Sugammadex: How Much are You Willing to Pay?

**Objectives**
- The learner will be able to:
  1. Appropriately describe the profile of Bridion® - Sugammadex
  2. Effectively describe proper use and potential adverse effects of Bridion® - Sugammadex
  3. Describe the value of Bridion® - Sugammadex

**Clinical Application**
- **Indications:**
  - Used for adults undergoing surgery for the reversal of neuromuscular blockade (NMB) induced by rocuronium or vecuronium
  - Not indicated: reverse blockade of depolarizing neuromuscular blocking agents (e.g. succinylcholine)
  - Not indicated for use in ICU setting

- **Contraindications:**
  - Hypersensitivity to sugammadex or any component of the product

- **Precautions:**
  - Severe renal impairment or dialysis-dependent patients (Not Recommended)
  - Caution: mild-to-moderate renal impairment (no dosage adjustment)

- **Pregnancy:**
  - No available human data
  - In animal studies, fetal birthweight was reduced when 8x human dose was administered
  - Reverse Oral Contraception up to 7 days

- **Lactation:**
  - Excretion in human breast milk (Unknown)
  - Present in animal milk

**Pharmacology**
- **Mechanism of Action**
  - Cyclodextrin forms a 1:1 complex with rocuronium and vecuronium – “mopping it up”
  - This reduces the amount of free NMB agent in plasma available to bind to Ach receptor
  - In turn, the concentration gradient favors movement of NMB agent away from the neuromuscular junction
Structure

- Rocuronium molecule is docked inside the lipophilic core of SUGAMMADEX
- The negatively charged carboxy-ethyl groups hold rocuronium tightly

SUGAMMADEX BINDING REACTION

<table>
<thead>
<tr>
<th>DRUG</th>
<th>SPEED OF REACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROCURONIUM</td>
<td>25</td>
</tr>
<tr>
<td>VECURONIUM</td>
<td>10.0</td>
</tr>
<tr>
<td>PANCURONIUM</td>
<td>2.6</td>
</tr>
<tr>
<td>ATRACTORIUM</td>
<td>0.005</td>
</tr>
<tr>
<td>SUCCINYL CHOLINE</td>
<td>0</td>
</tr>
</tbody>
</table>

ROCURONIUM > VECURONIUM > PANCURONIUM

Drug Interactions

TWO TYPES OF BINDING INTERACTIONS

1. DISPLACEMENT
   Another drug binding to sugammadex, displacing NMBA, causing rise in free NMBA concentration
   ✔ Potential risk of RE-OCURRENCE OF NMB

2. Capture
   Sugammadex binding another drug, decreasing its free concentrations
   ✔ Potential risk of reduction in efficacy

Drug Interactions

- The highest affinity constant - for REMIFENTANIL (0.2% of the affinity constant of sugammadex with rocuronium)
- PROGESTOGENS and ESTROGENS show some affinity for sugammadex (affinity 2-22% of that of rocuronium)
- Hormonal contraceptives: must recommend additional, non-hormonal method of contraception for next 7 days
- Toremifene (estrogen binding agent):
  - Used to treat advanced breast cancer
  - Recovery can be delayed
Bridion® Sugammadex

Side Effects & Adverse Effects

Side effects are dose-dependent

- **Common** (2-4 mg/kg) (16 mg/kg) [placebo]:
  - Nausea (23%) (26%) (23%)
  - Vomiting (11%) (15%) (10%)

- **Serious** (2-4 mg/kg) (16 mg/kg) [placebo]:
  - Prolonged QT interval (1%) (6%) (1%)
  - Bradycardia (1%) (5%) (1%)
  - Hypotension (4%) (3.3%) (4%)
  - Anaphylaxis (0%) (3%) (0%)

Dosing Information

- **2-4 mg/kg IV bolus** based on actual body weight depending on blockade status

- **Immediate Reversal**: 16 mg/kg IV bolus based on actual body weight
  - This dose has only been studied for rocuronium reversal

Clinical Trials

Bridion vs. neostigmine reversal agent for NMB induced by rocuronium or vecuronium at reappearance of T2 (Moderate Blockade)

_Eur J Anaesthesiol_ 2001;18:99

Clinical Trials

- **Purpose**: Comparing the efficacy of sugammadex with neostigmine given with glycopyrrolate or atropine in antagonizing block produced by aminosteroidal NMBAs
- **Design**:
  - Randomized, single-dose, active-controlled, safety-assessor blinded trial of 98 patients
  - Sugammadex 2.0 mg/kg or neostigmine 50 μg/kg plus glycopyrrolate 10 μg/kg were administered intravenously in randomized order

Clinical Trials

- **Included**: Adult patients scheduled for surgery under general anesthesia in the supine position
  - ≥ 18 years old
  - ASA class 1 to 3
- **Primary outcome**: Recovery time after reversal agent administration
  - measured as train of four ratio (T4/T1) of 0.9

Clinical Trials

- **Serious adverse effects reported**:
  - 2 subjects in the sugammadex group
  - 3 in the neostigmine group
- **Adverse effects were not attributed to the study drug**
Clinical Trials

- Sugammadex achieved significantly faster recovery of T4/T1 ratio to 0.9 compared with neostigmine after neuromuscular block with rocuronium
- Outliers and variability of recovery times were significantly lower following reversal with sugammadex

Recovery from Neuromuscular Blockade

- Decrease in NMBA concentration
  - Metabolism
  - Excretion
- Increase in acetylcholine

Neostigmine

- Anticholinesterase
- Increase acetylcholine concentration at the NMJ
- Displaces the NMB from the NMJ via competition

PROBLEMS WITH NEOSTIGMINE

- Residual Paralysis: which is real . . .
- Recurarization
- Cholinergic Side Effects
  - Require an Anticholinergic to counter Cholinergic Side Effects
    - Additional Side effects from Anticholinergic

Outcomes: Respiratory Complications (OSA)

Objective:

- Compare sugammadex and neostigmine
  1. regarding the efficacy in reversing rocuronium-induced neuromuscular block
  2. incidence of post-operative respiratory complications
  3. costs in patients undergoing surgery for the treatment of obstructive sleep apnoea (OSA).

Bridion® - Sugammadex

Cost Comparison

<table>
<thead>
<tr>
<th>Neuromuscular Blocking and Reversal Agents</th>
<th>AWP Pricing</th>
<th>Unit dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugammadex 200 mg/2 ml SDV</td>
<td>$1140</td>
<td>$66</td>
</tr>
<tr>
<td>Neostigmine (Bloxiverz) 1 mg/ml 10 ml MDV</td>
<td>$1185</td>
<td>$118.75</td>
</tr>
<tr>
<td>Glycopyrrolate (Robinul) 0.2 mg/ml SDV</td>
<td>$500</td>
<td>$50.00</td>
</tr>
</tbody>
</table>

AWP pricing as of 2/26/2016

Outcomes: Respiratory Complications (OSA)

- **OR Duration**
  - 72.4 vs. 96.6 min.

- **PACU Duration**
  - 22.9 vs. 36.3 min.


Cost-Effectiveness

**OBJECTIVES:**
the budget impact and the cost-effectiveness of SGX in the routine reversal of patients with neuromuscular block (NMB) from the Spanish National Health System perspective.

**METHODS:**
- **Decision-analytic (DA) simulation** of the probability of experiencing an adverse effect and the direct costs produced by each treatment alternative.
- **Budget impact model (BIM):** developed to assess the mean treatment costs per patient, accounting for the time that SGX could save in the:
  1. operating room (OR),
  2. shortening the time to extubation,
  3. accelerating the movement of patients in and out of the OR


<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A (%)</th>
<th>Group B (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-related complications</td>
<td>14.1</td>
<td>15.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Hypovolemia</td>
<td>11.2</td>
<td>9.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>10.2</td>
<td>10.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.1</td>
<td>2.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2.0</td>
<td>2.0</td>
<td>-</td>
</tr>
</tbody>
</table>

Net Benefit:
- $339.26/37 cases
Cost-Effectiveness

RESULTS:

"In the routine reversal of patients, ROC SGX is associated with higher costs than the spontaneous reversal or neostigmine/atropine".

But, it is higher LYG (Life Years Gained) for SGX.

Cost-effectiveness range of SGX vs. neostigmine/atropine

- 13,260 and 4,976 per LYG

BIM (Budget Impact Model)

- SGX saves 108 - 171 minutes of OR time (Capacity: 1 - 2 more procedures)
- Total Budget Savings: $1,672.27 - $2,389.12 per OR per day.

Objectives:

- Sugammadex in the reversal of patients with neuromuscular block.
- Impact on the number of patients with residual neuromuscular block.
- Value in Health, 19(7), A366. doi:10.1016/S1098-3015(10)74801-4

Cost-Effectiveness

Objective:

The aim of the study is to determine the potential cost impact of use of Sugammadex.

In settings where patients have full neuromuscular recovery (Train-of-four ratio ≥ 0.9) prior to extubation, the economic impact of Sugammadex is related to a reduction in recovery and operating room (OR) staff times.

In settings where full neuromuscular recovery is not verified, economic impact primarily derives from avoided complications of residual neuromuscular blockade.

This study aimed to determine the potential cost impact of use of Sugammadex.

Cost-Effectiveness

Conclusion:

1. SGX would be a cost-effective alternative for the routine reversal of patients with NMB
2. Cost-saving strategy due to the increase of the turn over of the OR

Loss: $22,068.71 cost saving from treatment of complications of residual neuromuscular blockade.

Total cost saving strategy due to the increase of the turn over of the OR

Cost-Effectiveness

Results:

At the institutional level, Annual cost saving was $992.90 if all patients had full neuromuscular recovery in the OR prior to extubation.

A $22,068.71 cost saving from treatment of complications was estimated for Sugammadex versus Neostigmine.

Conclusions: Although cost of acquiring Sugammadex is considerably higher than Neostigmine, the cost offsets for hospitals might be substantial.

Cost-Effectiveness

Objective:

The aim of the study is to evaluate the clinical and economic impact of introducing a rocuronium–neostigmine–sugammadex strategy into a cisatracurium–neostigmine regimen for neuromuscular block (NMB) management.

Results:

- rocuronium–neostigmine–sugammadex strategy into a cisatracurium–neostigmine regimen reduced the average cost of NMB management by 36%, from $24.84/case to $15.89/case.
- Sugammadex: first-choice reversal drug (3%) exhibited:
  1. Significantly better TTO ratios at extubation (P<0.001)
  2. Discharged to the surgical ward (P=0.001) more rapidly than controls.

Cost-Effectiveness

Economic benefit in avoiding postoperative residual curarization (PORC)

- Average savings on ICU admissions $16,183.32 ($11,128.12–$28,483.27)

Conclusion

1. Eliminated PORC and associated morbidities
2. Reduced the costs of NMB management
3. Promoted rapid turnover of patients in operating rooms
4. Total cost-effectiveness counteracts the disadvantages of high "unit" cost.