Anaphylaxis to rocuronium

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Reports about anaphylactic and anaphylactoid reactions to rocuronium have increased recently. We report two new cases of documented grade III anaphylaxis, leading to death in one patient. The first case occurred in an 81-year-old ASA II woman scheduled for emergency abdominal surgery. Severe hypotension and tachycardia were observed after rocuronium, without bronchospasm. Neosynephrine allowed rapid resuscitation, and the patient recovered fully. The second patient was a 64-year-old ASA II man scheduled for abdominal surgery. Severe haemodynamic instability and bronchospasm occurred after rocuronium. Despite immediate life support, the postoperative period was complicated by persistent low systolic pressure, acute respiratory distress syndrome, acute renal failure, disseminated intravascular coagulation and pancreatitis, leading to the death of the patient.

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Rocuronium has been available in France since 1994. It is a widely used aminosteroidal non-depolarizing neuromuscular blocking agent that shares many pharmacological features with vecuronium. It has the advantage of a more rapid onset time,1 which has led many anaesthetists to use rocuronium rather than vecuronium.2 Case reports,3–12 and correspondence,13–14 about both anaphylaxis (characteristic clinical symptoms, positive allergological tests) and anaphylactoid reactions (unusual clinical symptoms and reaction not mediated by IgE) after rocuronium have increased recently. Such reactions are often life-threatening and may be fatal.1–14 One fatality following rocuronium has already been reported.2 We report two new cases of documented grade III anaphylaxis, leading to death in one patient.

Case reports

Case 1 was an 81-year-old ASA II woman scheduled for emergency abdominal surgery in March 2000. Her past medical history included a nervous breakdown and atrial fibrillation. Her medication consisted of fluoxetine and verapamil. She had previously undergone eight general anaesthetic procedures, including orthopaedic (knee and hip) surgery, and repair of a genital prolapse. Induction was achieved with thiopental 350 mg and succinylcholine 80 mg. Following loss of consciousness, the trachea was intubated. Twenty min later and before skin incision, rocuronium 30 mg and sufentanil 10 µg were administered. One min later, the patient exhibited narrow complex tachycardia (156 beat min⁻¹), severe hypotension (45/32 mm Hg), and weak chest erythema, but did not develop bronchospasm. Incremental doses of neosynephrine up to 200 µg were given, and both heart rate and arterial pressure returned to basal values. Because of the rapid resuscitation, surgery was not cancelled. After surgery, the patient was transferred to the recovery room and her trachea was extubated 1 h later. She recovered fully and was discharged 6 days later.

Blood samples obtained at 30 min and 1 h, and urine sampled at 3 h after the reaction demonstrated increased levels of histamine (19.7 and 6.7 nmol ml⁻¹, respectively; normal value <6 nmol ml⁻¹), and tryptase (27.9 and 19.2 nmol ml⁻¹, respectively; normal value <13.5 nmol ml⁻¹) but normal urinary methylhistamine. Specific IgE antibodies against quaternary ammonium ions and rocuronium measured during the reaction were negative. Cutaneous tests were performed by an allergologist 6 weeks later. Skin-prick testing produced wheals <3 mm in the negative control and 10 × 8 mm in the positive (codeine sulfate) control. Skin-prick testing confirmed the diagnosis of anaphylaxis to rocuronium (8 × 7 mm). A positive skin test was also
observed with the other aminosteroidal neuromuscular blocking agents (pancuronium: 9×10 mm; vecuronium: 8×9 mm), but not with the benzylisoquinolinium neuromuscular blocking agents (<3 mm). Intradermal tests were positive to rocuronium (1:100 dilution), with a wheal of 11.5 mm and flare of 35 mm, but negative to succinylcholine (1:10 dilution).

Case 2 was a 64-year-old ASA II man scheduled for hernia repair in November 2000. Previous general anaesthesia for umbilical hernia repair and melanoma resection had been uneventful. His medical history included venous thromboembolism and obesity and he was treated with oral anticoagulants (acenocoumarol). Anaesthesia was induced with sufentanil 15 g and propofol 400 mg. Following loss of the eyelash reflex, rocuronium 50 mg was administered and the trachea was intubated. Shortly after rocuronium administration, the patient developed bronchospasm, hypotension (50/30 mm Hg), tachycardia (135 beat min⁻¹), and generalized erythema. The patient was resuscitated with oral anticoagulants (acenocoumarol).

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Blood samples obtained at 30 min and 1 h, and urine sampled at 3 h after the reaction demonstrated elevated levels of histamine (>100 and 44.6 nmol ml⁻¹, respectively; normal value <6 nmol ml⁻¹), mast cell tryptase (>200 nmol ml⁻¹ for both blood samples; normal value <13.5 nmol ml⁻¹) and urinary methylhistamine (10 318 nmol litre⁻¹ or 849 nmol mmol creatinine⁻¹; normal value <170 nmol mmol creatinine⁻¹), in keeping with anaphylaxis. Specific IgE antibodies against quaternary ammonium compounds were detected (QAS-radioimmunoassay technique: 3.5%) with positive radioimmunoassay inhibition by rocuronium (63%).

Discussion

We report two more anaphylactic reactions to rocuronium, leading to the death of one patient. According to the Ring and Messmer classification, these two cases were considered to be grade III.\(^{17}\)

In the first case, the patient did not exhibit any reaction when she received succinylcholine whereas 20 min later, she developed an anaphylactic reaction immediately after rocuronium. Skin tests were highly positive (1/100) to rocuronium, but negative to atracurium, a well-known histamine-releasing drug, suggesting an IgE-mediated reaction. The patient may have been previously sensitized to steroidal neuromuscular blocking agents (she had already undergone eight general anaesthetic procedures), without cross-reactivity to atracurium or succinylcholine. Specific IgE antibodies against quaternary ammonium ions were negative. This negative result is not rare, as IgE may have been consumed during the reaction. The technique has only 85% sensitivity.\(^{15}\) Therefore, the lack of specific IgE detection during such an adverse effect does not rule out an anaphylactic origin.

In contrast, there is no doubt that the second case documents a typical anaphylactic reaction because of the clinical presentation and the increase in mast cell tryptase and specific IgE antibodies against rocuronium. Despite rapid resuscitation, the patient died after developing multiple organ failure. Such a fatal event has already been described with rocuronium and has been documented with other neuromuscular blocking agents.\(^{2}\)

The use of rocuronium is increasing and it is not surprising that reports of side-effects such as anaphylaxis increase concomitantly.\(^{2–14}\) A high ‘rocuronium-mediated anaphylaxis rate’ is suspected by some authors,\(^ {2, 9–11}\) who recommended close monitoring of such adverse events. We agree with this recommendation. We would like also to emphasize that neuromuscular blocking agents are the main drugs responsible for life-threatening episodes during anaesthesia, but such agents are not always necessary surgically. There are several studies of the ability to intubate without neuromuscular blocking agents.\(^ {18}\) Between 1995 and 2000 the use of muscles relaxants in intubated patients decreased from 100% to 25% in our institution, without any related adverse events. We believe full reporting is important to study the potential risks of anaphylaxis to rocuronium.

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