The use of sugammadex for the reversal of vecuronium-induced neuromuscular block following intracranial surgery

Zbigniew Karwacki, Seweryn Niewiadomski, Marta Rzaska

Department of Neuroanaesthesiology, Medical University of Gdańsk, Poland

Abstract

Background: Total intravenous anaesthesia with propofol and remifentanil is widely used in neuroanaesthesiology and enables the quick recovery and early neurological assessment of patients. The administration of muscle relaxants carries a risk of residual relaxation following surgery. The administration of a suitable dose of sugammadex reverses the neuromuscular block irrespective of its depth and has none of the side effects associated with acetylcholinesterase inhibitors. The aim of the present study was to evaluate the usefulness of sugammadex for the reversal of vecuronium-induced effects following intracranial surgery.

Method: The study involved 38 women who underwent supratentorial tumour removal. These women were randomly divided into two groups. Total intravenous anaesthesia with propofol and remifentanil using target-controlled infusion was administered according to the Schnider and Minto models, respectively. Endotracheal intubation was performed after the target concentrations of propofol and remifentanil reached 4 µg mL⁻¹ and 4 ng mL⁻¹, respectively. Vecuronium (100 µg kg⁻¹) was administered, and no response to TOF stimulation was observed. Relaxation was continued via the continuous infusion of vecuronium (0.8–1.2 µg kg⁻¹ min⁻¹) to provide a TOF of 2 throughout the surgery. In group I, neuromuscular conduction was restored with intravenous sugammadex (2 mg kg⁻¹), whereas in group II, no reversal agents were administered.

Results: The times of the return of spontaneous breathing, extubation, eye opening (both spontaneous and in response to a verbal command) were found to be longer in group II than group I.

Conclusion: The use of sugammadex following craniotomy accelerates the achievement of optimal extubation conditions.

Key words: neuromuscular block, reversal agent, sugammadex, craniotomy, target-controlled infusion
into two groups of 19 individuals each. The exclusion criteria were obesity, cardiovascular diseases, diabetes mellitus, and kidney and liver failure.

Forty-five minutes prior to anaesthesia, the patients were orally premedicated with 0.2 mg kg⁻¹ midazolam. Anaesthesia was induced and maintained with total intravenous anaesthesia with propofol and remifentanil using target-controlled infusion. Perfusor Space infusion pumps (B. Braun Melsungen AG, Melsungen, Germany) were applied, and the Schnider and Minto models were adhered to for the administrations of propofol and remifentanil, respectively. During the procedure, the target concentrations of propofol and remifentanil in the brain tissue were adjusted such that the haemodynamic parameters did not exceed 20% of the baseline values. Propofol and remifentanil were infused until the final skin sutures were placed. Endotracheal intubation was performed after the target concentrations of propofol and remifentanil reached 4 µg mL⁻¹ and 4 ng mL⁻¹, respectively. Vecuronium (100 µg kg⁻¹ of) was administered, and no response to TOF stimulation was observed. Muscle relaxation was continued via the continuous infusion of vecuronium (0.8–1.2 µg kg⁻¹ min⁻¹) to provide a TOF of 2 during the surgery. Vecuronium was infused until the completion of the surgery. The degree of neuromuscular block was monitored using an acceleromyograph (TOF-Watch, Orga-
of the surgery. The degree of neuromuscular block was maintained with normoventilation (ETCO₂ within the range of 35−39 mm Hg), the lungs were ventilated with a 1:1 mixture of air and oxygen in a half-closed circular system.

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of the surgery. The degree of neuromuscular block was maintained with normoventilation (ETCO₂ within the range of 35−39 mm Hg), the lungs were ventilated with a 1:1 mixture of air and oxygen in a half-closed circular system.

In group I, the neuromuscular conduction after surgery was restored with intravenous sugammadex (Bridion, MSD, Dublin, Ireland) at a dose of 2 mg kg⁻¹. In group II, no reversal agents were used.

Thirty minutes prior to the completion of surgery, an intravenous infusion of tramadol (100 mg) and metamizole (2.5 g) was initiated to ensure early postoperative analgesia. The heart rate (HR), systolic (SysBP), diastolic (DiaBP) and mean (MABP) arterial blood pressures and the rectal core temperature were continuously monitored. The body temperature was maintained within the range of 37.5 ± 0.5°C using a warming system.

The values of the parameters were analysed at the following points of anaesthesia: TO (baseline), T1 (initiation of propofol and remifentanil infusion), T2 (target concentrations of propofol and remifentanil reached), T3 (intubation), T4 (one minute after intubation), T5 (two minutes after intubation), T6 (head fixation in the Mayfield head clamp), T7 (one minute after head fixation), T8 (prior to the skin incision), T9 (one minute after the skin incision), T10 (before bone flap removal), T11 (one minute after bone flap removal), T12 (before the opening of the opening), T13 (one minute after meninx opening), T14 (access stage), T15 (tumour resection stage), T16 (before meninx closure), T17 (one minute after meninx closure), T18 (before bone flap insertion), T19 (one minute after insertion), T20 (initiation of the soft integument closure), T21 (completion of the skin sutures), T22 (administration of the sugammadex) T23 (extubation), and T24 (3 minutes after extubation). Moreover, analyses of the total consumptions of propofol, remifentanil and vecuronium, the time of the return of spontaneous breathing return at V₁ > 4 mL kg⁻¹, the time to extubation (TOF-R > 0.9), and the times of spontaneous and verbally commanded eye opening were performed.

The statistical analyses were performed using GraphPad InStat, version 3.10 (GraphPad Software Inc., La Jolla, USA). The results are presented as the means ± the SD. The distributions of the data were examined with the Kolmogorov-Smirnov test. Dunnett’s tests were used for the intergroup comparisons, and Mann-Whitney tests were used for intergroup comparisons. P < 0.05 was considered statistically significant.

RESULTS
The study groups did not differ in age, height or body weight (Table 1). The distribution of the natures of the proliferative processes is presented in Fig. 1. The distributions of the target concentrations of propofol and remifentanil are provided in Table 2. The statistical analysis did not reveal any significant intergroup differences across the successive stages of anaesthesia.

Table 1. Characteristics of the study population (mean ± SD)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I</th>
<th>Group II</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>52.1 ± 14.1</td>
<td>53.1 ± 18.1</td>
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<tr>
<td>Height (m)</td>
<td>1.66 ± 0.05</td>
<td>1.71 ± 0.06</td>
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<tr>
<td>Body mass (kg)</td>
<td>64.3 ± 19.7</td>
<td>70.8 ± 13.2</td>
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No inter-group differences in HR, SysBP, DiaBP, MABP or core temperature were observed at the individual observation points (Figs 2–5).

Moreover, there were no differences in the consumptions of propofol, remifentanil or vecuronium (Table 3).

The times of the return of spontaneous breathing, extubation, and spontaneous and verbally commanded eye opening were found to be longer in group II than in group I (Table 4).

DISCUSSION
Data from the Central Brain Tumour Registry of the United States reveal that more than 64 thousand new disease cases occurred in 2011, and 80% of these cases involved...
Table 2. Modes of the propofol and remifentanil infusions in the study groups*

<table>
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<th>T2</th>
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<td>2.3</td>
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<td>µg mL⁻¹</td>
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<tr>
<td>Remifentanil</td>
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<td>ng mL⁻¹</td>
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<td>µg mL⁻¹</td>
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<tr>
<td>Remifentanil</td>
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<td>1.1</td>
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<td>4.1</td>
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<td>2.7</td>
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<tr>
<td>ng mL⁻¹</td>
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<td>(0.0)</td>
<td>(1.4)</td>
<td>(1.5)</td>
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<td>(1.3)</td>
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</table>

* The data are presented as the means (SD)
Figure 2. Mean heart rates (the bars indicate the standard deviations)

Figure 3. Mean systolic arterial blood pressures (the bars indicate the standard deviations)

Figure 4. Mean diastolic arterial blood pressures (the bars indicate the standard deviations)
These criteria are fulfilled by sugammadex [22]. Used in a dose of 2 mg kg\(^{-1}\), sugammadex shortened the time to reach optimal extubation conditions. The times to the restoration of complete conduction following deep block induced with rocuronium or vecuronium are dose-dependent [23]. Sugammadex at 2 mg kg\(^{-1}\) restored complete conduction following vecuronium-induced block within 2.7 minutes, whereas neostigmine at a dose of 50 µg kg\(^{-1}\) requires 17.9 minutes [24]. The discrepancies with our observations likely resulted from the use of different methods of anaesthesia and procedures. Due to its high cost, the use of sugammadex is limited to certain indications [22]. Paton and colleagues [25] noted the potential economic benefits that result from the markedly shorter time required for the care of patients who receive sugammadex compared to patients who are administered neostigmine and glycopyrrolate.

CONCLUSION

The use of sugammadex used after craniotomy accelerates the achievement of optimal extubation conditions.

ACKNOWLEDGMENTS

1. The authors declare no financial disclosure.
2. The authors declare no conflict of interest.

References:


Table 3. Comparison of the consumptions of anaesthetic agents between the study groups*

<table>
<thead>
<tr>
<th>Agent</th>
<th>Group I</th>
<th>Group II</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction dose of propofol (mg)</td>
<td>109.4 ± 21.2</td>
<td>127.5 ± 21.2</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Induction dose of remifentanil (µg)</td>
<td>85.9 ± 21.2</td>
<td>95.4 ± 18.4</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Total dose of propofol (mg)</td>
<td>1410 ± 405</td>
<td>1490 ± 390</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Total dose of remifentanil (µg)</td>
<td>1226.7 ± 405</td>
<td>1338 ± 412</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Total dose of vecuronium (mg)</td>
<td>14.6 ± 3.4</td>
<td>15.1 ± 2.9</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

The data are presented as the means ± SD

Table 4. Intergroup comparisons of the times of anaesthesia and the returns of clinical markers of neuromuscular block*

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Group I</th>
<th>Group II</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of anaesthesia</td>
<td>108.5±21.2</td>
<td>125.5±21.3</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Return of spontaneous breathing</td>
<td>5.8 ± 3.8</td>
<td>13.2 ± 2.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Extubation (TOF-R &gt; 0.9)</td>
<td>9.9 ± 2.3</td>
<td>16.8 ± 3.4</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Eye opening to verbal command</td>
<td>10.4 ± 5.6</td>
<td>19.1 ± 3.6</td>
<td>&gt; 0.05</td>
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<tr>
<td>Spontaneous eye opening</td>
<td>13.2 ± 4.9</td>
<td>21.4 ± 4.5</td>
<td>&gt; 0.05</td>
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</table>

* The data are presented as the mean ± the standard deviation

Figure 5. Mean arterial blood pressures (the bars indicate the standard deviations)


Corresponding author: Zbigniew Karwacki, MD, PhD
Department of Neuroanaesthesiology
Medical University of Gdańsk
ul. Smoluchowskiego 17, 80–214 Gdańsk, Poland
e-mail: zk@ujmed.pl

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