

Neuromuscular Blocking Agent Infusions

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Disclosure

- The speaker has no actual or potential conflicts of interest in relation to this presentation

Objectives

- Understand the NMBA and Comfort Measures ordersets
- Identify the appropriate selection of medication therapies regarding paralytic therapies

Paralytics

- Paralytic infusions
 - Atracurium, cisatracurium, vecuronium, rocuronium
- Benefits
 - Prevent vent dyssynchrony
 - Decrease work of breathing
 - Improve oxygenation
- Reserved for severe cases
 - Weigh benefit vs risks (deconditioning, myopathy, weakness)

Initiation

- Initial sedation is key
 - Do not recommend analgesia or sedation changes after the patient is paralyzed
- Utilize order sets
 - Critical Care Neuromuscular Blocking Agent (NMBA)

Goals

- Goal for starting NMBA
 - RASS -4 to -5 and CPOT < 2 prior to paralyzing
 - Obtain baseline and Q4H TOF
 - Continuous analgesia and sedative required

Critical Care Pain Observation Tool

Indicator	Description	Score	
Facial expression	No muscular tension observed	Relaxed, neutral	0
	Presence of frowning, brow lowering, orbit tightening, and levator contraction	Tense	1
	All of the above facial movements plus eyelid tightly closed	Grimacing	2
Body movements	Does not move at all (does not necessarily mean absence of pain)	Absence of movements	0
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection	1
	Pulling tube, attempting to sit up, moving limbs/ thrashing, not following commands, striking at staff, trying to climb out of bed	Restlessness	2
Muscle tension Evaluation by passive flexion and extension of upper extremities	No resistance to passive movements	Relaxed	0
	Resistance to passive movements	Tense, rigid	1
	Strong resistance to passive movements, inability to complete them	Very tense or rigid	2
Compliance with the ventilator (intubated patients)	Alarms not activated, easy ventilation	Tolerating ventilator or movement	0
	Alarms stop spontaneously	Coughing but tolerating	1
	Asynchrony: blocking ventilation, alarms frequently activated	Fighting ventilator	2
OR			
Vocalization (extubated patients)	Talking in normal tone or no sound	Talking in normal tone or no sound	0
	Sighing, moaning	Sighing, moaning	1
	Crying out, sobbing	Crying out, sobbing	2
Total, range			0-8

Richmond Agitation-Sedation Scale

- RASS
 - 10-point scale
 - 4 levels of anxiety or agitation (+1 to +4)
 - 1 level to denote a calm and alert state (0)
 - 5 levels of sedation (−1 to −5)

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitation	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
−1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
−2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
−3	Moderate sedation	Any movement (but no eye contact) to voice
−4	Deep sedation	No response to voice, but any movement to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

Score	Term	Description
+4		Overtly combative or violent; immediate danger to staff
+3		Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2		Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1		Anxious or apprehensive but movements not aggressive or vigorous
0		Spontaneously pays attention to caregiver
−1		Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
−2		Briefly (less than 10 seconds) awakens with eye contact to voice
−3		Any movement (but no eye contact) to voice
−4		No response to voice, but any movement to physical stimulation
−5		No response to voice or physical stimulation

Train of Four

- Baseline number of amps used for TOF
 - Necessary to determine patient's response to any additional TOF testing
 - If no baseline number of Amps then use lowest setting on TOF machine
- Located in flowsheets→ Complex Assessments→ Neurological

Vital Signs Anticoag Assess **Complex Assessment** Intake/Output IV Assessment Intra Procedure Sedat... VS Complex Specialty Infusion Meds Pat | Complex Assessment

Search (Alt+Comma)

Hide All Show All

CHARTING TYPE ☒

NEUROLOGICAL ☒

Neurological ☒

Glasgow Coma Scale ☒

Post tPA Assessment ☒

Sedation Scales ☒

Spontaneous Awak... ☒

Confusion Assessm... ☒

Reflexes ☒

Train of Four ☒

Accordian Expanded View All

1m 5m 10m 15m 30m 1h 2h 4h 8h 24h Based On: 0700 | Reset | Now

	1132	1400	1600	1606	Last Filed
Oculovestibular					
Train of Four					
Baseline Number of Amps (Train of Four)	5		5	5	
Twitches (Train of Four)	3		3	2	
Number of Amps (Train of Four)	5		5	5	
Location	Right facial nerve		Right facial nerve	Left facial nerv...	
Brief Neuro Check					
1-Level of consciousness				0	

Train of Four

Train-of-four (TOF) Nerve Stimulation						
<p><u>Target:</u> 1-2 twitches out of 4 or lowest effective dose</p> <ol style="list-style-type: none">1. Assess a baseline TOF prior to starting continuous infusion NMBA2. Check TOF 1 hour after infusion started and intervene as appropriate						
# of muscle twitches out of 4	% of receptor blockade	Intervention				
0 (over-paralyzed)	100%	<ol style="list-style-type: none">1. Stop infusion2. Recheck TOF every 15 minutes until 2 out of 4 twitches3. Once 2 out of 4, resume infusion at 50% of previous rate4. Repeat TOF in 1 hour				
1-2 (target TOF)	80-90%	<ol style="list-style-type: none">1. Continue at current rate2. Recheck TOF every 4 hours				
3-4 (under-paralyzed)	≤ 75%	<table><tr><td><u>Patient tolerating vent and achieving clinical goals:</u></td><td><u>Patient NOT tolerating ventilation:</u></td></tr><tr><td><ol style="list-style-type: none">1. Continue at current rate2. Recheck TOF in 4 hours</td><td><ol style="list-style-type: none">1. Increase infusion rate by 25%2. Recheck TOF in 1 hour</td></tr></table>	<u>Patient tolerating vent and achieving clinical goals:</u>	<u>Patient NOT tolerating ventilation:</u>	<ol style="list-style-type: none">1. Continue at current rate2. Recheck TOF in 4 hours	<ol style="list-style-type: none">1. Increase infusion rate by 25%2. Recheck TOF in 1 hour
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Order sets

- Critical Care Neuromuscular Blocking Agent (NMBA) Order set
 - Continuous infusion analgesia and sedation
 - Higher dosing range
 - Extra instructions to not titrate down analgesia and sedation while paralyzed

Practical Considerations

- Level 3 Analgesia
 - Fentanyl infusion
 - Hydromorphone infusion
- Level 3 Sedation
 - Midazolam infusion
 - Lorazepam infusion
 - Propofol infusion (high-dose)
- Consider drug shortages when selecting as changing analgesia/sedation after paralyzed is not recommended

Paralytics Reminders

- Mechanical ventilation is required
- NMBAAs do NOT have any analgesic or sedative effects
- Do NOT decrease sedation after the NMBA infusion has been started
 - Utilize extreme caution if changes are necessary

Medications

NMBA	Atracurium (Tracurium)	Cisatracurium (Nimbex)	Vecuronium (Norcuron)
Concentration	500 mg / 100 mL	200 mg / 100 mL	100 mg / 250 mL
Bolus Dosing	0.5 mg/kg over 30-60 seconds	0.1 mg/kg over 30-60 seconds	0.1 mg/kg over 30-60 seconds
Initial Infusion Rate	10 mcg/kg/min	3 mcg/kg/min	1 mcg/kg/min
OhioHealth Recommended Maximum Rate	17.5 mcg/kg/min	10 mcg/kg/min	1.5 mcg/kg/min
Alaris Pump Hard Max	30 mcg/kg/min	19 mcg/kg/min	2.6 mcg/kg/min
Time to maximal blockade (min)	3-5	2-3	3-4

NMBA	Atracurium (Tracurium)	Cisatracurium (Nimbex)	Vecuronium (Norcuron)
Duration (min)	25-35	45-60	35-45
Elimination	5-10% renal Hofmann Elimination	Hofmann Elimination	Hepatic via hydrolysis then ~50% bile excretion; metabolites excreted renally
Active metabolites	None	None	3-Desacetylvecuronium (half the activity of vecuronium)
Histamine release	Yes (dose-dependent)	No	No
Prolonged blockade	Rare	Rare	Yes

NMBA	Atracurium (Tracurium)	Cisatracurium (Nimbex)	Vecuronium (Norcuron)
Clinical Considerations	<p>Dose-dependent histamine mediated hypotension and worsening of bronchospasm</p> <p>Neurotoxic metabolite of Hoffman Elimination (laudanosine) may accumulate in patients with organ dysfunction and cause seizures</p>	<p>Consider avoiding in therapeutic hypothermia (prolongs Hofmann elimination)</p> <p>Lower dose compared to atracurium required therefore lower concern for laudanosine accumulation</p>	<p>Avoid in renal/hepatic impairment</p> <p>Concern for prolonged blockade</p>
Place in Therapy	Agent of choice in renal or hepatic dysfunction	Agent of choice in renal or hepatic dysfunction (when atracurium NOT available)	In light of drug shortages, consider first-line for patients WITHOUT renal or hepatic dysfunction

Moderate to severe ARDS requiring NMBA for ventilator synchrony
Ensure Critical Care NMBA Order Set is ordered (RASS -5 to -4 and eye care)



Trial vecuronium 10mg IV push prn
Desired effect?

Yes



Continue with 10mg IV push
every 30 min prn for ventilator
synchrony

No



Does the patient have evidence of
hepatic OR renal failure?

Yes



No



Start atracurium or cisatracurium
infusion. Re-evaluate necessity of
NMBA daily. Reassess daily for
resolution of hepatic and/or renal
failure. Upon resolution if NMBA still
required, consider vecuronium infusion.

Consider vecuronium infusion. Re-evaluate
necessity of NMBA daily. Reassess daily for
development of hepatic and/or renal failure.
**If patient develops hepatic or renal failure,
transition to atracurium or cisatracurium
infusion.**

NMBA Dosing Considerations

- Dosing based on IBW or adjusted body weight is recommended for obese patients
- Titrate to a train of four (TOF) of 1-2 out of 4
 - 80-90% of receptors blocked or lowest effective dose

Infusion Rate Considerations

Considerations During NMBA

- Maintain rates of analgesic and sedation infusions
 - May increase if physiologic signs indicating wakefulness
 - Unexplained tachycardia, hypertension, spontaneous movement despite
 - Do NOT decrease infusion rates once NMBA initiated
 - Only appropriate if NMBA stopped and confirmation of recovery by TOF

Sedation and Analgesia Transitions

- Recommended to not transition sedative/analgesic infusion unless clinical decline anticipated
 - Concern for PRIS, tachyphylaxis, hyperalgesia
- Consider boluses of new agents to help facilitate quicker transition
 - Consider pharmacokinetics of different medications
- Reach out to your resources

Complications of NMBAs

Complications of NMBAs	Management
Corneal abrasion and keratitis	Ocular lubricants
Venous thromboembolism	VTE prophylaxis
Decreased lymphatic flow	Raise head of the bed
Skin breakdown	Frequent turning
Slowed gastric motility	Promotility agents
Peripheral muscle & diaphragmatic atrophy	Range of motion
Pneumonia	Elevate head of bed, oral care, and suctioning

Withdrawal of NMBA

Compassionate Extubation Planning

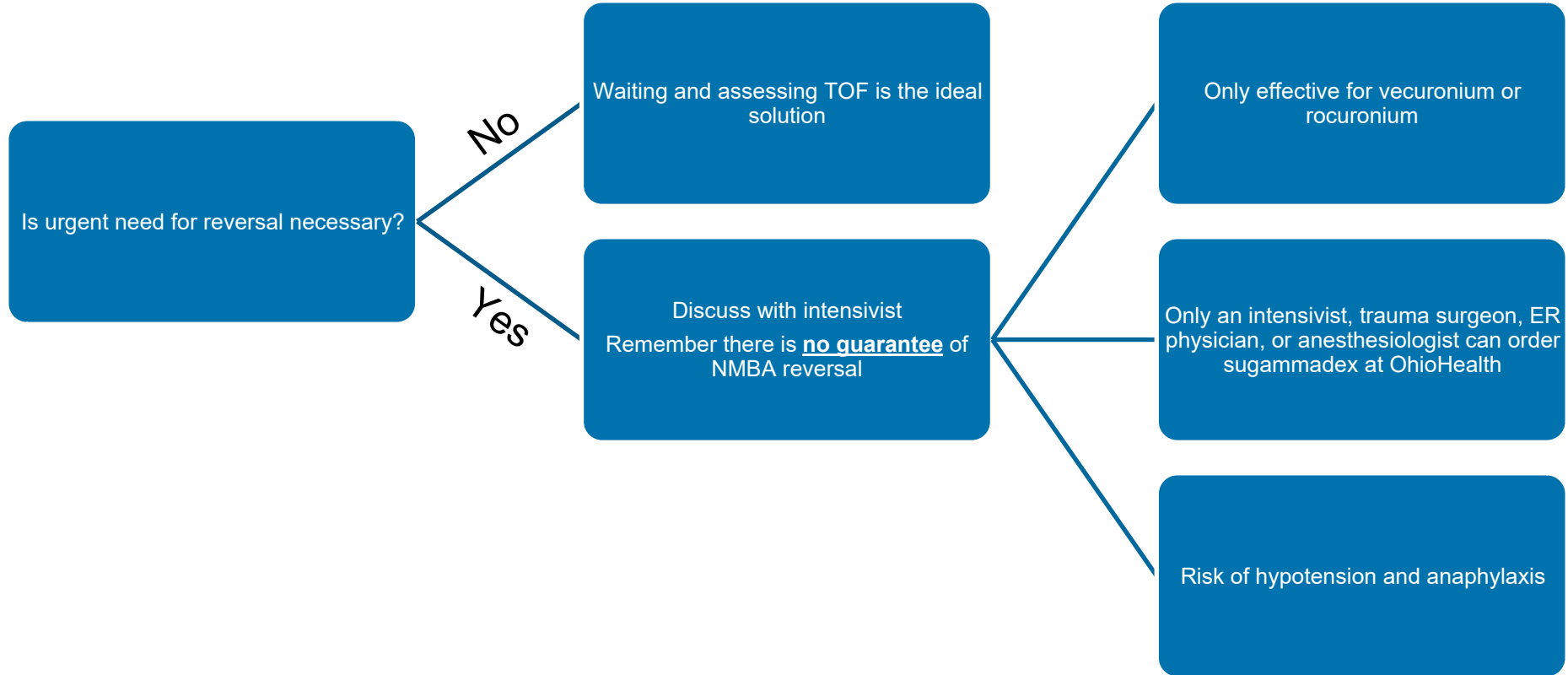
- Stop the paralytic drip and wait 3 half-lives to **reassess** TOF

Drug	Time to wait to reassess TOF prior to extubation if on INFUSION
Atracurium	60 min
Cisatracurium	60 min
Rocuronium	7 hours (or longer in renal/hepatic failure)
Vecuronium	210 min (or longer in renal/hepatic failure)

Compassionate Extubation Planning

- Assess TOF
 - TOF = 4/4
 - Proceed with withdrawal of mechanical ventilation
 - Ensure comfort medications have been initiated
 - TOF \neq 4/4
 - Wait another half-life and re-assess TOF
 - Patients can have residual effects of NMBA in liver or renal dysfunction

Reversal Agent - Sugammadex



Withdrawal Orderset

- Critical Care Redirection to Comfort Measures for Terminally Ill Patients
 - Operationalizes medications and nursing instructions
 - Medications
 - Based on renal function and current medications
 - Comfort and assessment orders
- Care should be individualized
 - Orderset is intended to guide practice

Sedation

- Typically stop sedation infusion 15 minutes prior to extubation
- Can be continued if necessary for patient comfort

Nursing Manage possible propofol drip prior to extubation

Routine, Once, First occurrence today at 1445

Specify: Manage possible propofol drip prior to extubation

IF patient is on a propofol drip at time of pre-medication for extubation (i.e. 15 minutes before extubation), discontinue the propofol drip at that time., Hold until Condition is met, Sign & Hold


Pre-medications

- Provider decision based on patient's perceived comfort level prior to extubation
- Based on CrCl and current medications

☐  CrCL LESS than 30, Dialysis patient, or allergic to morphine analogues

Select the current opioid infusion status:

- ☐ Patient currently has a fentaNYL infusion
- ☐ Patient currently has a NON-fentaNYL opioid infusion (morphine, HYDROmorphone, etc.)
- ☐ Patient currently does NOT have an opioid infusion (morphine, fentaNYL, HYDROmorphone, etc.)

☒  CrCl = 30 or GREATER

- ☐ Patient currently has a morphine infusion
- ☐ Patient currently has a NON-morphine opioid infusion (fentaNYL, HYDROmorphone, etc.)
- ☐ Patient currently does NOT have an opioid infusion (morphine, fentaNYL, HYDROmorphone, etc.)

Pre-medications – 15 minutes prior to extubation

- CrCl < 30 mL/min
 - Bolus fentanyl 100 mcg IV
- CrCl ≥ 30 mL/min
 - Bolus morphine 8 mg IV
- All patients
 - Stop continuous analgesia infusions
 - Lorazepam 1 mg IV
 - Glycopyrrolate 0.2 mg IV

Doses should be individualized base on patient requirements from prior day

Analgesia/Dyspnea Post-Extubation

▼ Analgesia/ Dyspnea Medications

- ☒ ⓘ Post-extubation analgesia (select one)

CareConnect cannot calculate a current CrCl.

(No SCr within last 72 hours, no height or weight documented, etc.)

Select the most appropriate choice:

- ☐ For CrCl LESS than 30, Dialysis patient, or allergic to morphine analogues: fentanyl (SUBLIMAZE) injection
50 mcg, Intravenous, Every 15 min PRN, pain/ dyspnea per nonverbal signs of pain: negative vocalization, furrowed brow, facial grimace., Hold until Condition is met, Contact provider for increased dose if patient requires 3 PRN doses of opioid within 1 hour.
- ☐ For CrCl = 30 or GREATER: morphine injection
4 mg, Intravenous, Every 15 min PRN, pain/ dyspnea per nonverbal signs of pain: negative vocalization, furrowed brow, facial grimace., Hold until Condition is met, Contact provider for increased dose if patient requires 3 PRN doses of opioid within 1 hour.

▼ Sedation Medications

- ☒ LORazepam (ATIVAN) injection 0.5 mg
0.5 mg, Intravenous, Every 15 min PRN, anxiety, agitation, Starting today at 1538, Hold until Condition is met
Contact provider for increased dose if patient requires 3 PRN doses benzodiazepine within 1 hour.
VESICANT
Sign and Hold

Take-Aways

- Determine appropriate analgesia and sedation
- **Always achieve goal RASS prior to NMBA**
- Facilitate prompt verification and/or delivery of analgesia/sedation +/- NMBA
- Utilize appropriate NMBA and withdrawal ordersets

