Using Sugammadex in Pediatric Patients?

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Objectives

At the end of this presentation, the audience will be able to:
- Review the mechanism and pharmacokinetics of sugammadex
- Describe the side effects and possible complications of sugammadex
- Discuss the trials and case reports on the use of sugammadex in the pediatric population

What is Sugammadex?

- Modified gamma cyclodextrin
- Forms a 1:1 complex with aminosteroid neuromuscular blocking agent molecules
- Reversal dose depends on depth of neuromuscular block

Why is it important?

- 28% of pediatric patients have been found to have a residual block
  - Severe block in 6.5%
- Greater potency and clinical duration of rocuronium in children
- Increased risk of post-operative apnea in pediatric patients

Pharmacology

- Metabolism: no metabolites, renally excreted unchanged
- Elimination half-life ~ 100 minutes
- No significant cardiovascular or hemodynamic adverse effects
- Obesity: use actual body weight to prevent recurarization

Disclosures

- No conflict of interest
Dosage

- Rocuronium and vecuronium:
  - ≥ 2 twitches = 2 mg/kg
  - 1-2 post-tetanic twitches = 4 mg/kg
- Rocuronium only: 16 mg/kg if there is a clinical need to reverse neuromuscular blockade soon after a single dose of 1.2 mg/kg
- Not recommended in patients with severe renal impairment, including dialysis-dependent patients

Warnings and Interactions

- Contraindications: known hypersensitivity
- Warnings:
  - Anaphylaxis
  - Marked bradycardia
- Adverse reactions:
  - Vomiting, pain, nausea, hypotension, headache
- Drug interactions:
  - Toremifene, hormonal contraceptives
  - Incompatible with verapamil, ondansetron, and ranitidine

Sugammadex in pediatric patients?

- Multicenter, randomized, parallel-group, dose-finding, safety-assessor blinded study
- May 2005-2006, 6 European centers
- 0.6 mg/kg rocuronium
  - Sugammadex 0.5, 1, 2 or 4 mg/kg, or placebo at reappearance of T2
- Results: dose-response relation in all groups but infants due to small n
- No recurrence of blockade, inadequate reversal, significant QT prolongation, or other abnormalities
**Prospective, comparative, randomized clinical study**

**August 2013-July 2014, Egypt**

**Two groups:** neostigmine 0.04 mg/kg with atropine 0.02 mg/kg, or sugammadex 4 mg/kg

**Primary endpoint:** time to recovery of TOF to 90% after rocuronium

**Results:** the sugammadex group had a statistically significant shorter time to TOF ratio of 90%

**No evidence of recurarization in any patient**

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**Randomized double-blinded clinical trial**

**2 groups:** sugammadex 2 mg/kg vs. neostigmine 0.06 mg/kg + atropine 0.02 mg/kg at emergence of T2

**Results:**
- Sugammadex group: more complete muscle strength rates
- Neostigmine group: TOF9 and extubation times were significantly longer

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**Prospective, randomized study from Turkey**

**2 groups:** group RN = neostigmine 0.03 mg/kg + atropine 0.01 mg/kg; group RS = sugammadex 2 mg/kg

**Results:**
- Group RN: higher extubation time and TOF rate, lower TOF rate at extubation, longer time to reach TOF > 0.9

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**Table 3: Mean time from administration of rocuronium till T2**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Neostigmine</th>
<th>Sugammadex</th>
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<tbody>
<tr>
<td>Mean time from administration</td>
<td>166 ± 58</td>
<td>144 ± 33</td>
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<td>of rocuronium till T2</td>
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<td>Mean time for recovery of the</td>
<td>35 ± 8</td>
<td>14 ± 12.29</td>
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<td>TOF ratio to 90%</td>
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Data are represented as mean ± SD; *P < 0.05 in comparison to neostigmine group; SD: Standard deviation; TOF: Train of four
Train-of-four recovery precedes twitch recovery during reversal with sugammadex in pediatric patients: A retrospective analysis

Ricardo Vivas Carlos1 • Marcelo Luis Alexandre Torres2 • Hans Donald de Beer5

- Retrospective analysis to investigate the relationship of the recovery of T1 height and TOF ratio
- January 2016–June 2017
- 2 groups: sugammadex 2 or 4 mg/kg, based on depth of block
- Results: same T1 and TOF ratio behavior in pediatric patients compared to adults

Table 2

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (years)</th>
<th>Number of infants</th>
<th>Number of controls</th>
<th>Time 1 (s)</th>
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Effect of Reversal of Neuromuscular Blockade with Sugammadex versus Usual Care on Bleeding Risk in a Randomized Study of Surgical Patients

Nels Fehr-Meyer, M.D., Ph.D., Henri Fennema, Ph.D., Sam Schulman, M.D., Ph.D., Victor Ramirez, M.D., Michael Pogorzelski, M.D., Marked Böhrer, M.D., Hannes Wolf, M.D., Marcel Speck, R.N., C.R.N.A., Christina McCarney Sikk, B.S., Deborah Williams-Herman, M.D., Tiffany Voci, M.S., Anise Siegelaub, M.D., Ph.D.

- Randomized, parallel-group, double-blind trial
- October 2011-September 2012, 22 centers in Austria, Belgium, and Germany
- 2 groups: sugammadex 4 mg/kg or usual care (neostigmine + glycopyrrolate or atropine, or placebo/spontaneous recovery)
- Results: treatment with sugammadex 4 mg/kg was not associated with an increased bleeding risk in surgical patients as compared with usual care
Take Home Points

- Dosages: 2 mg/kg, 4 mg/kg, OR 16 mg/kg (rocuronium only)
- Interacts with OCPs: use back-up method for 7 days
- Multiple studies have demonstrated effectiveness of sugammadex compared to neostigmine and placebo
- No significant side effects

Questions?

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References

- https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022225lbl.pdf