Reversibility of rocuronium-induced profound neuromuscular blockade with sugammadex in neonates.

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Background
- Sugammadex is a selective relaxant binding agent specifically designed to encapsulate rocuronium, which can, therefore, promptly restore neuromuscular function regardless of any levels of neuromuscular block as the dose is increased.
- During rocuronium-induced profound neuromuscular blockade, sugammadex 4 mg kg⁻¹ is recommended to reverse rapidly in adult patients.
- However, the age-related change in efficacy of sugammadex and an adequate dose of sugammadex in pediatric patients has not been completely investigated.
- We observed sugammadex-facilitated recovery in 10 neonatal patients from deep rocuronium-induced neuromuscular block quantified by a mode of the post-tetanic count (PTC).

Neuromuscular monitoring using acceleromyography
1. After induction of anesthesia, contraction of the adductor pollicis muscle in response to ulnar nerve train-of-four (TOF) stimulation was acceleromyographically quantified using a TOF-Watch SX™.
2. Twitch responses were stabilized using 1 Hz single twitch stimulation for 1 min and calibrated using the CAL1 mode.
3. Thereafter, the ulnar nerve was repeatedly stimulated in a TOF mode at 2 Hz every 15 s.
4. When surgical procedure had been done and the 1-2 PTC reappeared, a bolus dose of sugammadex 4 mg kg⁻¹ was administered to facilitate the recovery to a TOF ratio of 0.9.

Rocuronium and sugammadex dosing
1. After stabilization of the TOF responses, all patients received an intravenous bolus dose of 0.6 mg/kg rocuronium.
2. Tracheal intubation was performed after the maximum neuromuscular blockade had been attained. Anesthesia was maintained with iv fentanyl (1 μg/kg), remifentanil and 2–3% end-tidal concentration of sevoflurane. Some patients were performed caudal block for postoperative analgesia.
3. Subsequently, intense rocuronium-induced block was determined every 6 min using the post-tetanic count (PTC). When the first response to the PTC stimulus was detected, 0.2 mg/kg rocuronium was additionally administered throughout the surgery.
4. When surgical procedure had been done and the 1-2 PTC reappeared, a bolus dose of sugammadex 4 mg kg⁻¹ was administered to facilitate the recovery to a TOF ratio of 0.9.

Measurement items
- The time from the administration of intubating dose of rocuronium to the maximum depression of T1 (Onset time).
- The time from the administration of intubating dose of rocuronium until recovery of the first detectable PTC (Time to PTC≥1).
- The time for facilitated recovery to a TOF ratio of 0.9 following sugammadex administration (Time to TOF=0.9).
- The time to recover to a TOF ratio of 0.9 following sugammadex administration (Time to TOF=0.9).
- The time from the administration of intubating dose of rocuronium to the maximum depression of T1 (Onset time).
- The time from the administration of intubating dose of rocuronium until recovery of the first detectable PTC (Time to PTC≥1).
- The time for facilitated recovery to a TOF ratio of 0.9 following sugammadex administration (Time to TOF=0.9).

Results
- The data from 6 patients were deleted from the study because of some troubles in neuromuscular monitoring like baseline drift and incomplete recovery of twitch responses. In results, the data from 4 neonate were analyzed as bellows.

Table 1

<table>
<thead>
<tr>
<th>Age (day)</th>
<th>Gender</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Onset time (sec)</th>
<th>Time to PTC≥1 (min)</th>
<th>Time to TOF 0.9 (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>M</td>
<td>52.5</td>
<td>4.1</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>M</td>
<td>48.4</td>
<td>3.8</td>
<td>69</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>F</td>
<td>45.2</td>
<td>2.5</td>
<td>117</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>M</td>
<td>48.9</td>
<td>3.8</td>
<td>39</td>
<td>34</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>23.8 (2.6)</td>
<td>M 3 : F 1</td>
<td>48.8 (2.6)</td>
<td>3.6 (0.6)</td>
<td>67.9 (30.7)</td>
<td>34.0 (6.8)</td>
</tr>
</tbody>
</table>

Discussion
- It was reported that sugammadex dose-dependently quickened the time to recover to a TOF ratio of 0.9 from deep rocuronium-induced neuromuscular blockade in adults (2 mg kg⁻¹ : 3.2 min vs. 4 mg kg⁻¹ : 1.7 min, Duvaldestin P. et al. Anesth Analg 2010; 110: 74).
- It is therefore recommended that the dose of sugammadex for the reversal of rocuronium-induced deep neuromuscular block is 4 mg/kg in adult patients.
- As shown in Table 1, the mean (SD) time from an administration of sugammadex to recover to a TOF ratio of 0.9 were 41.0 (16.4) s. All 10 patients were safely extubated and did not show any symptoms of recurarization. It is therefore suggested that 4 mg/kg of sugammadex may be an adequate dose for the reversal from rocuronium-induced deep block also in neonates.
- Sensitivity to rocuronium is significantly higher in neonates and infants than adults, as shown in differences in the effective doses of rocuronium between two generations (Fig 1).
  - Neuromuscular junction is not still mature in neonates and infants.
  - The number of nicotinic acetylcholine receptors may be considerably lower in neonates.
  - It is therefore suggested that required molecules of rocuronium to obtain the same depth of neuromuscular block may be less in neonates, when compared with adults.
  - Based on the idea, necessary molecules of sugammadex to adequately reverse the same depth of rocuronium-induced neuromuscular block may be less in infants.
  - It is therefore possible that a lower dose of sugammadex (< 4 mg/kg) may be sufficient to reverse rocuronium-induced deep block in neonates.

Conclusion
- This case study demonstrate that sugammadex 4 mg kg⁻¹ may adequately and rapidly reverse rocuronium-induced profound neuromuscular block even in neonates.
- Further studies are warranted to determine the optimum dosing of sugammadex in neonates.