NEUROMUSCULAR BLOCKING AGENTS - ICU

PURPOSE: To outline the management of patients receiving neuromuscular blocking agents.

SUPPORTIVE DATA: Neuromuscular blocking agents (NMBA) primarily block the access of acetylcholine to the endplate at the neuromuscular junction, thereby producing skeletal muscle paralysis.

NMBA are frequently used:

- for airway management (e.g. for intubation)
- to reduce impedance to mechanical ventilation,
- for suppression of patient movement during diagnostic procedures,
- for shivering secondary to therapeutic hypothermia
- to control intra-abdominal pressure.

The typical sequence of paralysis begins with the ocular muscles, then digits, abdominal muscles, intercostal muscles and the diaphragm. Upon discontinuation of NMBA, muscle function is regained in the reverse direction, beginning with the diaphragm. NMBA reversal agents include pyridostigmine, edrophonium, and neostigmine. Sugammadex for NMBA induced by rocuronium and vecuronium. Patients with renal failure may require dialysis to remove NMBA.

Contraindications for NMBA use include history of upper/lower motor neuron disease.

Succinylcholine has many contraindications and is not used as a continuous infusion:

- Myasthenia gravis
- Known pseudocholinersterase deficiency
- Hyperkalemia
- Acute major burns
- Major crush injuries
- Severe intra-abdominal infection
- Spinal cord injured patients, prolonged immobilization
- History of malignant hyperthermia

Dantrolene is given for Malignant Hyperthermia related to Succinylcholine administration.
These drugs paralyze skeletal muscles but do not alter consciousness or relieve pain or anxiety.
Paralytics must be administered in combination with adequate sedation/analgesia (ensure RASS -4 to -5 prior to initiating NMBA continuous infusion).

Patients receiving NMBA must be receiving artificial ventilation with appropriate vent settings (i.e. No CPAP).

ASSESSMENT:

1. Assess concentration, dose, and verify accurate pump settings within 1 hour of assuming responsibility for care of the patient.
2. Assess dose and verify accurate pump settings with every rate change.
3. Assess for ineffective respiratory paralysis every 1 hour:
   - Spontaneous respirations
   - Increased Peak Inspiratory Pressure on ventilator
   - Asynchrony with the ventilator

4. Assess the following a minimum of every 2 hours:
   - Vital signs
   - Level of consciousness
   - Pupillary changes (except NICU)

- Muscle movement
- Oxygen saturation
- Electrocardiogram (ECG) for dysrhythmias, ST changes
- Physiologic signs of pain and anxiety

5. Assess for signs/symptoms of malignant hyperthermia after succinylcholine administration:
   - Dramatic rise in temperature
   - Tachycardia
   - Tachypnea
   - Muscle rigidity
   - Increase in CO2

6. Assess the other indications of ineffective paralysis and sedation a minimum of every 2 hours:
   - Ineffective paralysis
     - Blinking
     - Tongue movement
     - Twitching
   - Ineffective sedation
     - Sweat above brow
     - Tachycardia, hypertension, change in vital signs with stimulation

7. Assess the following a minimum of every 2-4 hours as ordered:
   - Breath sounds
   - Skin integrity
   - Ocular moisture

8. Assess degree of paralysis with peripheral nerve stimulator (PNS)/Train of Four (TOF) (except Pediatrics/NICU):
   - Verify correct electrode placement is over ulnar or facial nerve
   - Assess twitch response using Train of Four (TOF) mode. 1-2 out of 4 contractions represents the preferred percentage of muscular blockade (75-90%
   - Assess TOF
     - Prior to initiation of NMBA (to obtain baseline)
     - A minimum of every 4 hours
     - 30 minutes after each dose titration
   - If TOF equals:
     - 0/4, decrease rate per provider's order
     - 1/4 or 2/4, continue same infusion rate
     - Greater than or equal to 3/4, and signs of inadequate paralysis, increase rate per provider's order.

9. Monitor the following daily or as drawn:
   - Creatinine and BUN
   - Electrolytes (K^+, Ca^+, Mg^{++})
   - Blood gases
   - Liver function tests (LFTs)

ANALGESIA/SEDATION:

10. Obtain initial order for analgesia and sedation
11. Initiate analgesia and sedation prior to administering NMBA
12. Use CPOT pain scale, titrate analgesia for CPOT less than 3
13. Sedate to proper RASS level -4 or -5 (Deep sedation to unarousable)
14. Consult with provider for dosage changes according to patient response.

ADMINISTRATION:

15. Administer NMBA, order to include:
    - Type of NMBA
    - Dosage (see table)
    - TOF titration parameters as applicable
    - Route

SAFETY:

16. High alert medication, verification with two licensed staff members
17. Ensure secure and patent airway.
18. Give Baseline of TOF for hand off report
19. Administer ocular lubricants as ordered.

NMBA DISCONTINUATION:

20. Discontinue NMBA as ordered. Turn off infusion. **DO NOT titrate.**
21. **Discontinue NMBA before discontinuing sedation/analgesia.**

REPORTABLE CONDITIONS:

22. Notify provider for:
    - Inadequate paralysis and/or sedation
    - Development of complications or signs of respiratory infection
    - Residual paresis/paralysis after cessation of NMBA
    - Signs/symptoms of malignant hyperthermia
    - Vital sign changes, decrease in O2 saturation

PATIENT/CAREGIVER EDUCATION:

23. Instruct on the following:
    - Purpose of NMBA therapy
    - Purpose of PNS/TOF
    - Need for sensory stimulation as patient can still hear, smell and feel

ADDITIONAL STANDARDS

24. Refer to the following as indicated:
    - Immobility
    - Mechanical Ventilation
    - Sedation and Analgesics (Intravenous) – ICU
    - Propofol
    - Ketamine

DOCUMENTATION:

25. Document in accordance with “documentation standards”
26. Document RASS and CPOT prior to infusion of paralytic
27. Document Assume Pain Present (APP) when on paralytic
28. Document TOF/PNS In Orchid ICU Systems- customize TOF/PNS – select nerve stimulated- indicate level/amps – document Baseline – document twitches

NMBA DOSES

	Adult	Pediatrics
Vecuronium bromide (Norcuron)		
Loading	0.1 mg/kg	0.08 – 0.1 mg/kg
Intermittent	0.04-0.06 mg/kg	0.1 mg/kg (children greater than 1 week old)
Continuous	Usual starting dose: 0.8 mcg/kg/minute Maximum dose: 1.2 mcg/kg/minute Adjust dosage in liver or renal disease	1-1.5 mcg/kg/minute (infant greater than 1 week – 1 Year old) 1.5-2.5 mcg/kg/minute (children greater than 1 year old) Adjust dosage in liver or renal disease
Cistracurium besylate (Nimbex)		
Loading	0.1 mg/kg	0.1 mg/kg for children 2-12 years old
Intermittent	1-2 mcg/kg	Children 2-12 years: 0.1mg/kg followed by maintenance dose of 0.03 mg/kg as needed to maintain neuromuscular blockade Children greater than 12 years 0.15-0.2 mg/kg followed by maintenance dose of 0.03 mg/kg 40-65 minutes later or as needed to maintain neuromuscular blockade
Continuous	Usual starting dose: 2.5 mcg/kg/minute Maximum dose: 10 mcg/kg/minute	1-4 mcg/kg/minute for children greater than or equal to 2 years old

Initial date approved:	Reviewed and approved by:	Revision Date:
02/94	Critical Care Committee Professional Practice Committee Pharmacy & Therapeutics Committee Nurse Executive Council Attending Staff Association Executive Committee	95, 97, 00, 03, 08/05, 12/05, 03/08, 12/11, 08/15, 03/22

REFERENCE

Consult: LAC+USC Pharmacy, 2021

Murray M. J., Cowen J., DeBlock H., et al. (2002). Clinical guidelines for sustained neuromuscular blockade in the adult critically ill patient. *Critical Care Medicine*, 30:142-156.

Tietze, K. J. (2010). Use of neuromuscular blocking medications in critically ill patients. Retrieved from UpToDate.com

AACN Procedure Manual for High Acuity, Progressive, and Critical Care. 7th Edition. Debra L. Wiegand. Elsevier. (2017)

Addendum:

Quick Reference for Neuromuscular Blocking Agents (NMBA) Continuous Infusions - ICU

Neuromuscular Blocking Agents (NMBA) – Continuous Infusions - ICU

Medication Names	• Cisatracurium (Nimbex) • Vecuronium (Norcuron)
Mechanism of Action	• Blocks neural transmission at the myoneural junction. • Causes skeletal muscle paralysis but does not alter consciousness or pain
Indication/Use	• To facilitate mechanical ventilation • For shivering from therapeutic hypothermia
Prior to administration	• Ensure patient is intubated on full ventilator support • Ensure adequate analgesia and sedation are ordered and achieved. Titrate to ordered Richmond Agitation Sedation Scale (RASS) and/or Critical-Care Pain Observation Tool (CPOT). Recommended: - CPOT < 3 - RASS -4 • Perform baseline peripheral nerve testing train of four (TOF) at ulnar site to determine the required milliamperes required to achieve 4/4 twitches. Document (e.g. 1/4 twitch at level 6) • Start NMBA ONLY after the above are accomplished
Usual Dosage range	Adults • Cisatracurium 0.5-10mcg/kg/min • Vecuronium 0.8-1.7mcg/kg/min Infants (1 week – 1 year): • Cisatracurium: 1-2 mcg/kg/minute • Vecuronium: 0.8-1.7 mcg/kg/minute Children > 1 year: • Cisatracurium: 1-4 mcg/kg/minute • Vecuronium: 0.8-2.5 mcg/kg/minute
Sedation/ Analgesia	• Required Sedation/ Analgesics should be maintained while on NMBA; do not titrate down • Do not use RASS or CPOT once NMBA is initiated • Document “Assume Pain Present” (APP) for pain assessment • Sedation/Analgesics may include Propofol, Midazolam, Ketamine, Fentanyl - Dexmedetomidine (Precedex) **alone should NOT be used with NMBA**

Nursing Physical Assessment/Monitoring	• Ineffective paralysis
	  - Spontaneous movement
	  - Ventilator asynchrony
	  - Increased PIP
	  - Shivering
	  - Attempting to blink
	  - Tongue twitching
	• TOF q 4 hours and 30 minutes after each rate change
	TOF goal is 1-2 twitches out of four (1-2/4) at the same level at which the Baseline was observed. Change dose **as ordered**
	  - 0/4 twitches: patient is too paralyzed – decrease NMBA dose
	  - 1-2/4 twitches: just right; maintain dose
	  - 3-4/4 twitches: inadequate paralysis – increase dose of NMBA
	Note: Generally, 1-2/4 twitches is optimal, however collaborate with provider regarding if other parameters should be used for optimizing dosage. For example, 4/4 twitches may be optimal for a patient not fighting the ventilator and whose oxygenation is improving.
	• Signs of ineffective sedation; assess for:
	  - Sweat above brow
	  - Tachycardia, hypertension, change in vital signs with stimulation

Maintenance	• Lubricate eyes with artificial tears as ordered • Tape eyes shut; do not use gauze • DVT prophylaxis as ordered • Ventilator associated pneumonia prevention • Turn patient every 2 hours, asses skin
Adverse Reactions	• Bradycardia • Hypotension • Myopathy
NBMA/ Sedation Holiday	• First turn off NMBA as ordered • Reassess TOF within 30 minutes; goal TOF 3-4/4 twitches; indicates paralytic has metabolized • RASS should be -4 DEEP sedation; RASS of higher number than -4 indicates patient is not adequately sedated • Perform sedation awakening trial as per policy
Discontinuation	• NMBA should be discontinued without weaning off • Discontinue NMBA FIRST, then titrate sedation/analgesia to goal • Previous pain/sedation assessment tool of CPOT or RASS can be used when NMBA is off