New Perspectives on Neuromuscular Blockade and Reversal--A Relaxed Update

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While this presentation was developed independently of influences or financial incentives from Merck, I do disclose that I have consulted for Merck Sharp & Dohme and received any monies or benefits to present this information to you today. If you have any questions about my involvement with Merck please do not hesitate to contact me at sarah.giron@med.usc.edu.

My Disclosure To You:
Presentation Objectives

Review and discuss the physiologic and pharmacological roles of neuromuscular blockade in the care of the surgical patient.

Establish the implications of neuromuscular blockade in current CRNA practice.

Compare alternative, new neuromuscular blockade modalities.

Review current neuromuscular blocking agents and current reversal options for surgical patients.

Present neuromuscular blockade monitoring styles and compare their use in current CRNA practice.

Discuss the implications of neuromuscular blockade in the care of the surgical patient.

And finally, discuss the physiologic and pharmacologic roles of neuromuscular blockade.
The Neuromuscular Junction (NMJ) is the synapse between a motor nerve terminal and muscle fibers. As a motor nerve potential reaches the terminal, calcium channels open and cause acetylcholine (Ach) to be released. This leads to the opening of acetylcholine receptors on the motor end plate of muscle fibers, resulting in muscle contraction.

Motor nerve terminal

Muscle fibers

Muscle end plate

Motor end plate

Synaptic vesicles

Calcium channels

Acetylcholine receptors

Motor end plate

The Neuromuscular Junction

Physiologic Review

Neuromuscular Blockade

A Quick Anatomic and
Once Ach combines with both alpha subunits of the nicotinic receptor, the channel is opened causing $K^+$ to diffuse out and $Na^+$ and $Ca^{2+}$ to diffuse in. This diffusion initiates a depolarization which, if it reaches the threshold potential, initiates an action potential that causes muscle contraction.
It All Started with Curare
A Relaxing History...

- 1884: First published study on Curare
- 1941: Curare first used in surgical patients
- 1949: Gallamine & Metocurine developed
- 1951: Succinylcholine developed
- 1958: First nerve stimulator introduced
- 1964-68: The first steroidal NMBAs introduced: Alcuronium and Pancuronium
- 1971: Vecuronium & Atracurium introduced
- 1981: Rocuronium & Cisatracurium developed
- 1991: Mivacurium introduced
- 1994: Rocuronium & Cisatracurium developed
- 2000: Rapacuronium introduced

Depolarizing vs. Non-Depolarizing Muscle Relaxants

Depolarizing Muscle Relaxants:

Succinylcholine (Sux)

Sux is the only depolarizing muscle relaxant in clinical use. It has a rapid onset (30-60 sec) and short duration (3-5 min).

Unlike Non-Depolarizers, Sux's action in muscle relaxation occurs because it mimics the action of Ach. Neuromuscular blockade develops because the depolarized membrane cannot respond to Ach normally. This can be caused by receptor desensitization, ion channel blockade, or entrance of Sux into the skeletal muscle cytoplasm (Phase II blockade).

A single large dose, repeated doses or a continuous infusion leads to postjunctional membranes that do not respond to Ach normally. This can be caused by receptor desensitization, ion channel blockade or entrance of Sux into the skeletal muscle cytoplasm (Phase II blockade).
Side Effects of Succinylcholine

**Why We Like It:**
- Spontaneous ventilation by the patient resumes rather quickly.

**Why We Don't:**
- Cardiac Dysrhythmias
  - Bradycardia, junctional rhythms, and sinus arrest.
- Hyperkalemia
  - Sustained opening of postjunctional receptors are associated with leakages of K+ on average 0.5 meq/liter. Hyperkalemia may occur in patients with muscular dystrophy, burns, any time there's a skeletal muscle atrophy (96 hrs to 6 months after injury).
- Myalgia
- Fasciculations (ouch!)

Quick Key:
- Spontaneous venous ventilation by the patient resumes rather than by the patient's spontaneous ventilation.
Side Effects of Succinylcholine

Myoglobinuria
From skeletal muscle damage.

Increased Intragastric Pressure
Secondary to intensity of muscle fasciculations.

Increased Intraocular Pressure
Maximum increases seen 2-4 min after administration and can last 5-10 min.

Increased ICP
Sustained skeletal muscle contraction
Incomplete jaw relaxation and masseter muscle rigidity can be seen occasionally in children.

Malignant Hyperthermia
Can be seen occasionally in children.
Non-Depolarizing Muscle Relaxants

Unlike Sux, Non-Depolarizing Muscle Relaxants (NDMRs) act through competitive antagonism at the NMJ. Only one alpha subunit on the nicotinic receptor needs to be blocked to prevent action potential propagation.

Non-Depolarizing Muscle Relaxants

https://www.bedfordlabs.com/our_products/online_catalog/products/vecuronium.html
https://www.anesthesiologyhub.com/nimbex.html
https://www.anesthesiologyhub.com/mivacron.html
https://www.hospira.com/products_and_services/drugs/PANCURONIUM_BROMIDE
A Summary
Spontaneous Reversal of NDMR

- Spontaneous reversal is slow and unpredictable.
- Residual block is associated with rare but potentially serious risks: aspiration, impaired hypoxic ventilatory response.

<table>
<thead>
<tr>
<th>Time (Range) (min) to Spontaneous Reversal (TOF Ratio 0.8)</th>
<th>NDMR (dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 (19–30) Mivacurium (0.15 mg/kg)</td>
<td></td>
</tr>
<tr>
<td>50 (28–76) Rocuronium (0.6 mg/kg)</td>
<td></td>
</tr>
<tr>
<td>60 (45–117) Vecuronium (0.08 mg/kg)</td>
<td></td>
</tr>
<tr>
<td>65 (40–78) Cisatracurium (0.1 mg/kg)</td>
<td></td>
</tr>
<tr>
<td>69 (58–79) Atracurium (0.5 mg/kg)</td>
<td></td>
</tr>
</tbody>
</table>

Let’s Talk About How We Monitor Paralysis

When neuromuscular blocking agents are administered, monitor neuromuscular response. Also monitor recovery to assess depth of blockade and degree of recovery. Monitor neuromuscular function to assess when neuromuscular blocking agents are working.

AANA Standards of Nurse Anesthesia Practice, p. 2

http://en.wikipedia.org/wiki/Neuromuscular_monitoring
http://en.wikipedia.org/wiki/Neuromuscular_monitoring
http://neuromuscular-monitoring.anesthesia-research.com/
http://salestores.com/sunmed81053601.html

Train of Four Ratio (T4)
Central muscles recover earlier than peripheral muscles (i.e., your diaphragm recovers faster than you adductor pollicis).

However, your corrugator supercilii recovers faster than the upper airway and adductor pollicis (i.e., overestimates the degree of recovery).

A TOF ratio ≥ 0.9 at the adductor pollicis is considered adequate recovery.

http://intraoperativeneuromonitoring.com/ta-in-of-four/
**Subjective vs. Objective Monitoring**

**Subjective Monitoring**
- Also known as Qualitative monitoring.
- Usually performed with a peripheral nerve stimulator and visual or tactile assessment of twitches and fade.
- Performed in less than 40% of patients.


Once the TOF ratio exceeds 0.40, most clinicians cannot detect touch or visual fade. 17% of patients' tests are performed in less than 10% of cases.

**Objective Monitoring**
- Also known as Quantitative monitoring.
- Usually performed with a nerve stimulator that can calculate TOF ratio.
- Performed in less than 17% of patients.

4. From New to ICU blog, 2016/3/1

Also known as Quantitative Monitoring.
How do we measure reversal in NDMR?

### Clinical Response

<table>
<thead>
<tr>
<th>% of Receptors Blocked</th>
<th>Twitches</th>
<th>Clinical Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>99-100</td>
<td>95</td>
<td>Diaphragm Moves</td>
</tr>
<tr>
<td>90</td>
<td>1 Twitch</td>
<td>Abdominal relaxation</td>
</tr>
<tr>
<td>95</td>
<td>0 Twitches</td>
<td>Facial Patient</td>
</tr>
<tr>
<td>99-100</td>
<td>0 Twitches</td>
<td>Blocked on TOF-Twitches</td>
</tr>
</tbody>
</table>

### Head Lift and Hand-Grip

- 99-100 % twitches: Tidal Volume and Vital Capacity Normal
- 75 % twitches: Abdominal relaxation adequate for most abdominal procedures
- 70 % twitches: Capillary refill normal
- 50 % twitches: Pass inspiratory pressure test
- 30 % twitches: Sustained head lift and hand-grip

### 5-sec Tetanic Fade

- The 5-sec head lift was unable to identify TOF ratios as low as 0.5 in more than 70% of patients.
- 5-sec tetanic fade can only be reliably detected in patients with TOF ratios less than 0.3.

### References
Why Reverse Neuromuscular Blockade?

- To facilitate spontaneous respiration and ventilation.
- Shorten time in the operating room.
- Avoid residual block and its associated risks.
- Reversal of NDMR is associated with decreased risk of postoperative mortality and coma.
- Decrease the risk of patients experiencing the very unpleasant effects of residual block.
- 20-40% of patients experience residual NMB in the PACU.

References:
Disadvantages of Anticholinesterases

- These agents cannot reverse profound blockade.
- Adequate reversal is not always possible and there is always a risk of residual blockade (National Averages site 16-42% have residual block in the PACU). 1
- Murphy et al. showed that 88% of patients have residual block at extubation. 1
- Kopman et al. showed that 50% of patients have residual blockade in the PACU. 2

Onset times of anticholinesterases are different:

- Endrophonium 1-2 min
- Neostigmine 7-11 min

Critical events that they face that require emergency intervention:

- PACU nurses report that residual NMB is one of the three most blockades in PACU.

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Side Effects:

- Decreases in blood pressure secondary to decreases in SVR
- Bradycardia
- Poorly metabolized by renal
- Decreased IOP
- Miosis
- Increased airway resistance
- Bronchoconstriction and increase production of secretions
- Increased incidence of PONV
- Enhances motility of GI tract
- Enhances gastric secretions
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- Increased incidence of PONV
- Enhances motility of GI tract
- Enhances gastric secretions

Therefore, these agents should be administered with an anticholinergic!
Anticholinergics

- Used for their sedative and antispasmodic properties
- Treatment for bradycardia (Atropine more so than Glycopyrolate or Scopolamine)
- Given concomitantly with an anticholinesterase for reversal of muscle blockade

- Central Anticholinergic Syndrome: CNS manifestations such as restlessness, somnolence, hallucinations, and unconsciousness can result.

- Side Effects:
  - Prevention of motion sickness
  - Bronchodilation
  - Relaxes biliary and urethral smooth muscle

- Used for their sedative and antispasmodic properties
<table>
<thead>
<tr>
<th>Drug</th>
<th>Sedation</th>
<th>Antispasmodic</th>
<th>Antiemetic</th>
<th>Cessation</th>
<th>MYODYNAMICS</th>
<th>CYLOPLEGIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine</td>
<td>0</td>
<td>+++</td>
<td>+</td>
<td>0</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>+++</td>
<td>+</td>
<td>0</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>+++</td>
<td>+</td>
<td></td>
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</tr>
</tbody>
</table>

**Anticholinergics cont.**
INFOGRAPHICS IN ANESTHESIOLOGY

411 Innate Immune Dysfunction in Trauma Patients: From Pathophysiology to Treatment (Clinical Concepts and Commentary)

Recent insights into posttraumatic immune dysfunction have defined new targets for immunointervention that hold promise for improving outcomes in such critically ill patients.

271 High Intraoperative Inspired Oxygen Does Not Increase Postoperative Supplemental Oxygen Requirements

High inspired oxygen may be reasonable in lower risk surgery to improve wound oxygenation.

347 Accuracy of Ultrasound-guided Nerve Blocks of the Cervical Zygapophysial Joints

Ultrasound imaging was an accurate technique for cervical zygapophysial joint nerve blocks in volunteers. See the accompanying Editorial View on page 236.

353 Estimation of the Contribution of Norketamine to Ketamine-induced Acute Pain Relief and Neurocognitive Impairment in Healthy Volunteers

Norketamine has an effect opposite to that of ketamine on pain relief.

399 Severe Emergence Agitation after Myringotomy in a 3-yr-old Child (Case Scenario)

Emergence agitation, the associated risk factors, and its prevention and treatment are discussed.

243 Factors Affecting Admission to Anesthesiology Residency in the United States: Choosing the Future of Our Specialty

The proportion of anesthesiology residents from U.S. medical schools has more than doubled since 1995. This retrospective cohort study evaluated the 2010 and 2011 residency applicants to determine the factors that influence selection. Although age and gender were not factors, schools were likely influenced by bias. This study suggests the potential for age and gender bias in the selection process. See the accompanying Editorial View on page 230.

302 What Factors Affect Intrapartum Maternal Temperature?

APPROSPECTIVE COHORT STUDY: MATERNAL INTRAPARTUM TEMPERATURE

The cause of rises in intrapartum maternal temperature is not known. In this prospective study of 81 women scheduled for labor induction, hourly oral temperatures were recorded and analyzed based on race, body weight, blood pressure, epidural analgesia, and epidural duration. This study suggests that epidural analgesia alone does not increase the risk of high temperatures in intrapartum women.

321 Postoperative QT Interval Prolongation in Patients Undergoing Noncardiac Surgery under General Anesthesia

Electrocardiograms (ECG) can identify abnormal cardiac repolarization by observation of a prolonged QT interval. QT interval prolongation is often caused by drugs and can result in sudden cardiac death. In this study, ECGs were recorded before and after surgery, and correlation coefficients were determined. Drugs and QT interval prolongation is not known, further study is warranted to determine the clinical relevance.

THIS MONTH IN

1. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Deshur MA, Benson J, Newmark RL, Maher CE: Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: A randomized controlled trial of the effect on neuromuscular and clinical recovery. ANESTHESIOLOGY 2018; 128:27–37


PACU = postanesthesia care unit; TOF = train-of-four.
What is Sugammadex?

Sugammadex is a cyclodextrin, a cyclic oligosaccharide carbohydrate that is capable of encapsulating "guest" molecules. It helps to structurally component γ-cyclodextrin and sugar component and γ-cyclodextrin. Sugammadex refers to the structural component γ-cyclodextrin and sugar component. Sugammadex is usually renally excreted. It decreases gastric ulceration, increases bioavailability and stability, increases bioavailability to enhance solubility and a number of oral medications from ibuprofen to metoprolol to omeprazole to decrease gastric ulceration. Sugammadex preparations are currently used in a number of oral medications. Sugammadex is FDA approved for use in US in December 2015. First commercially available 2008. Known as Bridion® worldwide.


https://www.merckconnect.com/bri/dosing.html?hcpUser=yes
What is Sugammadex cont.

Very water soluble (hydrophilic outside, hydrophobic inside)

Forms a 1:1 complex with Roc or Vec.

Works on Aminosteroidal NMDRs (Vec > Roc).

Low dissociation rate.

Is now referred to as a Selective Relaxant Binding Agent (SRBA).

It is not a receptor drug, it is a container drug.

Contraindicated in severe renal impairment patients.

Sugammadex is a NMB reversal agent. For use in adult surgical patients only. For reversal of only Rocuronium and Vecuronium. Is available as a 100 mg/cc preparation in 2 cc and 5 cc vials.

The speed in which the reversal takes place is dependent on the level of relaxation and dose of Sugammadex. It is dose dependent. Sugammadex is administered IV.

Through inactivation, a concentration gradient occurs shifting the NMB away from the NMJ, reversing paralysis. The mechanism of action involves involving encapsulating and inactivating Roc or Vec. Incompatible with verapamil and ranitidine.

Adминистartion
Hormonal contraceptives can become less effective secondary to a lowering of the free plasma concentrations.

Counsel your female patients of child-bearing age to use backup contraception 7 days after surgery.

Dosing

No dose adjustments need to be made in patients with normal renal function.

However, it is contraindicated in severe renal impairment. No dose adjustment necessary for mild to moderate renal impairment. No dose adjustments need to be made in geriatric, cardiac, or pulmonary patients with normal renal function. However, it is contraindicated in severe renal impairment.

Administration

Homonal contraceptives can become less effective.
Dosing is based on actual body weight, not ideal body weight. Dosing is based on the degree of muscle relaxation.

- For 2/4 TOF twitches, the dose is 2 mg/kg.
- For 1-2 PTC twitches, the dose is 4 mg/kg.
- To reverse RSI, dose of Roc, 16 mg/kg should be administered 3 min after the RSI dose.

Be sure to give the recommended dose or you may run into recurrence of NMB/recurarization.
If neuromuscular blockade would need to be re-established after a reversal with Sugammadex, Sux, Mivacurium, Cisatracurium or Atracurium could be considered.

If an aminosteroidal NMB is used, follow the table below:

<table>
<thead>
<tr>
<th>NMBA &amp; Dose to be Administered</th>
<th>Minimum Waiting Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 mg/Kg Rocuronium</td>
<td>4 hours</td>
</tr>
<tr>
<td>0.6 mg/Kg Rocuronium</td>
<td></td>
</tr>
<tr>
<td>1.2 mg/Kg Rocuronium</td>
<td>5 minutes</td>
</tr>
</tbody>
</table>

Re-administration of Roc or Vec after Reversal with Sugammadex (up to 4 mg/Kg)

- If neuromuscular blockade would need to be re-established after a reversal with Sugammadex, Sux, Mivacurium, Cisatracurium or Atracurium, could be established.
Pharmacokinetics

- Sugammadex is renally excreted.
- More than 90% is excreted in the urine over 24 hours.
- The Et1/2 is 2 hours in an adult with normal renal function.
- Vd is 11-14 liters in adults with normal renal function.
- Plasma clearance is 88 cc/min.
- No metabolites.
- No difference in pharmacokinetics with respect to gender or race.
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Adverse Effects

- Hypersensitivity reactions, including anaphylaxis, have been reported.
- Hypersensitivity occurred with Sugammadex.
- Bradycardia has been reported.
- Risk of prolonged NMB.
- While no anticholinergic needs to be administered with Sugammadex, treat appropriately.
- The incidence cited is 0.3% or 1/299 subjects.
- While the 16 mg/kg dose.
- Sugammadex might not work on certain patients—Monitor always!
Tolerability

- Risk of bleeding:
  - Doses up to 16 mg/kg have been reported to increase coagulation values by 25% for 1 hour.
  - However, the clinical trial did not show an increase in blood loss or anemia.
  - Be aware, especially if your patient has a known coagulopathy, if they are receiving therapeutic anticoagulation/thromboprophylaxis.

For More Information visit:
www.clinicaltrials.gov
Studies
P07038 looked at coagulation issues
P06042 looked at the hypersensitivity

https://www.npg.org.uk/collections/search/portrait/mw62694/Breathing-a-vein
<table>
<thead>
<tr>
<th>NMB Agent</th>
<th>Sugammadex</th>
<th>Vecuronium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocuronium</td>
<td>2.7 minutes</td>
<td>21.5 minutes</td>
</tr>
<tr>
<td>Glycerophosphate/Neostigmine/Glycopyrrolate</td>
<td>Sugammadex</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>NA</td>
<td>2.1 minutes</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>NA</td>
<td>2.7 minutes</td>
</tr>
</tbody>
</table>

**Median Time to Full Reversal (TOF ratio to 0.9) from Deep Blockade (PTC 1-2)**

<table>
<thead>
<tr>
<th>NMB Agent</th>
<th>Sugammadex</th>
<th>Vecuronium</th>
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<tbody>
<tr>
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<td>2 minutes</td>
<td>2.1 minutes</td>
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<td>Glycerophosphate/Neostigmine/Glycopyrrolate</td>
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<td>2.1 minutes</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>21 minutes</td>
<td>2.1 minutes</td>
</tr>
</tbody>
</table>

**Median Time to Full Reversal (TOF ratio to 0.9) from Moderate Blockade (T2)**

<table>
<thead>
<tr>
<th>NMB Agent</th>
<th>Sugammadex</th>
<th>Vecuronium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocuronium</td>
<td>2.7 minutes</td>
<td>21.5 minutes</td>
</tr>
<tr>
<td>Glycerophosphate/Neostigmine/Glycopyrrolate</td>
<td>Sugammadex</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>2.7 minutes</td>
<td>21.5 minutes</td>
</tr>
</tbody>
</table>

**Just How Fast Is It?**
Looking to the Future

If I have seen further than others, it is by standing upon the shoulders of giants. - Isaac Newton

If I have seen further than others, it is by standing upon the shoulders of giants.

Gantacurium

A new class of isoquinoline NMB known as chlorofumarates. Developed as an ultra short acting, rapid onset NMB. Metabolized by cysteine adduction and pH-sensitive hydrolysis. Metabolites have no neuromuscular properties. No renal and hepatic involvement in elimination.
Pharmacodynamics/Pharmacokinetics

- In human trials, the ED95 of Gantcurium was found to be 0.19 mg/kg.
- Onset time is less than 3 min, however at 4 X ED95 dose, onset time can be shortened to 1.5 min.
- Duration of action is ~10-15 min (spontaneous reversal to TOF ≥ 0.9).
- Can be reversed with an anticholinesterase. Can be reversed with L-cysteine in humans, reversed to TOF ≥ 0.9 in 3.8 min.
- Preferably edrophonium with its peak effect at 2 min.
- Can be reversed with an aminolipase.
- In a bolus dose of 10-50 mg/kg for reversal, no toxicity.
- Cysteine is an amino acid used in parenteral nutrition. Used in parenteral nutrition.
- In human trials, the ED95 of Gantcurium was found to be 0.19 mg/kg. Depending on when it is administered for reversal, can shorten the duration of action by 2-6 min.
- Depending on when it is administered for reversal, no toxicity.
Side Effects

- Dose dependent transient cardiovascular side effects have been observed in humans.
  - Usually reported at doses of 3 X ED₉⁵.
  - Evidence by hypotension and reflex tachycardia.
- Humans show significant dose dependent histamine release:
  - Present in doses of 4 X ED₉⁵.
  - At lower doses (2.5 X ED₉⁵), no histamine release.
- Humans show significant flushing and reflex tachycardia.

Evidence by hypotension and reflex tachycardia.

[References]
Other New Horizons...

Other isoquinoline fumarate agents

CW002
CW011

Reversed by administration of the amino acid cysteine.

CW002 and CW011 have slower reversal time and longer duration of action than Gantacurium.

https://www.redbubble.com/people/compoundchem/works/1380542

A GUIDE TO THE TWENTY COMMON AMINO ACIDS

8-20 amino acids poster
Other New Horizons...

Tropinyl Diester Derivatives

These are alkaloids similar in structure to atropine and scopolamine.

These are alkaloids similar in structure to atropine and scopolamine.

No cumulative effects with infusion.

Rapid onset (~1 min)

Short Duration (5-11 min)

Reversed with an anticholinesterase.

Some cardiac side effects.

In animal studies, dose-dependent hypotension.

Some cardiac effects.

Rapidity of onset (45-60 sec)

Duration of effect (3/4 duration of Rocuronium (~half sec))

TAAC3 DRAC 6-4

G-1-64

Calabadions

Calabadions 1 and 2 are part of the molecular container family Cucurbit[n]urils. First reversal agents to reverse both aminosteroid and benzylisoquinolinium NMBs. Works by flexing its glycoluril backbone to accommodate both roc and cis. Benzylisoquinolines make up 1/3 of the market volume of NMBs.

No signs of recurarization. In preclinical trials, 90-150 mg/kg of Calabadion 1 was able to reverse rocuronium and cisatracurium to a TOF ≥ 0.9 within 1-2 min (84 vs. 87 sec). No effects on heart rate, blood pressure or ABG parameters. Fast renal elimination: 90-100% within 1 hour. Interestingly may also be aminosteroid and reverse both roc and cis. Hoffman et al., (2013). Anesthesiol. 119 (2), 317-325.

Fast renal elimination:

No effects on heart rate, blood pressure or ABG parameters.

87 sec).

0.9 within 1-2 min (84 vs. 85) cisatracurium to a TOF ≥ rocuronium and was able to reverse 1 mg/kg of Calabadion 1 in preclinical trials; 90-150

Calabadions
In Conclusion

Our current practice in NMB is improving, but it is still far from perfect. Patient safety is of the utmost priority. We currently administer muscle relaxation and reverse it in a very complex manner. Objective or quantitative monitoring of NMB needs to be utilized. Many agents, many side effects. Sugammadex offers a new way to reverse Roc and Vec.

Promising new drugs for NMB and reversal are coming, are we ready? Many agents, many side effects.

Objective or quantitative monitoring of NMB needs to be utilized. Very complex manner. 

We currently administer muscle relaxation and reverse it in a very complex manner. Patient safety is of the utmost priority.

In Conclusion