 minutes	20-35 minutes	5-10% renal, Hoffman elimination	• High doses may cause histamine release, resulting in hypotension, tachycardia • Toxic metabolite: laudanosine – no neuromuscular blocking properties, CNS stimulant that accumulates in renal insufficiency → may lead to CNS excitation/seizures • Effects and duration may be more variable in elderly patients
Cisatracurium	0.1-0.2 mg/kg (round to nearest 2 mg)	2-3 minutes	35-45 minutes	5-10% renal, Hoffman elimination	• Does not affect BP and HR • Relatively long duration of action
Rocuronium	0.6-1.0 mg/kg (round to nearest 50 mg)	1-3 minutes	30-60 minutes	33% renal ~75% hepatic	• **Accumulation may occur in patients with cirrhosis (more prominent) or renal impairment** • Vagal blockade at higher doses; weakly blocks muscarinic stimulation (bradycardia may occur) • Rapid onset and intermittent duration make it a viable option for intermittent paralysis
Vecuronium	0.1-0.2 mg/kg (round to nearest 10 mg)	3-4 minutes	35-45 minutes	50% renal 35-50% hepatic	• **Accumulation may occur in patients with liver impairment or anuric patients** • Minimal histamine release; vagal blockade at higher doses • Less cardiovascular effects than other NMBAs

Weight-based dosing is based on actual body weight for non-obese patients.* ***Obese patients should be dosed using an adjusted body weight.*

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Concomitant Therapies:

- Continuous infusion sedative recommended (RASS goal -5 prior to initiation)
    - Ensure all other active sedative medications have RASS goal modified to -5
- Artificial tears ointment Q1H PRN dry eyes
    - In order comments: Please apply to both eyes every time room is entered. KEEP TUBE AT BEDSIDE, MUST NOT RE-ENTER OMNICELL ONCE INSIDE PATIENT ROOM

Drug Interactions:

Decrease activity of NMBAs

- Calcium
- Carbamazepine
- Phenytoin
- Ranitidine

Prolong activity of NMBAs

- Antibiotics: aminoglycosides, vancomycin, clindamycin, tetracyclines
- Cardiac medications: beta blockers, calcium channel blockers, furosemide
- Steroids
- Cyclosporine

Monitoring:

- Before paralysis:
    - Baseline TOF (indicating site and voltage), RASS at -5
- During paralysis:
    - Ventilator synchrony, O2 saturations, PaO2:FiO2, ABG as needed, renal and hepatic dysfunction, vitals
- When discontinuing paralysis:
    - Monitor TOF and once achieved 3 to 4 twitches, can proceed to lighten sedation if necessary to assess neurologic function

References:

- Atracurium Besylate Injection [prescribing information]. Chicago, IL; Meitheal Pharmaceuticals Inc.: 2018.
- Nimbex (cisatracurium besylate) [prescribing information]. North Chicago, IL; AbbVie Inc; 2019.
- Rocuronium Bromide [prescribing information]. Deerfield, IL: Baxter Healthcare Corporation; March 2019.
- Vecuronium Bromide for Injection [prescribing information]. Rockford, IL: Mylan; 2018.
- Murray MJ, Deblock H, Erstad B, et al. Clinical Practice Guidelines for Sustained Neuromuscular Blockade in the Adult Critically Ill Patient. Crit Care Med. 2016;44(11):2079-2103.
- Greenberg SB, Vender J. The use of neuromuscular blocking agents in the ICU: where are we now?. Crit Care Med. 2013;41(5):1332-44.
- Ingrande J, Lemmens HJ. Dose adjustment of anaesthetics in the morbidly obese. Br J Anaesth. 2010;105 Suppl 1:i16-23

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ARDS requiring ventilator synchrony

STANDARD OF CARE

Cisatracurium 15 mg IVP followed by 7.5 mcg/kg/min infusion x 48 hours

- Repeat bolus of 20mg IVP x 1 if end-inspiratory plateau pressure remains ≥ 32 cm H20 for > 10 minutes despite deep sedation (RASS -5) and/or decreasing V_t and PEEP
- Max 2 additional boluses

If cisatracurium unavailable

Rocuronium 0.6 – 1 mg/kg (rounded to nearest 50 mg) IVP followed by 8 mcg/kg/min infusion titrated to ventilator synchrony (max 12 mcg/kg/min).

If cisatracurium and rocuronium unavailable

Vecuronium 0.08-0.1 mg/kg (rounded to nearest 10 mg) IVP followed by 0.8 mcg/kg/min infusion titrated to ventilator synchrony (max 1.5 mcg/kg/min).

If cisatracurium, rocuronium, and vecuronium unavailable

Atracurium 0.4-0.5 mg/kg (rounded to nearest 50mg) IVP followed by 10 mcg/kg/min infusion titrated to ventilator synchrony (max 20 mcg/kg/min)

- Initial dose may be reduced to 0.3-0.4 mg/kg in patients with significant cardiovascular disease or asthma

IF SIGNIFICANT SHORTAGES REQUIRE CONSERVATION EFFORTS, USE INTERMITTENT DOSING BELOW

Rocuronium 0.6 – 1 mg/kg (round to nearest 50 mg) IVP PRN

If rocuronium unavailable

Significant hepatic (known cirrhosis) or renal dysfunction (CrCl < 10 ml/min)?

NO

Vecuronium 0.08 – 0.1 mg/kg (round to nearest 10 mg) IVP PRN

If vecuronium unavailable

Cisatracurium 0.1 – 0.2 mg/kg (round to nearest 2 mg) IVP PRN

YES

Cisatracurium 0.1 – 0.2 mg/kg (round to nearest 2 mg) IVP PRN

If cisatracurium unavailable

Vecuronium 0.08 – 0.1 mg/kg (round to nearest 10 mg) IVP PRN

If vecuronium and cisatracurium unavailable

Atracurium 0.4 – 0.5 mg/kg (round to nearest 50 mg) IVP PRN

*PRN dosing will be based on duration of sustained ventilator synchrony following **each** dose. Doses should not be given more frequently than q1hr