Clinical observations on reversal of rocuronium-induced residual neuromuscular blockade by sugammadex after thoracic surgery

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Abstract

Objective: After thoracic surgery, a complete reversal of neuromuscular blockade (NMB) facilitates ventilatory movements and expectoration and enhances the possibility of early physiotherapy. Therefore, the aim of the present study was to evaluate the clinical usefulness of sugammadex for reversal of NMB after anaesthesia for thoracic surgery.

Design: prospective case series.

Setting: university hospital.

Participants: 49 patients undergoing thoracic surgical procedures (25 thoracotomies, 11 video-assisted thoracoscopies and 13 mediastinosciopies) were included.

Interventions: Rocuronium was used for intubation and maintenance of NMB under continuous monitoring with TOF Watch SX acceleromyograph. Residual NMB at the end of surgery was reversed by administration of sugammadex 2 mg/kg BW.

Main results: All patients had a residual curarisation at the end of surgery (TOF: 27.02 ± 25.9%). Time to 100% TOF recovery after sugammadex averaged 2.46 ± 0.58 minutes. Thirty three out of 49 patients had mild hypothermia at the end of surgery. There was no difference in time needed for TOF recovery to 100% between hypothermic and normothermic patients (hypothermic: 2.46 ± 2.9 minutes, normothermic: 1.81 ± 0.76 minutes, p = 0.29). Postoperative shivering occurred in 67% of the patients.

Conclusions: We conclude that sugammadex allows fast and complete recovery of the neuromuscular function after thoracic surgical procedures even if mild hypothermia was present.

Keywords: thoracic anaesthesia, sugammadex, rocuronium, residual curarisation

Introduction

Sugammadex is the first selective relaxant binding drug used for the reversal of neuromuscular blockade (NMB) [1-3]. The chemical structure of the drug corresponds to a modified gamma-cyclodextrin molecule with a hydrophobic cavity responsible for encapsulating aminosteroid NMB agents and forming a stable, water-soluble complex. Sugammadex forms a very tight complex with rocuronium and vecuronium at a binding ratio of 1:1 at molecular level. Adequate doses of sugammadex (2-16 mg/kg BW) allow the reversal of rocuronium blockade of any depth within 3 minutes [4-6]. The mechanism of action of sugammadex differs from that of anticholinesterase agents such as neostigmine and edrophonium, commonly used for NMB reversal, because it does encapsulate neuromuscular blocking agents. Sugammadex rapidly decreases the plasma level of unbound relaxant molecules, resulting in a concentration gradient that favours the movement of rocuronium or vecuronium away from the neuromuscular junction into the plasma. The sugammadex-neuromuscular blocking agent complex
is excreted by the kidneys. In addition to the rapid onset of action, the administration of sugammadex is free from the parasympathetic side effects of anticholinesterase agents.

After thoracic surgery, a complete reversal of NMB facilitates ventilatory movements and expectoration and enhances the possibility of early physiotherapy. There are numerous potential limitations of neostigmine, such as its extremely variable speed of action [7, 8], its inability to reverse a deep block because of its ceiling effect [9], or its propensity to cause neuromuscular weakness if administered once the recovery is nearly complete [10].

Therefore, the aim of the present study was to evaluate the clinical usefulness of sugammadex for reversal of NMB after anaesthesia for thoracic surgery.

Methods

During the period between June and September 2009, 49 patients were included in this prospective, observational study. 25 patients underwent thoracotomy, 11 underwent video-assisted thoracoscopy (VATS) and 13 had mediastinoscopy (MSC). The study was approved by the local medical ethics committee and patients’ written informed consent was obtained.

All patients had general anaesthesia. For induction fentanyl 2 µg/kg and propofol 2 mg/kg were administered intravenously. Intubation of the trachea was facilitated using rocuronium 1 mg/kg for thoracotomies and VATSs. For MSCs 0.5 mg/kg rocuronium was administered. After thoracic surgery, a complete reversal of NMB was required for tracheal extubation. Body temperature was noted before sugammadex administration. Times from sugammadex to TOF 100% as well as times to extubation were recorded. Complete recovery (defined by a TOF ratio > 100%) was required for tracheal extubation.

Statistical analysis: Means and standard deviations were calculated and are reported for all values. TOF values of the three operation groups were pooled for a first analysis and the time to 100% TOF was determined. Thereafter patients were dichotomized into two groups: TOF < 20% and TOF > 20%. In these two groups we compared recovery times to TOF 100% and times to extubation. In a post hoc analysis we also compared recovery times between patients with body temperatures < 36°C and > 36°C. For comparison we selected cases with similar (30% ± 5%) initial TOF values. Wilcoxon test was used for statistical analysis, p < 0.05 was accepted as statistically significant difference.

Results

Patients’ data and results according to the type of interventions are summarised in Table 1. Three patients undergoing thoracotomy and 1 patient undergoing VATS received incremental doses of rocuronium. TOF zero was not measured in any case at the end of surgery, and none of the patients recovered spontaneously to TOF 100%. The average of pooled TOF ratios before administration of sugammadex was 27.02 ± 25.9%. Time to 100% TOF recovery after sugammadex averaged 2.46 ± 0.58 (Ranges: 1-15.5) minutes.
Patients with < 20% TOF ratio needed longer to recover to 100% (2.7 ± 2.6 minutes) compared to patients with TOF > 20% (1.52 ± 0.58 minutes, p < 0.05). There were no differences concerning the time to extubation according to pre-sugammadex TOF ratios (TOF < 20%: 5.7 ± 5.7 minutes, TOF > 20%: 6.75 ± 6.79 min, p = 0.58).

Core temperatures at the end of surgery were 35.4 ± 0.4 ºC for thoracotomies, 35.6 ± 0.3 ºC for VATS and 36.0 ± 0.3 ºC for MSC. Selected TOF ratios before administration of sugammadex in hypothermic patients (n = 33) were 25.8 ± 23.7%, and in normothermic patients (n = 16), 28.2 ± 28.5% (p = 0.75). There was no difference in the time needed for TOF recovery to 100% (hypothermic: 2.46 ± 2.9 min, normothermic: 1.81 ± 0.76 min, p = 0.29). Postoperative shivering occurred in 92% of the patients with thoracotomies (n = 23), in 81% of the patients with VATS (n = 9) and in none of the patients with MSC. All shivering patients had core temperature below 36 ºC, mildly hypothermic.

Table 1. Patients’ data, characteristics of treatment and results

<table>
<thead>
<tr>
<th></th>
<th>Thoracotomy</th>
<th>VATS</th>
<th>MSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>15/10</td>
<td>5/6</td>
<td>8/5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.2 ± 6.9</td>
<td>40.2 ± 20.6</td>
<td>43.3 ± 15.2</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>70.7 ± 16.2</td>
<td>66.3 ± 16.0</td>
<td>74.3 ± 18.9</td>
</tr>
<tr>
<td>Total dose of rocuronium (mg)</td>
<td>82.6 ± 18.6</td>
<td>70.4 ± 15.5</td>
<td>40.0 ± 11.7</td>
</tr>
<tr>
<td>Repetition of rocuronium (number of cases)</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Time between last rocuronium and sugammadex (min)</td>
<td>74.04 ± 40.5</td>
<td>67.9 ± 20.3</td>
<td>39.0 ± 17.7</td>
</tr>
<tr>
<td>TOF % at administration of sugammadex</td>
<td>23.7 ± 21.5</td>
<td>46.5 ± 31.6</td>
<td>16.7 ± 21.3</td>
</tr>
<tr>
<td>Time from sugammadex until TOF 100% (min)</td>
<td>2.46 ± 2.9</td>
<td>1.54 ± 0.52</td>
<td>2.0 ± 0.87</td>
</tr>
<tr>
<td>Time from sugammadex until extubation (min)</td>
<td>8.0 ± 8.1</td>
<td>4.7 ± 1.88</td>
<td>3.9 ± 1.55</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>167.6 ± 63.8</td>
<td>132.3 ± 54.4</td>
<td>41.8 ± 17.7</td>
</tr>
<tr>
<td>Core body temperature at the end of anaesthesia (ºC)</td>
<td>35.4 ± 0.4 ºC</td>
<td>35.6 ± 0.3 ºC</td>
<td>36.0 ± 0.3 ºC</td>
</tr>
</tbody>
</table>

Means and standard deviations are reported. VATS indicates video-assisted thoracoscopy, MSC indicates mediastinoscopy.

Discussion

We administered sugammadex for reversal of rocuronium-induced residual neuromuscular blockage after different types of thoracic surgical procedures. To the best of our knowledge this is the first study to evaluate the efficacy and safety of sugammadex in patients undergoing thoracic surgical interventions. We believe that assessment of NMB reversal in this patient group is of clinical importance because it may influence early postoperative complications. It is known from previous clinical studies that respiratory complications are observed in 15-20% after lung resection surgeries. These respiratory complications develop in relation to inappropriate pain treatment, inefficient cough and hypoventilation leading to atelectasis [11, 12]. It is conceivable that an incomplete reversal of the neuromuscular block may lead to respiratory muscle weakness and therewith a decreased coughing activity and expectation as well as hypoventilation. It has been proven that residual neuromuscular block results in respiratory complications in the postoperative setting [13].

At the end of surgery, residual blockade was found in all cases necessitating pharmacological reversal before extubation. Consistent with previous reports [4-6], administration of sugammadex resulted in a complete reversal of the neuromuscular block within 3 minutes as assessed by AMG monitoring and allowed ideal circumstances for extubation within 8 minutes on average after thoracotomies and within 5 and 4 minutes after VATS and MSC respectively (Table 1). Hypothermia did not influence the efficacy of sugammadex.

Based on the above, one might assume that administration of sugammadex would be ideal and may be advised routinely because it allows better ventilatory movements and expectation in the early postoperative phase and enhances the possibility of early physiotherapy without significant side effects. We observed after reversal of NMB by sugammadex that postoperative shivering occurred in a large proportion of patients after thoracotomies and VATSs. Shivering occurred in conjunction with core hypothermia measured at the end of surgery. It is known from previous observations that general anesthesia results in a decrease of core temperature by approximately 1-3 ºC and this decrease is most prominent 60 minutes after initiation of general anesthesia [14, 15]. Despite intraoperative warming of the lower part of the body by forced air system, mild hypothermia developed in our patients who underwent thoracotomies and VATSs since the vast majority of these procedures lasted for more than 2 hours. It is known that drugs used for
general anesthesia do decrease the shivering threshold [14]. It is important to note, that although core hypothermia develops frequently after thoracic surgical procedures [14], such a large proportion of postoperative shivering is not observed during the clinical practice. It is conceivable that if a fast and complete reversal of the NMB occurs at the end of anesthesia caused by sugammadex, the combination of the decreased shivering threshold along with core hypothermia may result in more pronounced shivering than usual. In fact, postoperative shivering has to be avoided because it increases metabolic needs, decreases the thermal comfort of the patients in the early postoperative period [16] and may also result in cardiac complications [16].

In addition, hypothermia is known to prolong residual NMB following the administration of non-depolarising NMB agents and may increase the risk of severe complications such as critical respiratory events or bronchoaspiration [17] if patients were extubated before restoration of NM function [18, 19]. In addition, increased oxygen demand by shivering may challenge respiratory capacity that cannot react efficiently to hypoxaemia under residual neuromuscular block [20].

The results of the present study raise the question whether the administration of sugammadex for rapid reversal of NMB is appropriate in mildly hypothermic patients, knowing that shivering may occur, or we should allow patients to recover spontaneously from the NMB and warm them up as much as possible before extubation. The better choice, of course, would be to maintain normal core temperature during surgery by improving the efficacy of patients’ warming, for instance by administering combined preventive measures (preshowing and administration of heating blankets) to avoid core hypothermia [21]. However, the development of mild hypothermia during long thoracic surgical procedures is not always avoidable; therefore the possibility of postoperative shivering should be taken into account when antagonising residual NMB with sugammadex in these situations.

We see one optimal field for using sugammadex for routine reversal of NMB after thoracic interventions and that is fast track thoracic surgery, and especially MSC. The concept of fast track procedures includes a multimodal approach that contains minimally invasive surgical technique, optimal pain control and aggressive postoperative rehabilitation by early physiotherapy and deambulation [22].

We conclude that sugammadex allows fast and complete recovery of the neuromuscular function after thoracic surgical procedures.

Conflict of interest
Nothing to declare

References
Observații clinice privind antagonizarea cu sugammadex a blocului neuromuscular cu rocuronium în chirurgia toracică

Rezumat

Obiectiv: După intervențiile chirurgicale pe torace, antagonizarea completă a blocului neuromuscular (BNM) facilitează mișcările ventilatorii și expectoratia, grăbind instituirea fizioterapiei. De aceea, scopul studiului de față a fost să evaluate utilizarea clinică a sugammadex-ului pentru antagonizarea BNM după anestezia pentru chirurgia toracică.

Design: Studiu prospectiv de cohortă

Loc: Spitalul Universitar

Participanți: 49 de pacienți cu intervenții chirurgicale pe torace (25 toracotomii, 11 toracoscopii video-asistate și 13 mediastinoscopii)

Metodă: BNM necesar pentru intubare și menținerea anesteziei realizat prin administrarea de rocuronium a fost monitorizat continuu cu ajutorul unui acceleromiograf TOF Watch SX. BNM rezidual prezent la sfârșitul operației a fost antagonizat cu sugammadex 2 mg/kg.

Rezultate: Toți pacienții au prezentat o curarizare reziduală la sfârșitul operației (TOF: 27.02 ± 25.9%). Timpul până la o recuperare TOF 100% după sugammadex a fost, în medie, de 2.46 ± 0.58 min. Din totalul de 49 pacienți, 33 au prezentat o hipotermie ușoară la sfârșitul operației. Nu s-au constatat diferențe în privința timpului necesar pentru recuperarea TOF 100% între pacienții hipotermici și cei normotermici (hipotermici: 2.46 ± 2.9 min, normotermici: 1.81 ± 0.76 min, p = 0.29). Frisonul s-a instalat postoperator la 67% dintre pacienți.

Concluzii: Administriarea de sugammadex asigură o recuperare rapidă și completă a funcției neuromusculare după chirurgia toracică, inclusiv în prezența hipotermiei.

Cuvinte cheie: anestezie toracică, sugammadex, rocuronium, curarizare reziduală