Sugammadex vs. neostigmine vs. spontaneous reversal in pulmonary complications post surgery

Allison Clemens PharmD
Background

- Sugammadex is a selective relaxant binding agent
  - Indicated for the reversal of rocuronium bromide, vecuronium bromide, and pancuronium bromide

- Neostigmine is an acetylcholinesterase inhibitor
  - Indicated for reversal of nondepolarizing neuromuscular blockade
  - Must be used with atropine or glycopyrrolate

ASA Status

1. A normal healthy patient
2. A patient with mild systemic disease
3. A patient with severe systemic disease
4. A patient with severe systemic disease that is a constant threat to life
5. A moribund patient who is not expected to survive without the operation
6. A declared brain-dead patient whose organs are being removed for donor purposes

Murphy GS. Minerva Anestesiol 2006; 72:97
## Previous Study

**Sugammadex versus neostigmine for reversal of neuromuscular blockade and postoperative pulmonary complications (STRONGER) trial**

<table>
<thead>
<tr>
<th>Objective</th>
<th>• Compare sugammadex to neostigmine for the reversal of neuromuscular blockade on incidence of major pulmonary concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>• The trial matched 22,856 patients in each treatment arm</td>
</tr>
<tr>
<td>Primary Outcome</td>
<td>• Major pulmonary complications after noncardiac inpatient surgery</td>
</tr>
</tbody>
</table>

Sugammadex versus neostigmine for reversal of neuromuscular blockade and postoperative pulmonary complications (STRONGER) trial

Results

- Out of the 45,712 patients studied 1,892 (4.1%) were diagnosis with the primary outcome
  - 3.5% Sugammadex vs 4.8% Neostigmine
  - Reduced pneumonia risk by 47%
    - adjusted odds ratio, 0.53; 95% CI, 0.44 to 0.62

Key Findings

- Sugammadex was associated with a 30% reduced risk of pulmonary complications
  - Adjusted odds ratio, 0.70; 95% CI, 0.63 to 0.77

Sugammadex is a neuromuscular blocking reversal agent that works by binding to steroidal NMBAs. Which of the following is not reversed by sugammadex?

a) Rocuronium  
b) Vecuronium  
c) Succinylcholine  
d) Pancuronium
Self-Assessment Question #1

Sugammadex is a neuromuscular blocking reversal agent that works by binding to steroidal NMBAs. Which of the following is not reversed by sugammadex?

a) Rocuronium  
b) Vecuronium  
c) Succinylcholine  
d) Pancuronium
Sugammadex is an attractive neuromuscular blocking reversal agent for many reasons. Which of the following is not an advantage of using sugammadex?

a) Sugammadex works faster than neostigmine plus atropine
b) Sugammadex can reverse deep neuromuscular paralysis
c) Sugammadex can be used in patients with reduced renal function
d) Sugammadex can be stored at room temperature
Self-Assessment Question #2

Sugammadex is an attractive neuromuscular blocking reversal agent for many reasons. Which of the following is not an advantage of using sugammadex?

a) Sugammadex works faster than neostigmine plus atropine
b) Sugammadex can reverse deep neuromuscular paralysis
c) Sugammadex can be used in patients with reduced renal function
d) Sugammadex can be stored at room temperature
Purpose

To evaluate if there is a meaningful, clinically significant reduction of pulmonary complications with sugammadex use vs neostigmine use or spontaneous reversal.
Setting

Parkview Health

- Not-for-profit, community-owned organization
- Northeast Indiana and northwest Ohio
- 10 hospital health system
  - Over 900 inpatient beds
  - Over 200 primary care clinics
- Completes >10,000 surgeries per year
Design

- Retrospective matched cohort
- Single center: Parkview Regional Medical Center (PRMC)
- Timeframe: January 2017 - January 2020

- Study groups

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugammadex Reversal</td>
<td>Neostigmine Reversal</td>
<td>Spontaneous Reversal</td>
</tr>
</tbody>
</table>
## Design

### Inclusion Criteria

- Completed surgical procedure at PRMC
- ≥ 18 years old
- Received general anesthesia
- Endotracheal intubation
- CrCl ≥ 30 mL/min
- Received rocuronium or vecuronium
- Index only procedure per admission or 30-day period

### Exclusion Criteria

- ≥ 90 years old
- Neuromuscular disease
- Malignant hyperthermia
- Burns
- No ASA status
- ASA ≥ 5
- Received both Sugammadex and Neostigmine
- Received NMBA after Sugammadex and Neostigmine
## Matching

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>ASA Score</th>
<th>BMI (kg/m²)</th>
<th>Procedure Type</th>
<th>Procedure Length (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 5 years of age</td>
<td>Male</td>
<td>1</td>
<td>&lt; 18.5</td>
<td>Abdominal</td>
<td>&lt; 1:30</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2</td>
<td>18.5-24.9</td>
<td>Thoracic</td>
<td>1:31 - 2:99</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>3</td>
<td>25-29.9</td>
<td>Other</td>
<td>&gt; 3:00</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4</td>
<td>&gt; 30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Endpoints

Primary
• Composite endpoint of pneumonia, respiratory failure, and other respiratory complications within 30 days of surgery

Secondary
• Pneumonia
• Respiratory failure
• Other respiratory complications
Patient Inclusion

N=19,481

Not meeting inclusion or exclusion criteria
N=10,003

Not meeting exact matching criteria
N=8,038

Sugammadex
N=380

Neostigmine
N=380

No Reversal
N=380
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sugammadex (N = 380)</th>
<th>Neostigmine (N = 380)</th>
<th>No Reversal (N = 380)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean + SD</td>
<td>57.7 ± 16.3</td>
<td>57.6 ± 16.3</td>
<td>57.7 ± 16.4</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>194 (51.1%)</td>
<td>194 (51.1%)</td>
<td>194 (51.1%)</td>
</tr>
<tr>
<td>Weight, kg + SD</td>
<td>90.9 ± 26.4</td>
<td>92.2 ± 26.6</td>
<td>90.7 ± 24.6</td>
</tr>
<tr>
<td>BMI, kg/m² + SD</td>
<td>31.5 ± 8.5</td>
<td>31.4 ± 8.3</td>
<td>31.3 ± 8.1</td>
</tr>
<tr>
<td>ASA, mean + SD</td>
<td>2.5 ± 0.6</td>
<td>2.8 ± 0.6</td>
<td>2.5 ± 0.6</td>
</tr>
</tbody>
</table>
## Comorbid Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Occurrence (N=1140)</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic pulmonary disease</td>
<td>38</td>
<td>-</td>
<td>-</td>
<td>0.997</td>
</tr>
<tr>
<td>Chronic Heart Failure</td>
<td>61</td>
<td>0.431</td>
<td>0.050-3.695</td>
<td>0.443</td>
</tr>
<tr>
<td>Hypertension</td>
<td>592</td>
<td>0.879</td>
<td>0.204-3.781</td>
<td>0.862</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>85</td>
<td>0.299</td>
<td>0.051-1.738</td>
<td>0.179</td>
</tr>
<tr>
<td>Coronary artery disease/ Acute coronary syndrome</td>
<td>188</td>
<td>0.827</td>
<td>0.156-4.378</td>
<td>0.823</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease/ Asthma</td>
<td>217</td>
<td>0.255</td>
<td>0.054-0.944</td>
<td>0.041</td>
</tr>
</tbody>
</table>

### Primary Outcome

- **Composite Pulmonary Complication**
  - Pneumonia, respiratory complications, and other respiratory complications within 30 days of surgery

<table>
<thead>
<tr>
<th></th>
<th>Sugammadex (N = 380)</th>
<th>Neostigmine (N = 380)</th>
<th>No Reversal (N = 380)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Complications, N (%)</td>
<td>5 (1.32%)</td>
<td>5 (1.32%)</td>
<td>2 (0.53%)</td>
</tr>
</tbody>
</table>
Primary Outcome

Composite Pulmonary Complications

- Sugammadex vs Neostigmine
  1.135 (0.322, 4.002)
  p-value = 0.884

- Sugammadex vs No reversal
  0.424 (0.081, 2.208)
  p-value = 0.308
Secondary Outcome

- Pneumonia, respiratory complications, and other respiratory complications

<table>
<thead>
<tr>
<th></th>
<th>Sugammadex (N = 380)</th>
<th>Neostigmine (N = 380)</th>
<th>No Reversal (N = 380)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia, N (%)</td>
<td>2 (0.53%)</td>
<td>2 (0.53%)</td>
<td>1 (0.26%)</td>
</tr>
<tr>
<td>Respiratory Complications, N (%)</td>
<td>0 (0%)</td>
<td>1 (0.26%)</td>
<td>1 (0.26%)</td>
</tr>
<tr>
<td>Other Respiratory Complications, N (%)</td>
<td>3 (0.79%)</td>
<td>2 (0.53%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Secondary Outcome

Sugammadex vs Neostigmine

- Pneumonia
  1 (0.14, 7.136)
  p-value = 1

- Respiratory Failure
  - (0, -)
  p-value = 0.994

- Other Respiratory Complications
  0.332 (0.034, 3.202)
  p-value = 0.340

Sugammadex vs No Reversal

- Pneumonia
  0.499 (0.045, 5.523)
  p-value = 0.571

- Respiratory Failure
  - (0, -)
  p-value = 0.994

- Other Respiratory Complications
  0 (0, -)
  p-value = 0.994
Results

Summary

• Comorbid conditions
  • An at-risk population was not identified

• Composite pulmonary complication
  • No statistically significant difference observed

• Pneumonia, respiratory complications, and other respiratory complications
  • No statistically significant difference observed
Limitations

• Single center, small sample size
• Large population of patients excluded
  • CrCl < 30 ml/min
  • Received both reversal agents
  • Missing medication documentation
  • Age > 90 yo
• Lack of train of four documentation
• Lack of standardized documentation in anesthesia notes
• Not able to complete a total cost of care analysis
Future Directions

- Cost analysis for total cost of care
- Collaborate with anesthesiologists to execute safe and cost-effective patient care
Conclusion

- Fewer post-operative pulmonary complications compared to national reported average

- No difference in pulmonary complications seen between trial arms

- Additional cost of Sugammadex did not provide an added benefit
Acknowledgements

Mentors

• Will Armstrong, PharmD, BCPS
• Tara Jellison, PharmD, MBA, FASHP
• Sarah Ferrell, PharmD, BCPPS
• Sarah Pfaehler, PharmD, MBA, BCPS
References

Sugammadex vs. Neostigmine vs. Spontaneous Reversal in pulmonary complications post surgery

Allison Clemens, PharmD
PGY1 Pharmacy Resident
Parkview Health | Fort Wayne, Indiana

The speaker has no actual or potential conflict of interest in relation to this presentation.