MUSCLE RELAXATION AND POSTOPERATIVE RESIDUAL

IS IT A CONCERN?

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DISCLOSURE

• Educational Speaker for Merck
LONG HISTORY OF MUSCLE RELAXANTS

- **1494** - Tales of travelers killed by darts (contained muscle relaxant product)
- **1800s** - Curare used by Indians as poison on arrow
- **1932** - Purified curare used to treat tetanus/spastic disorder
- **1940** – Curare used in ECT to prevent fractures
- **1951** - Succinylcholine first used in Stockholm
- **1954** - 6-fold increase in mortality in patients receiving curare
- **1940-1960** - Curare and Succinylcholine most commonly used NMBs
- **1960** - Pancuronium introduced as long-acting neuromuscular blocker (NMB)
- **1980s** – Atracurium and Vecuronium introduced
- **1990s** – Cisatracurium and Mivacurium introduced; mivacurium later taken off market
- **1994** - Rocuronium introduced
- **2006** – Mivacurium now available again in the U.S.
MOTOR ENDPLATE ANATOMY
Neuromuscular Transmission: The Neuromuscular Junction

Nerve

Muscle
HOW DO MUSCLES CONTRACT/DEPOLARIZE?

- Ach is released from the vesicles in the neuron and diffuses across the synaptic cleft.
- The synaptic cleft is small; thus, ACh reaches the muscle quickly.

With depolarization, ACh is released, moves across cleft and attaches to muscle.
Neuromuscular Transmission: Acetylcholine (Ach) Receptor
• Ach then interacts with nicotinic receptors on the motor end plate. (Receptors consist of 5 protein subunits)

• Only the alpha subunits bind to Ach.

• At the NMJ (post-junctional), these five subunits (α, α, β, γ, δ) are arranged to form an ion channel (has 2 alpha subunits)

• Both subunits must be occupied in order for the ion channel to open
Neuromuscular Transmission: Ach Receptor (continued)
• Normally **200 quanta** are released by each nerve impulse.

• After the endplate potential depolarizes/contracts, **Acetylcholinesterase** hydrolyzes the **Acetylcholine**, leading to muscle relaxation.

• Choline and acetate are then taken up into nerve terminal and recycled into new Acetylcholine

• The process starts again for the next contraction
<table>
<thead>
<tr>
<th>Depolarizing Muscle Relaxant</th>
<th>Non-Depolarizing Muscle Relaxants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aminosteroids</strong></td>
<td><strong>Benzylisoquinolines</strong></td>
</tr>
<tr>
<td>Succinylcholine/Anectine</td>
<td>Rocuronium/Zemuron</td>
</tr>
<tr>
<td></td>
<td>Cisatracurium/Nimbex</td>
</tr>
<tr>
<td></td>
<td>Vecuronium/Norcuron</td>
</tr>
<tr>
<td></td>
<td>Atracurium/Tracrium</td>
</tr>
<tr>
<td>Pancuronium/Pavulon</td>
<td>Mivacurium/Mivacron</td>
</tr>
</tbody>
</table>
DEPOLARIZING VS NON-DEPOLARIZING MUSCLE RELAXANTS

• Can be classified by mechanism used to block acetylcholine from binding to its receptor, which leads to muscle relaxation.

• **Depolarizing MR (Non-competitive agonists)**
  - Bind to Ach receptors, leading to an initial contraction called a fasciculation, followed by relaxation
  - Not hydrolyzed by acetylcholinesterase, therefore, they can bind to Ach receptors for a longer time.
  - Leads to persistent depolarization of the motor endplate

• **Non-Depolarizing MRs (Competitive antagonists)**
  - Compete with Ach for receptor binding, blocking the action of Ach (blocking contraction and leading to muscle relaxation).
IS IT NECESSARY TO MONITOR NEUROMUSCULAR BLOCKADE?

• Not monitoring neuromuscular blockade or not monitoring with a quantitative monitor increases incidence of postoperative residual

• **AANA:**
  • Since 1989, states that if administering a NMB, monitoring must be done (however, use of quantitative monitoring not specified)

• **ASA:**
  • Recognizes the importance but has not made a statement in regards to monitoring

MONITORING PARALYSIS

Injection of NMB agent

PTC stimulation

Twitch response

<table>
<thead>
<tr>
<th>Level of block</th>
<th>Onset</th>
<th>Intense block</th>
<th>Deep block</th>
<th>Moderate block</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to TOF</td>
<td>TOF count ≥1</td>
<td>TOF count 0</td>
<td>TOF count 0</td>
<td>TOF count 1-3</td>
<td>TOF ratio (T4/T1)</td>
</tr>
<tr>
<td>Response to PTC</td>
<td>PTC 0</td>
<td>PTC ≥1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

16 mg/kg  4 mg/kg  2 mg/kg
WHERE TO MONITOR

• **Adductor Pollicus Muscle (Ulnar nerve)**
  • Best and safer to monitor for recovery

• **Flexor Hallucis Brevis or Flexor Hallucis Longus Muscle (Posterior tibial nerve)**
  • Use if you cannot monitor the ulnar nerve (Ex: arms tucked)

• **Corrugator Supercilli Muscle (Facial nerve)**
  • Resembles diaphragm and laryngeal muscles; however, be cautious. You may have 4 twitches here but none at the wrist (most muscles still paralyzed)

  • Best to monitor for intubation
## Differential Resistance of Muscles to Neuromuscular Blockers

### Most Sensitive; Least Resistant

<table>
<thead>
<tr>
<th>Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngeal Muscles</td>
</tr>
<tr>
<td>Adductor Pollicis Muscle (wrist)</td>
</tr>
<tr>
<td><strong>(Monitor this for recovery)</strong></td>
</tr>
<tr>
<td>Corrugator Supercili Muscle</td>
</tr>
<tr>
<td><strong>(Monitor this to know when to intubate)</strong></td>
</tr>
<tr>
<td>Monitoring for recovery leads to increased incidence of postop residual compared to adductor pollicis m.</td>
</tr>
<tr>
<td>(These muscles return quickly like the diaphragm while the other muscles are still paralyzed)</td>
</tr>
<tr>
<td>Laryngeal Adductor Muscles</td>
</tr>
<tr>
<td>Diaphragm</td>
</tr>
</tbody>
</table>

### Least Sensitive; Most Resistant

<table>
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<th>Muscle</th>
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<td>Diaphragm</td>
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QUALITATIVE MONITORING

• Use of a peripheral nerve stimulator to determine TOF, twitch and/or fade
  • Subjective monitoring; tactile, visual testing
  • Even with 4/4 twitches, can still have up to 75% of receptors blocked
  • If 4/4 twitches and no post-tetanic fade, can still have a TOF ratio > 0.4 but < 0.9.

• With 4/4 twitches, one cannot detect the ratio if not using acceleromyography
• Not as accurate as a monitor that gives TOF + a TOF ratio
During a block with a NDMR, a tetanic stimulation (50 Hz or 100 Hz) will induce a transient increase in the amount of Ach released from the nerve ending; thus, a post-tetanic muscle contraction may occur.

This response to stimulation after tetanus can be used to gauge the depth of block when TOF shows no response.

The number of post-tetanic responses is inversely proportional to the depth of block: the fewer post-tetanic contractions are elicited, the deeper the depth of block.

In the illustration above, PTC = 4.

In the unblocked state, a 5-second, 50-Hz tetanic stimulation is generally 7-10 times that of a single stimulus and has no fade.

During a partial nondepolarizing neuromuscular block, a tetanic stimulation exhibits fade (decreases in strength over time).

The tetanic stimulation is followed by a 2- to 5-min period of post-tetanic facilitation (the response is increased).

If no post-tetanic fade noted, patient may still not be ready for extubation as TOF ratio may still be < 0.9.

Double burst stimulus normally done after patient has 4/4 twitches; done instead of checking tetany.

DBS: 2 brief, 50-Hz tetanic bursts 0.75 seconds apart. (Each burst consists of 3 stimuli that result in two sustained muscle contractions.)

D2 is checked for fade (less strong). The DBS ratio (D2/D1) approximates the TOF ratio.

When TOF ratio is not available, checking DBS is more sensitive than checking TOF & tetany.

However, once the TOF ratio exceeds 0.60, the fade cannot be seen/felt.

TOF ratio is a better way to determine residual.

Quantitative monitoring reduces likelihood of unrecognized significant residual muscle weakness in the postoperative period.

- Should improve patient safety

- APSF has concluded that residual NMB is a common, under-appreciated condition that contributes to adverse events in the postoperative period.

- Current literature still reports similar occurrence rates as those reported in 1979.
Moderate block: TOF of 3 twitches

TOF Ratio: Once 4 twitches are present, ratio can be calculated by comparing magnitude of 4th twitch to 1st twitch: 0.4 (40%).

The new STIMPOD NMS450 Nerve Stimulator and TOF Monitor (~ $1200.00)

- Gives a ratio of the amount of muscle reversal; more accurate than a TOF only; quantitative/objective

- The strength of each measured contraction is displayed graphically and the relevant ratios are calculated and also displayed

- The fine differences that can be detected by using accelerometry offer major advantages over determining contraction strength visually or tactiley.

- A research study by Murphy et al demonstrated that “unpleasant symptoms of muscle weakness are reduced and patient satisfaction is improved when quantitative acceleromyography monitoring is used in the OR.”

## HOW DEEP IS THE BLOCK?

<table>
<thead>
<tr>
<th>Depth of Block</th>
<th>Twitch Response</th>
<th>Normally, you should never have this deep a block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shallow</td>
<td>TOF count with 4 twitches with fade</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>TOF count with 1-3 twitches</td>
<td></td>
</tr>
<tr>
<td>Deep</td>
<td>No TOF count but with a post-tetanic contraction (PTC)</td>
<td></td>
</tr>
<tr>
<td>Extremely deep</td>
<td>No TOF count; No post-tetanic contraction</td>
<td></td>
</tr>
</tbody>
</table>
RISK OF USING A MUSCLE RELAXANT

• In a study published in the BMJ in 2012, the researchers reported that the use of an intermediate-acting, non-depolarizing NM blocker was associated with adverse postoperative respiratory outcomes:

  • Desaturation after extubation to an oxygen saturation 90% or less

  • Postoperative re-intubation requiring unplanned admission to an ICU and mechanical ventilation

• Qualitative monitoring (TOF followed by post-tetanic fade) did not significantly modify the risk, and reversal with neostigmine even increased the risk of severe postoperative respiratory failure.

WHY REVERSE NEUROMUSCULAR BLOCKADE?

• Postoperative residual occurs in 40%-80% of patients

• Large clinical trial in > 500 patients reported:
  • 45% of patients who received a single dose of intermediate acting NMB (without reversal) had a TOFR < 0.9 in PACU
  • Two hours after intermediate acting NMB given, TOFR was < 0.7 in 10% of pts and < 0.9 in 37% of patients.
  • Cautious titration of reversal using quantitative NM monitoring may decrease postop residual in PACU

APSF Newsletter Feb 2016
HOW DO REVERSALS WORK?

- **Reversing a depolarizing MR**
  - No reversal agent for a depolarizing agent (Succinylcholine); it wears off with time; very short-acting most of the time
  
  - *Succinylcholine is metabolized by* plasma cholinesterase *(pseudocholinesterase)* *which is slower than the acetylcholinesterase which metabolizes Ach at the NM junction.*

  - Since plasma cholinesterase is not found in the NMJ, *Sux’s action is terminated after it diffuses into the extracellular fluid* (not when it is metabolized).

  - Takes about 11 minutes
HOW DO REVERSALS WORK?

- **Reversing a non-depolarizing MR**

  - Reverse with cholinesterase inhibitor or sugammadex
  
  - Originally, guidelines stated to have at least one twitch returned before giving reversal.
  
  - If not, reversal may wear off and MR will still be on board, leading to the patient struggling to breathe
  
  - Postoperative residual is a real concern.
  
  - New guidelines suggest having **3-4 twitches** back before giving an anticholinesterase inhibitor for reversal.
  
  - Failure to give a reversal agent is the greatest risk for re-intubation in the next 48 hours postoperatively
ACETYLCHOLINESTERASE INHIBITORS-REVERSALS

- Inhibit hydrolysis of acetylcholine by competing with ACh for attachment to acetylcholinesterase at the site

- Buildup of ACh facilitates the transmission of impulses across the NM junction; this then kicks off the NDMR (rocuronium, etc)

- **Muscarinic cholinergic side effects:** SB, bronchospasm, salivation, intestinal spasm, incontinence, N & V
  - Give anticholinergics with reversals to prevent life-threatening SB

- Have a ceiling effect—more of the drug will have no effect and can induce muscle weakness and pharyngeal muscle relaxation

- Overdose of reversal agents may induce a cholinergic crisis characterized by SB, low B/P, bronchospasm, hypersecretions, GI hypermotility, nausea (controversial), weakness/paralysis, POPE.

- Unable to reverse deep levels of NMB (Ex: TOF of 0); should have 3-4 twitches before given
<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Dose (mg/kg)</th>
<th>Onset of Action (min)</th>
<th>Duration of Action (min)</th>
<th>Ach Bond</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Edrophonium</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fastest onset; give with atropine</td>
<td>0.5 to 1.0</td>
<td>1-6</td>
<td>30-60</td>
<td>Electrostatic</td>
<td>Pre-synaptic</td>
</tr>
<tr>
<td><strong>Neostigmine</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>“Fast onset”; give with glycopyrrolate</td>
<td>0.025 to 0.075</td>
<td>5-20</td>
<td>45-90</td>
<td>Covalent</td>
<td>Post-synaptic</td>
</tr>
<tr>
<td><strong>Pyridostigmine</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Slowest onset</td>
<td>0.1 to 0.3</td>
<td>10-20</td>
<td>60-120</td>
<td>Covalent</td>
<td>Post-synaptic</td>
</tr>
</tbody>
</table>
CONCERNS WITH ACETYLCHOLINESTERASE INHIBITORS (REVERSAL AGENTS)

• If neostigmine is “routinely” given when it is not needed, it can impair upper airway and diaphragmatic function by inducing a NMB (caused by accumulation of Ach at the motor endplate).

• If an inadequate dose of neostigmine is given or it’s given too early, its duration of action may be shorter than the elimination half life of rocuronium or vecuronium on board.
  
  • (This can happen if neostigmine is given before 3-4 twitches are returned).
POSTOPERATIVE RESIDUAL

• Defined originally as a recovery of the TOF ratio less than 0.7
  • Healthy volunteers described “uncomfortable symptoms” (visual disturbances, facial weakness, difficulty speaking/swallowing and generalized fatigue) with a TOF ratio 0.70-0.75

• Postop residual now defined as TOF Ratio < 0.9

• Remains a common but usually undetected occurrence in early postop period
  • Originally reported in 1979 (Viby-Mogensen-anesthesiologist) as having a 42% incidence in PACU
  • Recent studies report similar results (40-80% of patients)

• Not monitoring neuromuscular blockade or not monitoring with a quantitative monitor increases incidence
POSTOPERATIVE RESIDUAL

• Clinicians often mistakenly perceive how slowly/quickly a muscle relaxant spontaneously recovers

• Incidence of residual NM block (with or without reversal agent) leads to increased morbidity in the postoperative period
  • Inability to breathe: 38%
  • Hypoxemia: 38%
  • Muscle weakness: 16%
  • Airway obstruction: 10%
  • Respiratory failure: 8%

• Patients who had a TOF ratio < 0.9 experienced: swallowing difficulty, diplopia, unsteady feeling when sitting up (Fortier et al: A&A 2015; 121(2): 366-372).

• Volunteers who did not receive any opioids, benzodiazepines, induction agents or volatile agents and had a TOF < 0.9 experienced visual disturbances, difficulty speaking and swallowing, hypoxemia, generalized weakness, increased risk of aspiration, airway obstruction, atelectasis, reduced forced vital capacity, peak expiratory flow and inspiratory flow. (Murphy et al: Anesthesiology 2011; 115(5): 946-952).

• Postoperative residual can also lead to delayed discharge from PACU/hospital

• Patients who received paralysis and were not reversed were twice as likely to develop pneumonia (Bulka et al 2016)
ARE CLINICAL SIGNS AN EFFECTIVE WAY TO ASSESS REVERSAL? ARE THEY RELIABLE?

• No! Head lift, tidal volume, squeezing hand, clenching teeth on a tongue depressor are not good indicators of reversal—unpredictable and unreliable

• **TOF Ratio of 0.2**: Pt can smile

• **TOF Ratio of 0.5**: Pt can lift head off pillow

• **TOF Ratio of 0.6**: TOF monitor: 4/4 twitches and no post-tetanic fade

• **TOF Ratio of 0.7**: Pt can open eyes and squeeze hands but may have profound symptoms of muscle weakness, atelectasis—leading to pneumonia, visual disturbances, facial weakness, difficulty speaking/drinking
ARE CLINICAL SIGNS AN EFFECTIVE WAY TO ASSESS REVERSAL? ARE THEY RELIABLE?

• **TOF Ratio of 0.8:** Pt can have impaired pharyngeal function and swallowing, increased risk of aspiration

• **TOF Ratio < 0.9:** Pt may be able to bite down on tongue depressor but may have increased risk of postop hypoxemia, aspiration, obstruction on way to PACU, increased critical respiratory events, muscle weakness, delay in discharge

• **TOF Ratio > 0.9:** Pt is now ready for extubation; no residual is likely to be experienced
AT THE END OF SURGERY

• Some anesthesia providers give a muscle relaxant but do not monitor MR.

• At the end of the case, if they give a reversal, it is often a fixed dose of reversal with neostigmine and glycopyrrolate.

• Relaxation may be checked with a qualitative monitor; 4/4 twitches and also sustained tetany may be seen; not the best way to check for residual.

• When patient responds sluggishly, the anesthesia itself is blamed rather than postoperative residual.

• Many anesthesia providers are unfamiliar with TOF ratio.

• **New recommendations**: TOF ratio of 0.9 or > before extubating
Even a single intubating dose of an intermediate-acting muscle relaxant can last longer than 4 hours.

Clearly, the mere passage of time does not guarantee that the effect of a muscle relaxant has dissipated.
STRATEGIES TO PREVENT NM RESIDUAL

• Dosing of reversal should be individualized based on surgical necessity, patient factors and presence of co-existing diseases.

• Deep neuromuscular blockade should be avoided.

• Consideration should be given to succinylcholine or mivacron since they do not need to be reversed.

• Clinical tests (head lift, TV, grip strength) are unreliable predictors of recovery of NM function.

• Use of a quantitative monitor (acceleromyography) should be used so TOF ratio can be monitored.

• Monitoring the ulnar nerve/adductor pollicis muscle is important since it is the weakest link in the chain; if 4 strong twitches, this may indicate extubation readiness; however, TOF ratio > 0.9 is the only method to determine appropriate timing of extubation.

• Reversal should be routinely given & only when spontaneous muscle activity is present (3-4 twitches if neostigmine used). Even with a TOF count of 4/4 and no perceived fade, a low dose should be considered unless monitoring TOF ratio is done and TOF ratio is > 0.9.
STRATEGIES TO PREVENT NM RESIDUAL

- Having 3-4 twitches back before giving an anticholinesterase (neostigmine) is important.
  - Does not apply to sugammadex; consider using this if block is deep.
- Allowing sufficient time for reversal to work is necessary before extubating the patient.
- Neostigmine contributes to pharyngeal muscle weakness if given in the absence of neuromuscular blockade or if the reversal dose is too high.
- The use of tactile evaluation of TOF and DBS fade reduces, but does not eliminate, the incidence and degree of postoperative residual compared to the use of clinical signs to assess readiness.
- However, monitoring the TOF ratio reduces the incidence of postoperative residual even greater.
- Clinical signs are unpredictable and unreliable.
- A TOF ratio of 0.9 or > should be achieved prior to tracheal extubation.
THE LONG-AWAITED SUGAMMADEX!

- Reversal agent that does not involve Ach, nicotinic receptors or acetylcholinesterase
- Indicated for reversal of ANY DEPTH of NMB induced by rocuronium or vecuronium in adult patients
- Selectively binds to rocuronium or vecuronium to form a tight complex bond
- Reduction in the plasma results in a shift of the drug away from the NMJ and into the plasma where it is further bound and inactivated by sugammadex
- Excreted by kidneys; elimination ½ life: 2 hours
  - Do not use in patients on hemodialysis
  - Ok to use in patients with mild or moderate kidney impairment
  - Dosing is the same in patients with cardiac or pulmonary disease or in the elderly.
DOSAGE FOR REVERSAL

• PTC: 4 mg/kg to reverse rocuronium or vecuronium

• 2 twitches: 2 mg/kg to reverse rocuronium or vecuronium

• Emergency-deep block: 16 mg/kg to reverse rocuronium (cannot use to reverse vecuronium - deep block)
# Recommendations for Reversing Muscle Relaxants


<table>
<thead>
<tr>
<th>Depth of Block</th>
<th>Neostigmine Dose (mg/kg)</th>
<th>Sugammadex Dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTC of 0</td>
<td>Delay reversal</td>
<td>&gt; 4 mg/kg and up to 16 mg/kg</td>
</tr>
<tr>
<td>PTC of 1 or &gt;</td>
<td>Delay reversal</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>TOF count 2</td>
<td>Delay reversal</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>TOF count 3-4</td>
<td>0.05-0.07</td>
<td></td>
</tr>
<tr>
<td>TOF 4/4 and no tactile or visual</td>
<td>0.02-0.03</td>
<td>0.25-0.5 mg/kg</td>
</tr>
<tr>
<td>fade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOF ratio &gt; 0.9</td>
<td>No reversal necessary</td>
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</tr>
</tbody>
</table>
MONITORING TOF AND REVERSING

**Table:**

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<th>Level of block</th>
<th>Onset</th>
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**Injection of NMB agent**

**PTC stimulation**

**Twitch response**

16 mg/kg  4 mg/kg  2 mg/kg
• Patients who received Bridion recovered from rocuronium-induced moderate block quicker.
• Majority recovered to a TOF ratio of 0.9 within 5 minutes of administration (median 2.1” vs 29”)
• Generally, a TOF ratio of > 0.9 correlates with recovery from NMB

Recovery from a deep rocuronium-induced NMB is significantly faster with sugammadex 4 mg/kg vs neostigmine (2.7 minutes vs 29 minutes)

Sugammadex 16 mg/kg after rocuronium 1.2 mg/kg: 4.2 minutes (Sux: 7.1 minutes)

In study, researchers waited 3" before giving sugammadex for the emergent reversal, thus reversed in 1.2".
ADVANTAGES AND DISADVANTAGES OF SUGAMMADEX

- Reverses deep NMB along with mild and moderate blockade rapidly

- Emergent reversal of rocuronium for “Can’t ventilate, can’t intubate” (4.2”)

- Minimal adverse drug reactions (next slide)

- Rare allergic reaction, SB and questionable transient alteration in PT time (?lab error)

- Does not require use of anticholinergic agent to offset SB

- Only reverses aminosteroids; does not reverse benzylisoquinolines
DRUG INTERACTIONS WITH SUGAMMADEX

• **Hormonal contraceptives**
  • Sugammadex binds and decreases the serum concentration of contraceptives (estrogen and progestin); similar to “skipping a dose”
  • Must use non-hormonal method of contraception for 7 days following sugammadex (condoms, spermicides, diaphragms, sponges, cervical caps)

• **Toremifene**
  • Selective estrogen receptor modulator given for metastatic breast cancer or prostate cancer or soft tissue sarcoma
  • Interaction: Displacement of NMB from sugammadex

• **Physically incompatible with verapamil, ondansetron and ranitidine**
  • Flush IV line after giving these medications and before giving sugammadex
**REPEAT PARALYSIS AFTER SUGAMMADEX**

- Wait minimum amount of time before giving rocuronium again after reversing with bridion up to 4 mg/kg
  - 5” if **1.2 mg/kg rocuronium** is to be re-administered
  - 4 hours if **0.6 mg/kg rocuronium or 0.1 mg vecuronium** is to be re-administered
    - 24 hours if renal insufficiency; if you cannot wait 24 hours, then give 1.2 mg/kg rocuronium
  - 24 hours to re-paralyze if 16 mg/kg given for reversal

- When rocuronium 1.2 mg/kg given within 30” after bridion given, onset may be delayed by 4” and duration may be shortened by up to 15”

- If paralysis is needed within 24 hours after giving sugammadex, a benzylisoquinoline agent (non-steroidal NMB agent) such as **cisatracurium or atracurium**, can also be given
SUGGESTED USES FOR SUGAMMADEX

• Reversal of rocuronium or vecuronium, including deep block (TOF 0; PTC 1 or >)
  • Safer and quicker than waiting for 3-4 twitches
  • If dosed appropriately, full reversal will occur (TOF Ration > 0.90)

• Reversal in those at risk for obstruction or aspiration: elderly, morbidly obese, OSA pts

• Emergent reversal of rocuronium (16 mg/kg)

• Ventilation failure in the PACU after reversal with neostigmine or after no reversal
  • TOF ratio < 0.9 and symptomatic

• Wake-up test during spinal surgery

• Reversal in patients with NM diseases (Ex: myasthenia gravis, muscular dystrophy)
SUMMARY

• If a muscle relaxant is given, monitoring with a PNS should be done. Ideally, a quantitative monitor should be utilized to determine TOF ratio.

• If a muscle relaxant is given, it should normally be reversed.

• A TOF ratio of 0.9 or > should be achieved before extubating the patient.

• Dependence on clinical signs is associated with a high incidence of postoperative residual neuromuscular blockade.

• Sugammadex can be used to reverse all types of NM blockade, including deep blocks, without the side effects of neostigmine.
Thank you!
REFERENCES


REFERENCES


• Murphy, GS & Brull SJ: Residual NMB: Lessons unlearned. Part II: Methods to reduce the risk of residual weakness. A & A 2010; 111(1): 129-139.

• Van Pelt, M, Chitilian, HV & Eikerman, M: Multi-faceted initiative designed to improve safety of neuromuscular blockade. APSF Newsletter February 2016; 51-52.
HOW EXPENSIVE IS IT?
PRICE AT MY HOSPITAL

• Bridion 2 ml (200 mg): $89.06

• Bridion 5 ml (500 mg): $163.17

• Neostigmine 3 ml: $32.76; 10 ml: $68.00 (some institutions: $90.00)

• Glycopyrrolate 3 ml: $30.81; 5 ml: ~ $55.00

• Neostigmine 3 ml + Glycopyrrolate 3 ml: $63.57

• Neostigmine 3 ml X2 + Glycopyrrolate 3 ml X2: $127.14
<table>
<thead>
<tr>
<th>Qualitative Monitoring</th>
<th>Quantitative Monitoring</th>
<th>Type of Block</th>
<th>Reversal with Neostigmine</th>
<th>Reversal with Bridion</th>
</tr>
</thead>
<tbody>
<tr>
<td>No twitch; PTC of 0/8</td>
<td></td>
<td></td>
<td>WAIT</td>
<td>WAIT</td>
</tr>
<tr>
<td>No twitch; PTC of 2/8</td>
<td></td>
<td></td>
<td>WAIT</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>No twitch; PTC of 4/8</td>
<td></td>
<td></td>
<td>WAIT</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>No twitch; PTC of 6/8</td>
<td></td>
<td></td>
<td>WAIT</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>No twitch; PTC of 8/8</td>
<td></td>
<td></td>
<td>WAIT</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>TOF 1 / 4</td>
<td></td>
<td>Profound Block</td>
<td>WAIT</td>
<td></td>
</tr>
<tr>
<td>TOF2 / 4</td>
<td></td>
<td></td>
<td>WAIT</td>
<td>4 mg/kg</td>
</tr>
<tr>
<td>TOF 3 / 4</td>
<td></td>
<td>Shallow Block</td>
<td>0.05 - 0.07 mg/kg + glycopyrrolate</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>TOF 4/4 with fade</td>
<td>Can now obtain a TOF Ratio (&lt; 0.4)</td>
<td>Shallow Block</td>
<td>0.04-0.05 mg/kg + glycopyrrolate</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>TOF 4/4 without fade</td>
<td>TOF Ratio &gt; 0.4 but &lt; 0.9</td>
<td>Shallow Block</td>
<td>0.02-0.03 mg/kg + glycopyrrolate</td>
<td>1-2 mg/kg</td>
</tr>
<tr>
<td>TOF 4/4 without fade</td>
<td>TOF Ratio &gt; 0.9</td>
<td>No Block</td>
<td>NONE?</td>
<td>NONE?</td>
</tr>
</tbody>
</table>
MONITORING THE ULNAR NERVE
MONITORING THE POSTERIOR TIBIAL NERVE
Recovery of supercilli muscle of the eye (eyebrow wrinkles) is comparable to recovery of the diaphragm.

- Temporal branch of facial nerve

Recovery of orbicularis occuli muscle of the eye (eyelid closure) is comparable to recovery of the adductor pollicis muscle.

- Zygomatic branch of facial nerve
A study by DeBaene et al showed that 45% of patients had residual NMB in PACU after a single intubating dose of an intermediate-acting NDMR.

Two hours after administration of the NDMR, 37% of patients displayed TOFR < 0.9 with no reversal given.

Intermediate acting NDMRs have a duration of action of 30-90 minutes

Textbook-cited duration times do not guarantee full return of NM function, and clinically significant residual NMB can occur after the proposed duration.

NEOSTIGMINE VS SUGAMMADEX

• Meta-analysis comparing neostigmine to sugammadex; 13 articles and 1384 patients included

• Sugammadex was:
  • Faster in reversing NMB
  • More likely to be associated with higher TOF ratio values at extubation
  • Lower risk of postoperative residual after extubation
  • Significantly lower risk of adverse events: respiratory, cardiovascular and postoperative weakness

• Both assoc. with similar likelihood of PONV, pain, & neurologic adverse events

• Results from the meta-analysis suggest that sugammadex is superior to neostigmine since it reverses NMB faster and more reliably with a lower risk of adverse events.