Evaluation of Procedural Neuromuscular Blockade Reversal Time with Sugammadex versus Neostigmine plus Glycopyrrolate

Alex Metzger PharmD
PGY1 Pharmacy Practice Resident - SSM Health DePaul Hospital
Residency Program Director: Anthony Lucido PharmD, BCPS
Project Mentors: Heather Malcom PharmD, BCPS & Kim Doerhoff PharmD, BCPS
Disclosure

• No conflicts (financial or otherwise) to disclose
Learning Objective

• Identify differences in efficacy, safety, and cost between sugammadex and neostigmine plus glycopyrrolate for neuromuscular blockade reversal.
Research Question

• Do adult patients undergoing elective surgeries who received sugammadex for reversal of rocuronium or vecuronium induced neuromuscular blockade have a shorter neuromuscular blockade reversal time compared to patients who received neostigmine plus glycopyrrolate?
Background

– Rocuronium and vecuronium induced neuromuscular blockade reversal historically has been performed with neostigmine plus glycopyrrolate

– Sugammadex approved in 2015

– Price Differences:
  • Sugammadex 200mg/2ml: $119.68
  • Neostigmine 10mg/10ml: $22.00
  • Glycopyrrolate 0.4mg/2ml: $6.72

### Background cont.

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Hristovska et al&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Carron et al&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Paton et al&lt;sup&gt;4&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aim</strong></td>
<td>Meta-analysis</td>
<td>Meta-analysis</td>
<td>Systematic Review</td>
</tr>
<tr>
<td>To evaluate the efficacy and safety of sugammadex versus neostigmine in both moderate and profound neuromuscular blockade reversal</td>
<td>To evaluate the efficacy and safety of sugammadex versus neostigmine in neuromuscular blockade reversal</td>
<td>Economical evaluation of the difference in time saved with sugammadex versus neostigmine in neuromuscular blockade reversal</td>
<td></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Moderate: 10.22 min reduction Profound: 45.78 min reduction</td>
<td>Statistically significant quicker reversal Statistically significant lower adverse effects</td>
<td>Economically cost-effective when used in the operating room</td>
</tr>
<tr>
<td><strong>Year</strong></td>
<td>2017</td>
<td>2016</td>
<td>2010</td>
</tr>
</tbody>
</table>

---

Study Design

• Multi-center, non-blinded, retrospective study

Jan 1<sup>st</sup> 2019 to July 31<sup>st</sup> 2019

DePaul | St. Mary’s
St. Clare | St. Joseph’s West

SSM Health
Treatment Arms

Retrospective cohort arms

- Neostigmine plus glycopyrrolate for neuromuscular blockade reversal
- Sugammadex for neuromuscular blockade reversal
## Inclusion & Exclusion

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>- &gt; 18 years old</td>
<td>- Creatinine clearance</td>
</tr>
<tr>
<td>- Vecuronium or rocuronium neuromuscular blockade</td>
<td>≤ 50 ml/min</td>
</tr>
<tr>
<td>- Elective surgery</td>
<td>- Pregnant</td>
</tr>
<tr>
<td>- Located at SSM Health: DePaul, St. Mary’s, St. Clare,</td>
<td>- Breastfeeding</td>
</tr>
<tr>
<td>or St. Joseph’s West</td>
<td></td>
</tr>
</tbody>
</table>
Study Endpoints

Primary Endpoint

• Neuromuscular blockade reversal time

Secondary Endpoints

• Hypotension up to 6 hours following the procedure
• Bradycardia up to 6 hours following the procedure
Statistical Analysis

Mann-Whitney U
• Neuromuscular blockade reversal time

Chi-Square
• Hypotension up to 6 hours following procedure
• Bradycardia up to 6 hours following procedure

Descriptive statistics
• Baseline characteristics

* All statistical tests performed with Minitab v19 software

## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sugammadex (n=60)</th>
<th>Neostigmine/glycopyrrolate (n=60)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>51.4</td>
<td>43.2</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>42 females, 18 males</td>
<td>45 females, 15 males</td>
<td>0.540</td>
</tr>
<tr>
<td><strong>Hospital Breakdown</strong></td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>DPHC</td>
<td>25</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>SMHC</td>
<td>13</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>SCHC</td>
<td>13</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>SJHW</td>
<td>9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>102</td>
<td>91.9</td>
<td>0.025</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>35.2</td>
<td>32.4</td>
<td>0.129</td>
</tr>
<tr>
<td><strong>Height (in)</strong></td>
<td>67</td>
<td>66.2</td>
<td>0.557</td>
</tr>
<tr>
<td><strong>S.Cr</strong></td>
<td>0.8</td>
<td>0.82</td>
<td>0.727</td>
</tr>
<tr>
<td><strong>CrCl</strong></td>
<td>84.1</td>
<td>87.1</td>
<td>0.170</td>
</tr>
<tr>
<td><strong>ASA Score</strong></td>
<td>2.5</td>
<td>2.1</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Primary outcome

Neuromuscular Blockade Reversal Time

<table>
<thead>
<tr>
<th>Drug</th>
<th>Time of Neuromuscular Blockade Reversal (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugammadex</td>
<td>26.1</td>
</tr>
<tr>
<td>Neostigmine + Glycopyrrolate</td>
<td>26.0</td>
</tr>
</tbody>
</table>

p = 0.350
Secondary Outcomes

Hypotension up to 6 hrs post-procedure

- Sugammadex: 80% Yes, 20% No
- Neostigmine + glycopyrrolate: 55% Yes, 45% No

p = 0.003
Secondary Outcomes Cont.

Bradycardia up to 6 hrs post-procedure

- Sugammadex: 87% Yes, 13% No
- Neostigmine + glycopyrrolate: 75% Yes, 25% No

p = 0.104
Cost and Dosing Data

• average cost per minute in operating room: $31.31
  – neostigmine + glycopyrrolate would result in $3.13 in savings based on operating room time

• neostigmine + glycopyrrolate would result in $113.97 in savings based on the average amount of each medication utilized

• time + medications = total savings of $117.10
# Strengths & Limitations

<table>
<thead>
<tr>
<th><strong>Strengths</strong></th>
<th><strong>Limitations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Multi-center</td>
<td>- Small patient population</td>
</tr>
<tr>
<td>- Cost data</td>
<td>- Differences in surgical type</td>
</tr>
<tr>
<td>- Strict inclusion and exclusion criteria</td>
<td>- Baseline characteristic differences</td>
</tr>
<tr>
<td></td>
<td>- Limited safety data</td>
</tr>
<tr>
<td></td>
<td>- Low percent of accurate dosing</td>
</tr>
</tbody>
</table>
Correct Dosing Percentages

neostigmine
- Correct: 67%
- Incorrect: 33%

glycopyrrolate
- Correct: 87%
- Incorrect: 13%
sugammadex
- Correct: 35%
- Incorrect: 65%
Summary

• **Efficacy:**
  – There was no difference in neuromuscular blockade reversal time between the two arms

• **Safety:**
  – Sugammadex showed statistical significance in reducing rates of hypotension
  – No statistical difference seen in rates of bradycardia

• **Cost:**
  – Neostigmine + glycopyrrolate resulted in a $117.10 average cost savings per procedure
Future Plans

• Dosing issues:
  – Educate anesthesia staff about proper dosing per package inserts
  – Stress the risks and benefits of over or under dosing
  – Re-evaluate data to see if there is a difference when correct dosing is utilized
Future Plans Cont.

• Operating room staff:
  – Present the efficacy, safety, and cost data
  – Discuss any limitations they identify
  – Evaluate the switching back to neostigmine + glycopyrrolate
  – Standardize train of four
References


Evaluation of Procedural Neuromuscular Blockade Reversal Time with Sugammadex versus Neostigmine plus Glycopyrrolate

Alex Metzger PharmD
PGY1 Pharmacy Practice Resident - SSM Health DePaul Hospital
Residency Program Director: Anthony Lucido PharmD, BCPS
Project Mentors: Heather Malcom PharmD, BCPS & Kim Doerhoff PharmD, BCPS