

## Case report

# Sugammadex in the management of rocuronium-induced anaphylaxis

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### Editor's key points

- During an anaphylactic reaction to rocuronium, there was a poor response to standard treatment.
- Sugammadex given 19 min after rocuronium was associated with haemodynamic improvement.
- The exact role of sugammadex here is not clear but is worthy of investigation.
- However, this is an unlicensed use.

Anaphylaxis during anaesthesia is a rare event that in ~60–70% of cases is secondary to neuromuscular blocking agents. It has been suggested previously that the recent introduction of sugammadex may provide a novel therapeutic approach to the management of rocuronium-induced anaphylaxis. We describe the case of a 33-yr-old female who suffered a severe anaphylactic reaction to rocuronium, presenting with cardiovascular collapse on induction of anaesthesia. After 19 min of traditional management, she was given a bolus of sugammadex 500 mg. This was associated with an improvement in the adverse haemodynamic state. The underlying reasons for this are unclear, but sugammadex may potentially be a useful adjunct in the management of rocuronium-induced anaphylaxis.

**Keywords:** anaphylaxis; rocuronium; sugammadex

Accepted for publication: 8 November 2010

Anaphylaxis during anaesthesia is a rare but life-threatening event. Neuromuscular blocking drugs are thought to be responsible for between 60% and 70% of anaesthesia-induced reactions, with either rocuronium or succinylcholine being most commonly implicated.<sup>1–6</sup> The traditional management of anaphylaxis includes the elimination of ongoing patient exposure to the causative antigen,<sup>7</sup> although once an antigen has been administered i.v., this may not occur until metabolism or excretion of the antigen occurs. Sugammadex is a recently introduced selective relaxant binding agent that is licensed for the reversal of rocuronium- and vecuronium-induced neuromuscular block. Sugammadex essentially encapsulates the rocuronium molecule<sup>8</sup> which may, in cases of rocuronium anaphylaxis, potentially be of benefit.<sup>9</sup> We describe a case of severe rocuronium-induced anaphylaxis in which the administration of sugammadex, in addition to traditional treatment measures, was associated with the improvement in the adverse haemodynamic consequences.

### Case report

A 33-yr-old, 77 kg female was undergoing a laparoscopic procedure for the investigation of infertility. She had no major medical co-morbidities and smoked 10 cigarettes per day. Approximately 9 yr earlier, she had undergone uncomplicated general anaesthesia at our institution at which

time she received propofol, fentanyl, and rocuronium for induction. She described no allergies related to medication, food, or latex.

On arrival in the operating theatre, the baseline observations were an arterial pressure of 133/80 mm Hg, heart rate of 84 beats min<sup>-1</sup>, and oxygen saturation (Sp<sub>O</sub><sub>2</sub>) of 100%. A 17 G peripheral i.v. cannula was placed and, after pre-oxygenation, anaesthesia was induced with propofol 200 mg and fentanyl 300 µg. Once loss of consciousness was achieved, rocuronium 30 mg (0.39 mg kg<sup>-1</sup>) was given. No antibiotic was administered in the preoperative period or as part of the induction sequence. Within 30 s of the administration of rocuronium, the patient began to cough and a sinus tachycardia of 122 beats min<sup>-1</sup> was noted. Attempts were made to mask ventilate, but this proved difficult and the trachea was immediately intubated.

Post-intubation, despite visual confirmation of tracheal intubation, no carbon dioxide was detected on the capnograph and the airway pressures were elevated. The Sp<sub>O</sub><sub>2</sub> had decreased to 80%. Despite evidence of a tachycardia on the ECG monitor, a carotid pulse could not be detected and hence an emergency was immediately declared and cardiopulmonary resuscitation was commenced. Initial management consisted of chest compressions, i.v. fluids, and intermittent, escalating doses of i.v. epinephrine, starting with a bolus of 200 µg.

There was no response to the initial bolus of epinephrine and a further 800 µg was rapidly titrated, followed by bolus doses of 1 mg. Continuous chest compressions were administered with brief pauses every 2 min to check for a palpable pulse. Chest compressions were stopped on two occasions after a return of a palpable pulse. On both occasions, this was short-lived, and chest compressions were rapidly recommenced.

After ~19 min of resuscitation efforts, the patient had received a total of 4 mg of i.v. epinephrine, 2000 ml of lactated Ringer's solution, and 1500 ml of colloid. Further i.v. access had been obtained but despite multiple attempts, including the use of ultrasound, invasive arterial access could not be achieved secondary to the decreased cardiac output. Peripheral perfusion was poor with all four limbs appearing dusky and mottled. Non-invasive arterial pressure and Sp<sub>O</sub><sub>2</sub> were not recordable, and the ECG monitor showed a tachycardia of 148 beats min<sup>-1</sup>.

At this point, it was considered that the most likely cause of the patient's sudden and profound deterioration on induction was anaphylaxis, likely to be secondary to rocuronium. Despite appropriate traditional management, the situation was still critical. A decision was made to administer sugammadex to potentially mitigate the immunological effects of the rocuronium.

A dose of 500 mg (6.5 mg kg<sup>-1</sup>) was given while chest compressions were in progress. The last dose of epinephrine had been given 4 min previously. Approximately 45 s after administration and while chest compressions were in progress, the patient suddenly opened her eyes and reached for her tracheal tube. Her next recorded arterial pressure and Sp<sub>O</sub><sub>2</sub> (which had been unrecordable on administration of the sugammadex) were 111/56 mm Hg and 97%, respectively, with a heart rate of 126 beats min<sup>-1</sup>. This was recorded ~2 min after she had exhibited spontaneous movement.

The patient was sedated with a bolus of propofol and sedation was then maintained with sevoflurane. Over the subsequent 90 min, during which time the patient was transferred to an offsite intensive care unit, she received hydrocortisone 200 mg i.v., epinephrine 650 µg in divided doses, and metaraminol 1 mg. The vasopressor boluses were generally required in response to a deepening of her level of sedation to facilitate safe transfer and management. She was extubated within 30 min of arrival in the intensive care unit, and no further vasopressor support was required.

The patient made an uncomplicated recovery and was discharged home 48 h after the initial event with no recollection of the period between induction and her extubation in the intensive care unit. Her mast cell tryptase, taken 7.5 h after the event, was 62.9 µg litre<sup>-1</sup> (normal <14). She was followed up 4 weeks post the event at the specialist West Australian Anaesthetic Allergy Clinic. Intradermal skin testing was performed using 1:1000 dilution of 10 mg ml<sup>-1</sup> rocuronium with normal saline and 1:100 dilutions of fentanyl and propofol. A markedly positive persistent flair and wheal response was recorded at 20 min after injection at the

rocuronium test site and the histamine positive control, with negative responses at the other sites. Cross-sensitivity testing elicited positive reactions to succinylcholine, pancuronium, and vecuronium and negative responses to atracurium, cisatracurium, and mivacurium.

## Discussion

In this case report, the administration of sugammadex during an episode of confirmed rocuronium-induced anaphylaxis was associated temporally with a marked improvement in the patient's critical haemodynamic state. This was despite sugammadex being administered 19 min after the onset of the event. This case may potentially further support the consideration of the role of sugammadex in the management of rocuronium-induced anaphylaxis.

Anaphylaxis during anaesthesia is a rare event that is estimated to occur in between 1 in 3500 and 1 in 20 000 cases<sup>5 6</sup> and is associated with significant morbidity and mortality.<sup>5</sup> In the majority of anaesthesia-related reactions, neuromuscular blocking drugs are identified as being the causative agent, being responsible for between 58% and 69% of cases, followed by reactions to latex and antibiotics.<sup>2 10 11</sup> There also appears to be a marked female preponderance to anaesthesia-related reactions.<sup>2 10 11</sup> Rocuronium has been shown in a number of studies to be the most commonly implicated agent, although it is controversial as to whether this simply reflects its increased market share.<sup>12</sup>

Central to the management of anaphylaxis is the prevention of ongoing exposure to the potential antigen.<sup>6 7</sup> Unfortunately, once an agent has been administered i.v., it is very difficult to prevent ongoing exposure and the agent may sustain an anaphylactic response until it has been eliminated from the body.<sup>9</sup> Sugammadex is a recently developed drug that was specifically designed for the reversal of rocuronium-induced neuromuscular block.<sup>8</sup> In contrast to traditional reversal agents that work by competitive antagonism of the neuromuscular agent, sugammadex encapsulates the rocuronium molecule, negating its pharmacological effect, and essentially removing it from the circulation.<sup>8</sup> It has been suggested in correspondence in the scientific literature that sugammadex may be of potential therapeutic value in an episode of rocuronium-induced anaphylaxis.<sup>9</sup> Given the rare nature of such events, clinical trials of this situation are currently not possible.

There are a number of unanswered questions in relation to the use of sugammadex for this situation. As the sugammadex molecule does not completely encapsulate the rocuronium molecule,<sup>8</sup> it is unknown whether the antigenic portion of rocuronium would still be able to cross-link with IgE when it is bound by sugammadex.<sup>9</sup> Not all anaesthesia-related reactions are secondary to an IgE-mediated process,<sup>12</sup> and hence it is not clear whether sugammadex would be of benefit in these situations. In addition, sugammadex may also bind with other steroid compounds,<sup>13</sup> such as hydrocortisone, and potentially decrease their effect in the management of anaphylaxis. As anaphylaxis is traditionally thought of as a

cascade type of response, it is unclear whether the subsequent removal of the rocuronium would be of benefit, and this may vary on a case-by-case basis depending on the severity of the initial presentation. In addition, it is also unclear whether sugammadex would also be of benefit in vecuronium-induced anaphylaxis.

The optimal dose of sugammadex in this situation is unknown. Given that the theoretical aim of administration is to encapsulate all the circulating rocuronium molecules, it has been suggested that large doses (up to 16 mg kg<sup>-1</sup>) may be required.<sup>9</sup> This is likely to be dependent on both the initial dose of rocuronium administered and the elapsed time since administration. In this case, 500 mg (one ampoule, ~6.5 mg kg<sup>-1</sup>) was given because it was readily available. In this situation, it appeared to fully reverse the underlying neuromuscular block, as would be expected given the 19 min that had elapsed since rocuronium was given.<sup>14 15</sup>

In our case, the decision was made to administer sugammadex once it became clear that the underlying diagnosis was likely to be anaphylaxis. Given that it occurred immediately after induction and only three agents had been given as part of the induction process, it was considered that rocuronium was likely to be the cause. Traditional management had until that point failed to reverse or mitigate the underlying process. Other therapeutic options that could also be considered in similar situations include the administration of high doses of alpha agonists<sup>16 17</sup> or a vasopressin infusion.<sup>18</sup> The response to the administration of sugammadex consisted of an expected reversal of the patient's neuromuscular block in addition to being associated with an improvement in the patient's adverse haemodynamic state.

The potential reasons for the reversal of the haemodynamic state are unclear. As anaphylaxis is not necessarily an 'all or none' phenomenon,<sup>7</sup> it may be that the binding of the rocuronium molecule by sugammadex prevented further vasoactive mediator release and allowed the previously administered epinephrine to have increased efficacy. As the administration was also associated with reversal of the patient's neuromuscular block, it may be that the associated increase in muscle tone assisted with the restoration of venous return and cardiac output. It is also possible that the effect was purely by coincidence and that the reversal in her clinical condition was secondary to the epinephrine and fluid resuscitation that had been instituted. Other as yet unidentified processes may also have played a role.

In conclusion, in this case, the administration of sugammadex during rocuronium-induced anaphylaxis was associated with an improvement in the patient's haemodynamic state. The underlying reasons for this are unclear and given the rare nature of such presentations, it is likely that the evidence of benefit in similar situations will rely on isolated case reports. With this in mind and until further evidence is forthcoming, we would consider the role of sugammadex as that of a potential adjunct in cases of suspected rocuronium-induced anaphylaxis that is unresponsive to traditional

measures. Clinicians should be mindful that this is an unlicensed indication for the use of sugammadex.

## Conflict of interest

None declared.

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