

# Original Article

## Efficacy of sugammadex in rocuronium-induced or antibiotic-induced anaphylaxis. A case-control study

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### Summary

We report 13 cases of presumed rocuronium-induced anaphylaxis in which sugammadex was administered with the intention of reversing the immunological reaction. Of these 13 cases, eight (62%) were later confirmed to be type-1 hypersensitivity reactions to rocuronium, three (23%) were triggered by an antibiotic and two (15%) were non-immunologically mediated. Response to treatment was scored by the treating anaesthetist, and compared with haemodynamic and inotrope measurements from the resuscitation and anaesthetic records. Haemodynamic improvement was seen in only six (46%) cases, three of which were associated with a non-rocuronium trigger. Of the three cases in which the treating anaesthetist thought that sugammadex had been beneficial, one was not caused by rocuronium, one had no improvement in blood pressure and one required 8.5 times as much adrenaline in boluses after, compared with the period before, sugammadex administration. These data suggest that sugammadex does not modify the clinical course of a suspected hypersensitivity reaction.

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### Introduction

Intra-operative anaphylaxis is a potentially life-threatening complication of anaesthesia, and rocuronium is the most commonly implicated neuromuscular blocking drug in Western Australia [1, 2]. The introduction of sugammadex, a cyclodextrin able to encapsulate rocuronium and reverse neuromuscular blockade, has led to speculation that it may be effective in rocuronium-induced anaphylaxis. There are case reports of potential benefit [3–9] and one report of no perceived benefit [10]. In-vitro and in-vivo human models of anaphylaxis have not been able to demonstrate immunologically mediated attenuation of established anaphylaxis [11, 12]. We have raised theoretical objections about the plausibility of any such immunologically mediated benefits [11, 13–15]. For both ethical and

practical reasons, a controlled clinical trial investigating this use of sugammadex in humans is unlikely. As a consequence, case reports will continue to be the main source of further information. We sought to report all cases of presumed rocuronium-induced anaphylaxis treated with sugammadex in Western Australia. We anticipated that we would be able to compare, in an exploratory way, those cases that were treated with sugammadex and were subsequently confirmed to be triggered by rocuronium, with those that were not.

### Methods

Ethics approval was granted by the Health Department of Western Australia. All patients provided retrospective written informed consent.

The Western Australian Anaesthetic Drug Reaction Clinic (WAADRC) is a specialised diagnostic centre for the investigation of peri-operative allergic reactions, with records dating back to 1982. Between October 2010 and October 2014, all cases of presumed rocuronium-induced anaphylaxis referred to the WAADRC, in which sugammadex was administered during the period of physiological derangement and as part of the crisis management, were analysed. Details of the individual cases can be found in the online Supporting Information (Data S1).

Standard immunological investigation included history, analysis of anaesthetic and resuscitation records, intradermal skin testing and acute and baseline plasma mast cell tryptase levels (ImmunoCap Tryptase; Phadia Laboratory Systems, Uppsala, Sweden). The criteria for diagnosis of anaphylaxis have been previously described [2] and the severity of the reaction was graded according to the four-level scale described by Mertes et al. [16]. The dosage and timing of sugammadex administration(s) after reaction were also recorded.

Response to sugammadex was recorded as the treating anaesthetist's impression of effectiveness at the time of referral for investigation (definite/possible/no benefit). Retrospective case review was used to record data about blood pressure, cumulative adrenaline dose before and after treatment, duration of postoperative ventilation and signs and symptoms of anaphylaxis after emergence.

## Results

Thirteen cases of presumed rocuronium-induced anaphylaxis were referred to the WAADRC over four years (Table 1). All cases were administered rocuronium at the time of anaesthetic induction. One case (case 2) has previously been described in the literature [3].

The systolic pressure was higher immediately after sugammadex administration in 6/13 cases (46%). However, of the eight cases of rocuronium anaphylaxis, it was higher in only three cases (38%), compared with 3/5 cases of non-rocuronium anaphylaxis (60%).

Of the three cases in which the treating anaesthetist thought that sugammadex had resulted in a definite benefit, one (case 1) was not caused by

rocuronium, one (case 2) had no improvement in blood pressure and still required significant adrenaline boluses and an infusion after sugammadex, and the remaining case (case 11) required 8.5 times as much adrenaline in boluses in the period after sugammadex compared with the period before.

## Discussion

Although it has previously been hypothesised in individual case reports that sugammadex is effective in modifying the syndrome of anaphylaxis caused by rocuronium, data from this case series do not support that hypothesis, nor do in-vivo experimental evidence and theoretical objections that we have published previously [11], cautioning against including sugammadex in anaphylaxis treatment algorithms [11].

Several important observations can be made from this series, which have not been previously considered. Firstly, there were instances of reported haemodynamic improvement after sugammadex administration in cases that were not triggered by rocuronium. Secondly, not all cases that were caused by rocuronium had a treatment response to sugammadex. Thirdly, the case record did not always support the treating anaesthetist's impression of effectiveness. Fourthly, the severity of the anaphylactic response, the mast cell tryptase level and the therapeutic adrenaline doses varied markedly after rocuronium-triggered anaphylaxis.

Haemodynamic improvement was reported in two of the three cases of confirmed antibiotic anaphylaxis. If it is accepted that this benefit was real then it cannot be caused by the binding of sugammadex to the antibiotic and must be by some other mechanism that is independent of the triggering drug.

Of the eight cases of confirmed rocuronium anaphylaxis, the anaesthetist felt that sugammadex was not effective in three and only possibly effective in three more. There was no improvement in blood pressure in five cases, and no reduction in adrenaline requirement in six cases. This suggests that sugammadex cannot be relied upon as an effective treatment in anaphylaxis. This is important, given that the use of sugammadex is not without potential harm in anaphylaxis, having itself been reported to trigger anaphylaxis [17] and reversing neuromuscular blockade, complicating ventilation.

**Table 1** Immunological, dose, blood pressure, treatment and disposition data for 11 patients with presumed rocuronium-induced anaphylaxis in which sugammadex was administered.

| Case | Trigger     | Grade | Peak<br>MCT; $\mu\text{g.l}^{-1}$ | Sugammadex                   |                | Systolic BP; mmHg |              | Adrenaline dose; $\mu\text{g}$ |            |        | Time<br>intubated<br>in ICU; h |                      |                  |             |
|------|-------------|-------|-----------------------------------|------------------------------|----------------|-------------------|--------------|--------------------------------|------------|--------|--------------------------------|----------------------|------------------|-------------|
|      |             |       |                                   | Dose;<br>$\text{mg.kg}^{-1}$ | Timing;<br>min | Response          | Before       |                                | After      |        |                                | Before<br>sugammadex | After sugammadex |             |
|      |             |       |                                   |                              |                |                   | sugammadex   | After<br>sugammadex            | sugammadex | Bolus  |                                |                      | Infusion; h      | Disposition |
| 1    | Amoxicillin | 2     | 15.4                              | 13.8                         | 10             | Definite          | 110          | 135                            | 500        | 0      | —                              | ICU                  | 7                |             |
| 2    | Rocuronium  | 4     | 62.9                              | 6.5                          | 20             | Definite          | 115          | 111                            | 4000       | 650    | 1                              | ICU                  | 1                |             |
| 3    | Cefazolin   | 3     | 12.5                              | 14.7                         | 30             | Possible          | 90           | 110                            | 175        | 0      | 2                              | ICU                  | 14               |             |
| 4    | Rocuronium  | 3     | 29.7                              | 3.4                          | 2              | No                | Unrecordable | Unrecordable                   | 0          | 1000   | 2                              | ICU                  | 0                |             |
| 5    | None        | 2     | Not done                          | 3.4                          | 25             | Possible          | 140          | 140                            | 0          | 0      | —                              | Ward                 | —                |             |
| 6    | Rocuronium  | 2     | 9.3                               | 4.7                          | 12             | Possible          | 100          | 120                            | 20         | 40     | —                              | Ward                 | —                |             |
| 7    | Rocuronium  | 2     | 57.1                              | 5.4                          | 5              | Possible          | 140          | 140                            | 50         | 300 sc | —                              | ICU                  | 0                |             |
| 8    | None        | 2     | 5.4                               | 19.3                         | 20             | No                | 90           | 220                            | 500 im     | 0      | —                              | Ward                 | —                |             |
| 9    | Rocuronium  | 2     | 9.1                               | 5.6                          | 5              | Possible          | 60           | 90                             | 30         | 0      | —                              | ICU                  | 4                |             |
| 10   | Rocuronium  | 4     | 164                               | 4.7                          | 10             | No                | Unrecordable | Unrecordable                   | 3200       | 4000   | —                              | ICU                  | 48               |             |
| 11   | Rocuronium  | 3     | 9.3                               | 2.7                          | 25             | Definite          | 85           | 110                            | 20         | 170    | 0.5                            | ICU                  | 0                |             |
| 12   | Rocuronium  | 3     | 15.5                              | 8.2                          | 5              | No                | 47           | 49                             | 500        | 1000   | 7                              | ICU                  | 20               |             |
| 13   | Cefazolin   | 4     | 12.4                              | 10.0                         | 15             | No                | Unrecordable | Unrecordable                   | 1000       | 1000   | 16                             | ICU                  | 14               |             |

MCT, mast cell tryptase; sc, subcutaneous; im, intramuscular.

Anaesthetists' perceptions about the clinical benefit of sugammadex in anaphylaxis were subjective. Indeed, other clinicians present during the reported cases disagreed (personal communication). Of the eight cases of anaphylaxis confirmed to be due to rocuronium, in only two cases was there thought to be definite benefit (cases 2 and 11). According to the case records, however, after sugammadex administration, both patients were administered continued adrenaline boluses and infusion, their lungs were ventilated in an intensive care unit, and they developed significant generalised angioedema, severe abdominal pain and diarrhoea, indicating ongoing anaphylaxis.

From these subjective and objective findings, it follows that any treatment effect of sugammadex is independent of rocuronium-mediated anaphylaxis, either because there is no treatment effect, or because any treatment effect occurs via mechanisms that have not been proposed previously.

If a non-immunological treatment effect exists in anaphylaxis, it would need to explain why sugammadex is not effective in all cases of rocuronium anaphylaxis but effective in some cases of non-rocuronium or non-immune-mediated anaphylaxis. We hypothesise that sugammadex increases muscle tone by reversing neuromuscular blockade, compressing intramuscular and intra-abdominal vessels, and so reducing venous capacitance, increasing venous return and cardiac preload. Minimising anaesthetic drug administration during anaphylactic shock may lead to patient arousal and movement, exaggerating this effect. The importance of venous return in anaphylactic shock has been demonstrated in various settings, including cardiopulmonary bypass [18], out-of-hospital reactions [19], and emergency care [20] as through use of a pneumatic anti-shock garment [21]. It may be that sugammadex is effective only in anaphylaxis characterised by severe maldistributive shock, with insufficient volume resuscitation. Trendelenburg positioning and volume resuscitation may be just as effective techniques of improving unresponsive anaphylactic shock, without exposing the patient to any further harm associated with reversal of neuromuscular blockade during resuscitation.

In summary, our case series does not support the hypothesis that sugammadex modifies the immunological cascade of anaphylaxis. An alternative hypothesis,

that sugammadex administration in anaphylaxis improves cardiac preload, is more plausible, but is not without potential risk in its clinical implementation, compared with known effective methods of increasing venous return.

## Competing interests

No external funding and no competing interest declared.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Data S1** Details of individual cases.

## **Supporting Information 1: Details of individual cases**

### **Case 1**

Induction prior to dental implant surgery with fentanyl, propofol and rocuronium followed by dexamethasone, parecoxib and amoxicillin after which there was an increase in heart rate from 85 to 140bpm, decrease in SBP from 150 to 90mmHg, a generalized erythematous rash, moderate bronchospasm and a fall in SpO<sub>2</sub> to 88%. Anaphylaxis was immediately diagnosed and over the following ten minutes multiple 100mcg doses of adrenaline and intravenous fluids were administered with an effective but transient response. A presumptive diagnosis of rocuronium-induced anaphylaxis was made and hydrocortisone 250mg and sugammadex 1200mg were administered. After approximately two minutes heart rate fell from 150 to 100 and SBP rose to 135 and SpO<sub>2</sub> increased to 99% from a nadir of 77%. No further adrenaline was required. During subsequent central venous and arterial line placement the patient awoke and attempted to remove the endotracheal tube and was thus sedated and re-paralysed with atracurium. The patient was extubated after a night in the Intensive Care Unit (ICU), generalized oedema resolved after 24 hours and she made an uneventful recovery. Mast cell tryptase (MCT) was elevated at 15.4 mcg.L<sup>-1</sup> four hours post event. Intradermal skin testing five weeks post event was negative to all drugs administered except for a markedly positive response to 0.02 ml of amoxicillin 1mg.ml<sup>-1</sup>. The anaesthetist was strongly convinced the sugammadex was responsible for the patient's improvement.

### **Case 2**

This case has been previously reported (3). Profound cardiovascular collapse 8 minutes after induction with propofol, fentanyl and rocuronium prior to an elective laparoscopic procedure. At commencement of cardiopulmonary resuscitation non-invasive blood pressure was recorded as 36/19mmHg, SpO<sub>2</sub> 60%, heart rate 122bpm and end tidal carbon dioxide undetectable. After 3mg of adrenaline and 3500 ml of fluid had been administered with an only intermittent palpable pulse detectable during pauses from cardiac compressions SBP was recorded as 87 and a further 1mg

of adrenaline was administered. Three minutes later 500mg sugammadex was administered with immediate arousal of the patient associated with struggling. SBP was recorded at 115. Propofol was administered with a fall in blood pressure to 111/56 two minutes later. Approximately 14 minutes after the administration of sugammadex the blood pressure had fallen to 62/41. Multiple further bolus doses (650 mcg) and an infusion of adrenaline were required to maintain stability prior to and during transfer to an ICU at a different hospital. In transit through the Emergency Department the blood pressure was 60/38. After administration of metaraminol 0.5mg in the ICU the blood pressure was 78/40 and the endotracheal tube was removed. Hypotension persisted until midnight despite the administration of a further 4385ml of fluid. The patient's ICU stay was associated with severe abdominal pain, diarrhoea and marked generalized oedema. MCT 7.5 hours after the event was 62.9. Subsequent skin testing four weeks after the event confirmed rocuronium as the cause of the anaphylaxis. Most, but not all, of the staff present at the resuscitation were convinced the administration of sugammadex had improved the clinical condition of the patient.

### **Case 3**

Twenty minutes after induction prior to a planned laparoscopic bowel resection worsening hypotension, tachycardia and truncal erythema occurred. The hypotension was initially unresponsive to metaraminol and was less than 40 systolic for about 90 seconds. After incremental 25mcg doses of adrenaline (total dose 175mcg) and 3500 ml of crystalloid the blood pressure rose progressively to 100/30 after a further 15 minutes. Sugammadex 1400mg was then administered to treat what was presumed to be an anaphylactic reaction to rocuronium (approximately 35 minutes after induction) after which the blood pressure stabilized coincident with the institution of an adrenaline infusion. The case was abandoned and the patient transferred to the hospital's ICU where the patient remained intubated and dependent on a low dose adrenaline infusion until the following day. At an unidentified time late on the day of the event a MCT was measured at 12.5. A further 5 litres of fluid was administered. The angioedema, particularly of the face, was so severe that the patient was unrecognizable to relatives, and took several days to resolve. Intradermal skin testing three weeks after the event confirmed cephalosporins as the responsible agent and subsequent surgery was uneventful with vancomycin used as an

alternative antibiotic. The anaesthetist felt that the sugammadex had contributed to the clinical improvement.

#### **Case 4**

Ten minutes into an elective knee arthroscopy under general anaesthesia with a laryngeal mask 15mg of rocuronium was given to relieve mild laryngospasm. Blood pressure rapidly became unrecordable associated with marked erythema and piloerection. There was no increase in heart rate. Increasing incremental doses of adrenaline to a total of 1mg followed by an infusion of a further 1mg resulted in a stable blood pressure. The development of atrial fibrillation was reverted with amiodarone 300mg. Sugammadex 200 mg was administered immediately after the anaphylaxis was recognized but “it did not do much other than reverse any relaxation”. The surgery was completed during the resuscitation and the patient transferred to the ICU extubated and awake. There was no further haemodynamic instability but oedema of the hands and face persisted for 48 hours. MCT was measured at one hour and the following day with levels of 29.7 and 5.5 respectively. Intradermal skin testing was performed four weeks later negative to all drugs to which the patient was exposed except for a markedly positive reaction at the rocuronium test site.

#### **Case 5**

An atopic 65-yr-old male with mild asthma and dilated cardiomyopathy, ejection fraction of 35% and a biventricular pacemaker in-situ was anaesthetized for VT ablation. Of note was a history of intra-operative bronchospasm during a previous AF ablation. Shortly after induction of anaesthesia with propofol, fentanyl and rocuronium the patient developed severe bronchospasm, which temporarily responded to ventolin but rapidly returned. There were no other features of anaphylaxis. The working diagnosis was allergy to rocuronium and at approximately 30 minutes post induction sugammadex 400mg was administered followed by atracurium 50mg to maintain paralysis. This was associated with resolution of the bronchospasm. The five-hour procedure and the post-operative course were uneventful. A MCT assay was not performed and skin tests to all drugs used were negative. The conclusion subsequent to the immunological review was that this

reaction was probably not IgE mediated. The attending anaesthetist felt that the sugammadex was beneficial.

## **Case 6**

Induction with midazolam, fentanyl, propofol and rocuronium for internal fixation of an ankle fracture. Immediately after intubation a widespread erythema was noted coincident with a tachycardia of 130bpm and a SBP of 70 initially unresponsive to incremental 0.5mg doses of metaraminol. No bronchospasm was evident. After two 10 mcg doses of adrenaline and further increments of metaraminol SBP rose to 100 at which time sugammadex 400mg was administered with an increase in SBP to 120 but subsequently fell. Maintenance of blood pressure in the normal range required further doses of adrenaline but haemodynamic stability was maintained without vasopressors after a further 20 minutes. The surgery was abandoned and the patient woken without subsequent problems. MCT thirty minutes after onset of the reaction was 9.3 and 7.5 two and a half hours later. The procedure was completed four days later under spinal anaesthesia and sedation. The patient was temporarily lost to follow up but was investigated at the allergy clinic six months later. Intradermal skin testing was strongly positive at the rocuronium test site with cross sensitivity to suxamethonium and vecuronium. The attending anaesthetist was of the opinion that the sugammadex may have helped.

## **Case 7**

Anaesthesia with interscalene block followed by general anaesthesia with fentanyl, propofol and rocuronium prior to an elective shoulder arthroscopy. Cephazolin 300mg was given as a test dose followed by a further 700mg. During intubation the pulse rate was noted to be 130bpm. Immediately after intubation SBP was recorded as 57, the end tidal carbon dioxide was 23mmHg and the heart rate had fallen to 60bpm. ST segment depression was noted on the electrocardiogram. Metaraminol 2mg was administered with a rise in SBP to 70mmHg and a further 2mg bolus followed. Anaphylaxis was considered and 50mcg of adrenaline resulted in normalization of the SBP to 140 and heart rate of 130bpm. Sugammadex 350mg was given followed by a further 150mg. When reversal of paralysis was apparent the patient was awoken

and extubated. The patient now had swollen lips, complained of shortness of breath and a wheeze was apparent on auscultation. A further dose of 300mcg of adrenaline was given intramuscularly. The patient was observed on the ICU overnight and discharged home the following day. MCT at approximately one hour after the event was elevated at 57.1. Skin testing one month later confirmed rocuronium as the responsible agent with cross reactivity to suxamethonium and vecuronium. The attending anaesthetist felt that the sugammadex had a beneficial effect.

## **Case 8**

The patient, who had a history of a truncal and facial urticaria after a dental procedure and unspecified skin eruptions after cephalexin and non-steroidal anti-inflammatory drugs, was anaesthetized with midazolam, fentanyl, propofol and rocuronium prior to an elective laparoscopic procedure. Immediately after intubation the SBP had dropped to 55, pulse rate was 60 and a small increase in airway pressure was noted. Three 1mg doses of metaraminol were administered at minute intervals with an increase in SBP to 90. Generalized erythema and urticarial appeared. Over the next 15 minutes arterial and intravenous cannulae were placed and 2 litres of crystalloid infused. During this time cardiovascular stability was maintained but because of the ongoing skin changes 16mg.kg<sup>-1</sup> of sugammadex and 0.5mg of intramuscular adrenaline were administered to treat the presumed rocuronium induced anaphylaxis. Esmolol and glyceryl trinitrate were required to control blood pressure that was at times greater than 200mmHg. Two hours after induction of anaesthesia the patient was woken and extubated with all signs of allergy resolved. Serial mast cell tryptase assays were normal and skin testing four weeks later was unremarkable except for large transient flares at each intradermal injection site. The attending anaesthetist did not feel that the sugammadex altered the course of the reaction. After the immunological assessment it was felt that the reaction represented non-specific histamine release in a patient with a history of drug induced acute urticaria.

## **Case 9**

Induction prior to a laparoscopic sleeve gastrectomy with midazolam, propofol, fentanyl, rocuronium and sevoflurane. Immediately SBP fell to 60 associated with a heart rate of 115bpm,

generalized erythema and increased airway pressure. After multiple 0.5mg doses of metaraminol to a total of 3mg, without any response, 30mcg of adrenaline in divided doses was administered in conjunction with 500mg of sugammadex. Over the next 20 minutes the measured parameters returned to normal, the procedure was abandoned and the patient was transferred to the ICU where the patient remained stable and was extubated four hours later without sequelae. Six weeks later skin testing was strongly positive for rocuronium with unusual cross reactivity to only atracurium. MCT measured at one, three and seven hours with levels of 8.6, 9.1 and 3.7 respectively. The attending anaesthetist was of the opinion that the sugammadex had contributed to the improvement.

### **Case 10**

Scheduled thyroidectomy for the treatment of a multinodular goitre. One minute after the administration of rocuronium SpO<sub>2</sub> fell to 60%, heart rate increased to 140bpm and the pulse was barely palpable. Two successive 200mcg doses of adrenaline were ineffective. A further bolus of adrenaline 1mg had little effect and external cardiac massage was commenced followed by the administration of a further 1mg adrenaline. Three minutes later a further 1mg of adrenaline was given followed 2 minutes later by 400mg of sugammadex. Ventricular fibrillation followed and cardiac massage continued for 30 minutes during which a further 6mg of adrenaline was administered. Defibrillation was successful on the sixth attempt. Forty-five minutes after induction sinus rhythm returned with haemodynamic stability, cardiac massage was discontinued and a generalized erythema was noted with return of peripheral perfusion. The patient was transferred to ICU and actively cooled, sedated and ventilated. The patient's stay was complicated by a mild coagulopathy; acute lung injury and a troponin rise to 3.4 (normal < 0.03ug.L<sup>-1</sup>). Two days after admission to ICU the patient was extubated and subsequently made a full recovery. The mast cell tryptase level approximately one hour after the onset of the reaction was 164mcg.L<sup>-1</sup>. Skin testing four weeks post event was strongly positive for rocuronium with cross reactivity to vecuronium and mivacurium. The anaesthetist felt that the sugammadex had no impact on the course of the reaction.

### **Case 11**

Induction with fentanyl, midazolam, propofol and rocuronium prior to an elective microdiscectomy. SBP fell immediately from 160 to 70 associated with an increase in HR to 130bpm. There was some erythema but no bronchospasm. Incremental doses of metaraminol to 5mg had little effect. With adrenaline in 5mcg aliquots there was unsustained improvement in blood pressure so 200mg of sugammadex was given deliberately to reverse the anaphylaxis. There was no dramatic increase in blood pressure but over the next 20-30 minutes it increased and stabilized during which time central venous access was achieved and an adrenaline infusion commenced. The latter was weaned over 30 minutes, the surgery abandoned, the patient extubated and transferred to the ICU for monitoring over the next 30 hours. Angioedema of face and arms was marked and took a week to resolve completely. Mast cell tryptase was 9.3, 5.7 and 2.3 at 1, 5 and 15 hours respectively. Four weeks later skin testing was positive for rocuronium with no cross sensitivity. The anaesthetist was convinced that the sugammadex was beneficial and stated he would use it again in the same circumstance.

## **Case 12**

Induction with fentanyl, propofol, rocuronium and morphine prior to an appendicectomy. Immediate development of tachycardia of 160bpm and profound hypotension, SBP 35 and cyanosis. There was uncertainty about the diagnosis of anaphylaxis because of the lack of bronchospasm and an echocardiogram was performed to rule out a primary cardiac cause. Adrenaline 500mcg and sugammadex 600mg was administered with little response. Over the next hour 2.5 L of crystalloid and 0.5L of colloid was infused while central venous access and invasive blood pressure monitoring was instituted. Adrenaline 100mcg aliquots were administered that maintained SBP between 60 and 85. Surgery was abandoned and the patient was transferred intubated to the ICU, remaining sedated and ventilated until the following day. Because of a relative lack of response to an adrenaline infusion noradrenaline was added. Mast cell tryptase assays on blood drawn 4 hours and 24 hours post event were 15.5 and <1.0. The appendicitis was managed medically and the patient made a full recovery. Skin testing eight weeks post event was strongly positive to rocuronium with cross reactivity to vecuronium and pancuronium. The attending anaesthetist did not feel that the sugammadex had been beneficial.

### Case 13

Scheduled elective ulnar nerve transposition, induction with midazolam, fentanyl, propofol and rocuronium and concurrently administered cephazolin. First blood pressure post induction was normal, however the following was 40mmHg. This was associated with a generalised erythematous rash and tachycardia. There was no response to metaraminol and bolus doses of adrenaline were given with transient improvement. The patient rapidly became pulseless and cardiopulmonary resuscitation was commenced. During this resuscitation period 800mg of sugammadex was administered with no effect. After approximately 20 minutes the patient's condition improved. The patient was transferred to the intensive care, remaining on an adrenaline infusion for a total of 16 hours and before extubation the following morning. There was no further haemodynamic instability but face and upper limb oedema remained for 48 hours. A mast cell tryptase level, taken three hours after the onset of the reaction, was 12.4 before returning to normal limits the following morning 2.5. Ten days after the event the patient experienced a cerebellar infarction, which on further investigation was shown to be secondary to a vertebral artery dissection, the cause of which was not clear.