Reversal of Neuromuscular Blockade by Sugammadex after Continuous Infusion of Rocuronium in Patients Randomized to Sevoflurane or Propofol Maintenance Anesthesia

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Background: Sugammadex rapidly reverses neuromuscular blockade induced by bolus rocuronium doses, but it has not been investigated after continuous rocuronium infusion in surgical patients. We therefore examined the clinical effect of sugammadex for neuromuscular blockade induced by continuous rocuronium infusion in adults undergoing surgery under maintenance anesthesia with sevoflurane or propofol.

Methods: This four-center, comparative, parallel-group study, randomly assigned 52 adult patients (American Society of Anesthesiologists Class I-III) to maintenance anesthesia with sevoflurane or propofol. Neuromuscular blockade was induced by bolus injection of 0.6 mg/kg rocuronium followed by continuous infusion of 7 µg · kg⁻¹ · min⁻¹ rocuronium adjusted to maintain a neuromuscular blockade depth of zero response to train-of-four and a posttetanic count of no more than 10 responses. A single dose of 4 mg/kg sugammadex was administered at first twitch (T₁) and a posttetanic count of no more than 10 responses. A single neuromuscular blockade depth of zero response to train-of-four ratio of 0.9.

Results: Median recovery time from start of sugammadex administration to a train-of-four ratio of 0.9 in the sevoflurane and propofol groups was 1.3 and 1.2 min, respectively. The estimated difference in recovery time between groups was 9 s (95% confidence interval −6 to 26 s), entirely within the predefined equivalence interval. Median plasma rocuronium concentration just before sugammadex administration was 33% lower during maintenance anesthesia with sevoflurane than with propofol. Sugammadex was well tolerated. One adverse event (procedural hypotension) was considered to be probably related to sugammadex.

Conclusions: Single-dose sugammadex (4 mg/kg) after continuous rocuronium infusion is equally effective and well tolerated during maintenance anesthesia with sevoflurane or propofol

REVERSAL agents are often used to ensure the reversal of nondepolarizing neuromuscular blockade (NMB). The most widely used are the acetylcholinesterase inhibitors, neostigmine, and edrophonium. However, these agents are only partially effective against profound NMB, especially in the presence of volatile anesthetics such as sevoflurane, and may also be associated with adverse effects, such as cholinergic cardiovascular and gastrointestinal events.

Sugammadex is a modified gamma cyclodextrin specifically designed for the reversal of NMB induced by the steroidal neuromuscular blocking agent (NMBA) rocuronium. Sugammadex acts by encapsulating unbound rocuronium molecules and reducing their concentration at the neuromuscular junction. Studies in surgical patients have shown that sugammadex rapidly and safely reverses rocuronium- and vecuronium-induced NMB.

Unlike acetylcholinesterase inhibitors, sugammadex is also effective in the reversal of profound NMB. In previous studies with sugammadex, patients received NMBA as single or repeat bolus doses. No safety or clinical effect data have been published thus far on sugammadex after continuous infusion of rocuronium, although rocuronium infusion provides stable drug concentrations with a constant degree of paralysis, and its use has become increasingly common. However, continuous infusion of rocuronium has been demonstrated to significantly increase the recovery time after NMB compared with single bolus doses. In this study by Jellish and coworkers, the median recovery index (time required for the first twitch [T₁] of the train-of-four [TOF] to recover from 25% to 75% of baseline) after a single bolus dose of rocuronium was 17 min compared with a median recovery index of 24 min after continuous rocuronium infusion. Furthermore, some patients experienced spontaneous recovery times to a TOF ratio of 75% of over 70 min after infusion dosing of rocuronium, suggesting that patients undergoing prolonged infusion are likely to require the administration of a reversal agent.

In clinical practice, rocuronium is administered in combination with volatile agents such as sevoflurane, or with intravenously administered agents such as propofol. The neuromuscular-blocking effect of several NMBA, including rocuronium, are potentiated under sevoflurane anesthesia in contrast to propofol-based anesthesia; therefore, the properties of NMBA under those two anesthetic regimens have been extensively investi-
gated and compared.\textsuperscript{7,8} These studies have shown a delayed recovery induced by acetylcholinesterase inhibitors during sevoflurane anesthesia as compared to propofol anesthesia.\textsuperscript{8} The effects of sugammadex under maintenance anesthesia with sevoflurane and propofol have recently been investigated, but only after administration at reappearance of the second twitch of the TOF after a single bolus dose of rocuronium (representing a time of partial spontaneous recovery of neuromuscular function).\textsuperscript{9} This situation does differ from continuous infusion, as illustrated by the potentiating effect of volatile anesthetics, which is clinically most significant during infusion.\textsuperscript{7,10} Also, the rapid reversal of sugammadex has been explained by redistribution of rocuronium; during continuous infusion, the ability to redistribute the drug is decreased as a result of distribution compartment saturation.\textsuperscript{11} Thus, the question still remains to be answered whether volatile anesthetics do influence the clinical effect and safety of sugammadex when used for reversal from neuromuscular blockade induced by continuous infusion of rocuronium.

The primary objective of the present trial was to show equivalence in recovery from NMB after a single dose of sugammadex (4 mg/kg) administered at T\textsubscript{1} 3–10\% of baseline after continuous infusion of rocuronium in patients receiving maintenance anesthesia with propofol or sevoflurane. Secondary objectives were to investigate safety under these treatment conditions and to compare plasma rocuronium concentrations between groups before sugammadex administration.

Materials and Methods

Study Design and Patient Selection

This phase III, safety assessor-blinded trial (Nebula) was conducted between December 2006 and March 2007 at four surgical centers in Germany (Reutlingen, Kiel, Berlin, and Marburg). The protocol was centrally approved by the Independent Ethics Committee of the Marburg University Hospital, and written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent revisions, the International Conference on Harmonization guidelines, Good Clinical Practice, and current regulatory recommendations.

Patients were enrolled if they were aged 20–65 yr, American Society of Anesthesiologists physical status Class I–III, and scheduled to undergo surgery under general anesthesia with an expected duration of 2–5 h and requiring neuromuscular relaxation with an NMBA. Exclusion criteria were: neuromuscular disorder affecting NMB; an anatomical malformation that predicted difficult intubation; history of malignant hyperthermia, significant renal dysfunction, or allergy to medications used during general anesthesia; concurrent use of medications known to interfere with NMBAs (e.g., antibiotic, anticonvulsants, magnesium salts); and women who were pregnant, breastfeeding, or of childbearing potential and not using an adequate method of contraception.

Group Assignment

Patients were randomized to maintenance anesthesia with either propofol or sevoflurane by using a central randomization list system. Anesthesia was induced with an intravenous (IV) opioid and IV propofol and maintained with an IV opioid and either sevoflurane (target 1.5 vol\% end tidal) or propofol. Propofol and sevoflurane were administered according to routine clinical practice.

Study Procedures

Before tracheal intubation, all patients received a single IV bolus dose of 0.6 mg/kg rocuronium administered within 10 s into a fast-running saline infusion. This was followed by continuous infusion of 7 \( \mu \)g \cdot kg\(^{-1}\) \cdot min\(^{-1}\) rocuronium, with the dose adjusted to maintain a depth of NMB of zero response to TOF and a posttetanic count of no more than 10 responses during a period of at least 90 min. At the end of the rocuronium infusion, patients received a single bolus dose of 4 mg/kg sugammadex at a target NMB of T\textsubscript{1} of 3–10\%. Patients were not permitted to receive a second dose of sugammadex or an NMBA other than rocuronium during the monitoring of neuromuscular transmission. If further muscle relaxation was required after the administration of sugammadex, a nonsteroidal NMBA could be administered.

Neuromuscular function was monitored by acceleromyography at the adductor pollicis muscle using the TOF-Watch\textsuperscript{®} SX (Schering-Plough, Dublin, Ireland). After induction of anesthesia, the TOF-Watch\textsuperscript{®} SX was affixed to the arm and stabilized and calibrated in the operating room. Repetitive TOF stimulation was applied at the ulnar nerve every 15 s until the end of anesthesia. Neuromuscular data were collected via a transducer affixed to the thumb and transferred to a computer by means of the TOF-Watch\textsuperscript{®} SX Monitoring Program. Practical guidance on the set-up of this acceleromyographic technique was provided to each trial site to reduce variability.

Safety

All adverse events (AEs) and serious AEs, regardless of possible causal relationship with treatment, including signs of recurrent or residual NMB, were recorded and coded using MedDRA version 10.0 (International Federation of Pharmaceutical Manufacturers and Associations, Geneva, Switzerland). All subjective safety parameters were assessed by an investigator blinded to treatment randomization. Blood pressure and heart rate were recorded before administration of rocuronium before and at 2, 5, 10, and 30 min after administration of sugammadex, and at the postanesthetic visit (at least 10 h after administration of sugammadex). Respiratory rate was...
reported at screening and at the postanesthetic visit. Oxygen saturation (monitored by pulse oximetry with alarm set at less than 90% SpO₂) and respiratory rate were monitored for at least 1 h after recovery of the TOF ratio to 0.9. Any clinical evidence of NMB was reported. Continuous electrocardiographic monitoring of the QT-interval was undertaken intraoperatively and postoperatively, consistent with the routine anesthetic practices at the trial sites. Venous blood samples (10 ml per sample) for analysis of routine biochemistry and hematology variables (plus haptoglobin for possible hemolysis) were drawn before administration of rocuronium and at the postanesthetic visit. Abnormal laboratory/electrocardiogram/vital sign findings were recorded as AEs, depending on whether they were considered clinically relevant in the opinion of the investigator.

**Plasma Concentration Analysis**

Two venous blood samples (2 ml per sample) were drawn from each patient for plasma concentration analysis of rocuronium (one before administration of rocuronium and one within 2 min before administration of sugammadex). Rocuronium concentrations in plasma were determined by using a validated liquid chromatographic assay method with mass spectrometric detection at the Department of Bioanalytics, Schering-Plough, The Netherlands. Linearity was assessed over the range of 2 to 1,000 ng/ml. Lower limit of quantification was 2 ng/ml. The intraassay coefficient of variation was 3.2–11.2%, and the interassay coefficient of variation was 5.9–14.5%. The assay was carried out in full compliance with Good Laboratory Practice regulations.

**Statistical Analysis**

The primary clinical effect variable was time from start of administration of sugammadex to recovery of the TOF ratio to 0.9. The confidence interval (CI) approach was used to demonstrate equivalence in recovery of the TOF ratio to 0.9 between the two treatment groups.9 Equivalence was claimed if the two-sided 95% CI for the difference between the two groups was within the interval ranging from −1 min to +1 min. The 95% CI was obtained by using a nonparametric approach, with the estimated difference between treatment groups and corresponding two-sided 95% CI calculated according to the methods of Hodges-Lehmann and Moses.12 Other neuromuscular variables were time to recovery of the TOF ratio to 0.8 and 0.7, which were analyzed as for the primary clinical effect variable, and twitch height of T₁ at the start of sugammadex administration, which was not analyzed statistically.

The primary clinical effect analysis was performed on the intent-to-treat population, which included all randomized patients who received sugammadex and had at least one clinical effect measurement. All analyses were performed using SAS® version 9.1 (SAS Institute, Cary, NC).

Results

Patients

A total of 52 patients were initially randomized to receive maintenance anesthesia with either sevoflurane (n = 26) or propofol (n = 26). The dose of propofol administered for induction was in the 1.6–3.6 mg/kg range, and the propofol maintenance dose ranged from 0.5–10.2 mg · kg⁻¹ · h⁻¹. The target sevoflurane concentration was 1.5 vol% end tidal. Actual end tidal concentrations of sevoflurane were in the 0.5–3.0 vol% range; during the study period (time interval from sugammadex administration until attainment of a TOF ratio of 0.9), the sevoflurane concentration was constant for 17 of the 26 subjects, for whom mean (SD) sevoflurane concentration was 1.6% (0.3%). For one subject, administration of sevoflurane was stopped 9.5 min before sugammadex was administered, and the sevoflurane concentration varied after sugammadex between 0.5% and 2.7% for the remaining 8 subjects.

One patient in the propofol group discontinued from the study before anesthesia was started and before sugammadex was administered because of pretreatment AEs (severe vomiting and nausea) and was excluded from the intent-to-treat analysis. All other patients were subsequently treated, and none were discontinued prematurely. Core body temperature was monitored according to local procedures, for example via the nose or bladder, and maintained at 35°C or higher, except for one subject who was not covered due to surgery. Mean peripheral temperature (monitored continuously at the skin of the hand) was 35°C and was maintained at 32°C or higher in 48 of the 52 patients; for four patients, the temperature during set up was between 31.4°C and 31.8°C, but no abnormalities in the time to recovery were observed in these patients. Patient baseline characteristics are reported in table 1. Baseline characteristics were generally similar across the treatment groups, although the sevoflurane group included more American Society of Anesthesiologists Class II and fewer American
Table 1. Patient Baseline Characteristics (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>ASA Class</th>
<th>n (%)</th>
<th>Sevoflurane (n = 26)</th>
<th>Propofol (n = 25)</th>
<th>Total (n = 51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6 (23)</td>
<td>12 (48)</td>
<td>18 (35)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>19 (73)</td>
<td>11 (44)</td>
<td>30 (59)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1 (4)</td>
<td>2 (8)</td>
<td>3 (6)</td>
<td></td>
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ASA – American Society of Anesthesiologists; SD – standard deviation.

Society of Anesthesiologists Class I patients compared with the propofol group.

Clinical Effect

Recovery times from the start of sugammadex administration are summarized in table 2. All 51 subjects recovered to a TOF ratio of 0.9 within 2.5 min. Median recovery time from start of sugammadex administration to a TOF ratio of 0.9 was 1.3 min in the sevoflurane group and 1.2 min in the propofol group. The estimated difference in recovery time between the two groups was 9 s (95% CI, –6 to 20 s). This CI is entirely within the predefined equivalence interval; therefore, equivalence was shown. Times to recovery to TOF ratios of 0.8 and 0.7 from start of sugammadex administration were also equivalent between groups. Median time to recovery to a TOF ratio of 0.8 was 1.2 min in the sevoflurane group and 1.1 min in the propofol group, with an estimated difference of 6 s (95% CI, –2 to 16). Median time to recovery to a TOF ratio of 0.7 was 1.0 min in the sevoflurane group and 0.9 min in the propofol group, with an estimated difference of 6 s (95% CI, –3 to 13). The median infusion rate of rocuronium was slightly slower and the duration of infusion was shorter under sevoflurane compared with propofol maintenance anesthesia (0.45 vs. 0.46 mg · kg⁻¹ · h⁻¹ and

Table 2. Recovery Times from Start of Sugammadex Administration to a TOF Ratio of 0.9, 0.8, and 0.7 (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Time to Recovery, min</th>
<th>Sevoflurane (n = 26)</th>
<th>Propofol (n = 25)</th>
<th>Between-group Difference (95% CI), s</th>
</tr>
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<tbody>
<tr>
<td>TOF ratio of 0.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>1.3 (0.6–2.4)</td>
<td>1.2 (0.7–2.4)</td>
<td>9 (–6 to 20)</td>
</tr>
<tr>
<td>TOF ratio of 0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>1.2 (0.6–2.2)</td>
<td>1.1 (0.7–2.0)</td>
<td>6 (–2 to 16)</td>
</tr>
<tr>
<td>TOF ratio of 0.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>1.0 (0.6–1.7)</td>
<td>0.9 (0.7–2.0)</td>
<td>6 (–3 to 13)</td>
</tr>
<tr>
<td>TOF = train-of-four.</td>
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Table 3. Depth of Neuromuscular Blockade during Continuous Infusion of Rocuronium for a Period of at Least 90 min (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Depth of Neuromuscular Blockade*</th>
<th>Sevoflurane (n = 26)</th>
<th>Propofol (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10 PTC, n (%)</td>
<td>24 (92)</td>
<td>23 (92)</td>
</tr>
<tr>
<td>10 PTC u/i/20% T₁, n (%)</td>
<td>2 (8)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>&gt; 20% T₁, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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* For more than half of the total duration of continuous rocuronium infusion. PTC = posttetanic count.

2.1 vs. 2.6 h, respectively). Sugammadex was administered at a similar level of NMB in both groups (mean T₁ of 5.9% in the sevoflurane group and 6.7% in the propofol group). The available data did not indicate changes in maintenance anesthesia that affected the recovery to TOF ratios of 0.7, 0.8, or 0.9.

Plasma Concentrations

Maintenance anesthesia treatment had a statistically significant effect on plasma rocuronium concentration as measured just before administration of sugammadex (P < 0.05). Median plasma concentrations of rocuronium were 33% lower in the sevoflurane group than in the propofol group (959 [range 684–2,680] vs. 1,680 [range 951–2,650] ng/ml). Variability in concentrations (geometric coefficient of variation) was similar in both groups (30% in the sevoflurane group and 31% in the propofol group). Despite this difference in rocuronium plasma concentrations between groups, neuromuscular blockade was maintained to a similar degree during rocuronium infusion in the propofol and sevoflurane groups (table 3).

Safety

A total of 46 patients had at least one AE (92% of patients in the sevoflurane group and 88% in the propofol group). The most frequently reported AEs were procedural pain, constipation, and nausea. No serious AEs were reported, and no deaths occurred. No patients discontinued from the trial because of an AE. One patient had an AE that was considered by the investigator to be probably related to sugammadex administration. This was a report of procedural hypotension in a patient in the sevoflurane group that occurred 2 min after administration of sugammadex. The subject’s systolic/diastolic blood pressure dropped from 102/65 mmHg at baseline to 73/47 mmHg at the 2-min time point. The AE was considered to be mild in intensity and lasted 3 min. By 5 min postdose, the patient’s blood pressure had recovered to 96/62 mmHg. No markedly abnormal heart rate values (defined as being 120 beats/min or more or 50 beats/min or less, and an increase or decrease of 15 beat/min, respectively, from baseline) or alterations to the QT-interval were reported for any patient. There
were no clinically relevant differences between groups with regard to laboratory parameters, vital signs, or respiratory rate. There were no reports of residual NMB or reoccurrence of NMB based on neuromuscular monitoring. In addition, no patient had clinical evidence of residual NMB or reoccurrence of NMB (for example, respiratory difficulties) as determined by the investigator. In addition, there were no reports of changes in breath frequency or oxygen saturation during the study that would be suggestive of severe reoccurrence of NMB.

Discussion

This study showed that a single dose of sugammadex (4 mg/kg) administered at T1 3–10% after continuous infusion of rocuronium was equally effective for the reversal of NMB in patients, regardless of whether anesthesia was maintained with sevoflurane or propofol. Sugammadex has been previously shown to reverse NMB induced by continuous infusion of rocuronium in Rhesus monkeys. However, this was the first study in surgical patients to show that sugammadex effectively reverses NMB induced by continuous infusion of an NMBA. The median recovery time from the start of sugammadex administration to a TOF ratio of 0.9 was similar in the sevoflurane and propofol groups (1.3 and 1.2 min, respectively). These findings are in agreement with those from a recent study showing that recovery times after sugammadex administration (after a single bolus dose of rocuronium) are similar during sevoflurane and propofol maintenance anesthesia. In this study by Vanacker et al., mean time to recovery of the TOF ratio to 0.9 was 1.8 min in patients receiving 2.0 mg/kg sugammadex at reappearance of the second twitch of the TOF. In our study, reversal was carried out at a T1 value of less than 10%, which usually represents a TOF count of one.

To our knowledge, this is the first study to evaluate the clinical effect of sugammadex given for the reversal of rocuronium after a continuous IV infusion of this NMBA. The choice of the dose of sugammadex used in the current study was, therefore, based on previous dose-finding studies in surgical patients who received sugammadex at reappearance of the second twitch of the TOF or 1–2 posttetanic counts after single or maintenance bolus doses of rocuronium as well as on preclinical studies in animals that have received sugammadex reversal after continuous rocuronium infusion. For example, a study evaluating sugammadex after prolonged rocuronium-induced neuromuscular blockade to maintain a profound blockade of less than 10 posttetanic counts for 2 h suggested a somewhat more rapid reversal with 4 mg/kg sugammadex (median time to TOF 0.9 = 1.1 min) than with 2 mg/kg sugammadex (median time to TOF 0.9 = 1.8 min). This, together with the mode of rocuronium administration (redistribution of NMBA from the neuromuscular junction is likely to be reduced with continuous infusion when the peripheral compartment has become saturated) led us to the selection of a 4 mg/kg sugammadex dose rather than a lower dose.

Given the very rapid recovery achieved in this study with 4 mg/kg sugammadex administered at T1 values of 3–10% after NMB maintained at no more than 10 posttetanic counts by continuous rocuronium infusion, it is possible that a lower dose of sugammadex may also provide adequate times to recovery, depending on the individual’s elimination and redistribution of rocuronium. To confirm this hypothesis, further (dose-response) studies of sugammadex for reversal at T1 values of 3–10% will be required.

The recovery times reported in our study are faster than has been previously reported for the reversal of NMB with anticholinesterases. In one study, time to incomplete recovery (TOF ratio to 0.7) after cessation of continuous infusion of rocuronium was 7.5 min in patients given 50 µg/kg neostigmine and 9.3 min in patients given 1.0 mg/kg edrophonium at 10% of T1. Antagonism was significantly faster in patients reversed after a greater degree of spontaneous recovery had occurred (25% of T1), especially with edrophonium, but it was still slower than the reversal times we observed with sugammadex. Although it is not possible to directly compare these results with the reversal times reported in our study, these findings strongly suggest that sugammadex would provide more rapid reversal of NMB after continuous infusion of rocuronium than neostigmine or edrophonium.

The NMB effect of rocuronium is potentiated by volatile anesthetics, and this effect is clinically most significant when using a continuous infusion. In one previous study, rocuronium infusion requirements to maintain 95% twitch depression were reduced by 40% during anesthesia involving enflurane or isoflurane, compared with barbiturate-nitrous oxide- opioid anesthesia. In a study in children, the rocuronium infusion rate required to maintain stable 90–99% T1 depression was reduced by approximately 20% with halothane and isoflurane and by 50% with sevoflurane when compared with fentanyl-nitrous oxide anesthesia. A relatively small decrease (7%) in the total rocuronium infusion dose during sevoflurane anesthesia as compared to propofol anesthesia was observed in the current study. The rocuronium concentrations in plasma during the entire period of infusion are not known. Plasma rocuronium concentrations were only measured just before sugammadex administration; at this time point, the median concentration of rocuronium was 33% lower in the sevoflurane group as compared to the propofol group.

Previous reports have shown a similar pharmacokinetic profile of rocuronium, regarding volume of distribution, plasma clearance, and elimination half-life, after
continuous infusion as compared to that after administration of an IV bolus dose.\textsuperscript{19,20} However, as has also been reported in previous studies, we observed significant interpatient variability (of approximately 30\%) in plasma rocuronium concentrations in both the sevoflurane and propofol groups. Because of this, monitoring of neuromuscular transmission is necessary in patients receiving continuous infusion of rocuronium.\textsuperscript{5,18}

Sugammadex was well tolerated, with only one report of an AE considered at least possibly related to treatment. This was a case of mild procedural hypotension, which was classified as probably treatment-related, in a patient in the sevoflurane group occurring 2 min after administration of sugammadex. There was no clinical evidence of recurrent or residual NMB in any patient. There were no clinically relevant differences between sevoflurane and propofol groups with regard to laboratory parameters, vital signs, or respiratory rate.

In conclusion, a single dose of sugammadex after continuous infusion of rocuronium is equally effective for NMB reversal and well tolerated during maintenance anesthesia with sevoflurane or propofol.

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References

17. Shanks CA, Fragen RJ, Ding D: Continuous intravenous infusion of rocuronium (ORG 9426) in patients receiving balanced, enflurane, or isoflurane anaesthesia. Anesthesiology 1993; 78:649–51