

## Long-lasting potentiation of a single-dose of rocuronium by amikacin : case report

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**Abstract :** We report for the first time to our knowledge long-lasting (4 hours) potentiation of single intubating dose of rocuronium by a single bolus of amikacin given 55 minutes later in a woman having no precipitating factor (renal failure, hepatic failure, ionic disorder, other drugs influencing neuromuscular function). This patient had received the same rocuronium dose one month sooner in similar circumstances (without aminoglycoside antibiotic drug) and had not presented any prolonged neuromuscular blockade at this time.

Neuromuscular blockade should be monitored in every patient receiving aminoglycoside antibiotic with even a single intubating dose of neuromuscular blocking drug.

**Key words :** Neuromuscular blockade ; rocuronium ; amikacin ; potentiation.

### INTRODUCTION

Neuromuscular blocking agents can have multiple drug interactions that can lead to clinically significant potentiation. We report a case of long-lasting neuromuscular blockade due to synergism between a single dose of rocuronium and an amikacin injection.

### CASE REPORT

A 62 year old female was scheduled for a lumbar athrodesis. She had a Launois-Bensaude disease (subcutaneous fat deposition, thought to be genetic ; can be associated to alcoholic liver disease, with megaloblastic anaemia and polyneuropathy). She had history of hypertension, alcohol abuse but no evidence of polyneuropathy, gastro-duodenal ulcer, treated asthma and obesity (90 kg, 158 cm, BMI 36). No known allergy. She was taking beta-blocker, sartan, inhaled beta-2 mimetics and corticosteroids, oral theophylline. Preop lab, EKG and chest X-ray were without particularity. The procedure was performed under general anesthesia induced with 200 mg propofol, 25 µg sufentanil, 45 mg ketamine, 40 mg rocuronium, and main-

tained with desflurane. She received 2 g cefazoline as antibioprophyllaxis. Total duration was 140 minutes and there was no residual neuromuscular blockade (NMB) at the end of the procedure (train-of-four ratio (TOF) above 0,9, ulnar nerve stimulation at the wrist, thumb adduction measured by acceleromyography ; TOF-Watch®, Organon, Oss, The Netherlands). The patient could be then safely extubated ten minutes later.

Our patient didn't leave hospital and had to be reoperated one month later because of local infection at the scar site. Before reoperation, she received a ten days course of amoxicilline-clavulanate (2 g every 8 hours). Two days before operation serum creatinine was 1,18 mg/dl, CRP 37, GOT 76, GPT 34, gammaGT 37. Serum ions were normal, including calcium and magnesium.

The second procedure was performed under general anesthesia induced by exactly the same drugs including 40 mg rocuronium (a single induction bolus), and maintained by propofol (50 mg/hour) and sufentanil (5 to 10 mcg every 30-45 minutes). 55 minutes after induction of GA, patient received amikacin (1 gram over 30 minutes), by request of the surgeon. Surgery was without problem. Body temperature was kept above 35,5°C. At the end of the procedure, 120 minutes after induction of GA, she received 2 gram of propacetamol and 100 mg of tramadol (and no NSAID), but

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neuromuscular monitoring showed complete muscular blockade. We had to wait 230 minutes to recover the first response to TOF stimulation, and 18 more minutes to recover 4 responses but still with residual NMB (fading). We reversed NMB (2 mg neostigmine and 0,4 mg glycopyrrolate) and 10 minutes later, TOF ratio rise above 0,9 and the patient could be safely extubated. Blood samples taken 210 minutes after injection of rocuronium showed serum creatinine 0,8 mg/dl and serum amikacin 88 mcg/dl. Those results were obtained 210 minutes after initial bolus of rocuronium, 125 minutes after the end of infusion of amikacin, and 10 minutes before observing the first response at the neuromuscular stimulator.

## DISCUSSION

Many drugs are known to interact with neuromuscular blocking drugs (1). They include antibiotics, inhaled anesthetics, magnesium, lithium, local anesthetics, antiepileptic drugs, some diuretics (furosemide) and some other drugs. Some antibiotics have been proved to be very safe (e.g. beta-lactams) while others have proved to have neuromuscular properties by themselves (e.g. clindamycine). Aminoglycoside can interfere with neuromuscular transmission by inhibition of the cholinergic activity at a pre- and post-synaptic level (2).

In experimental animal studies, amikacin has been shown to induce NMB by itself at very high doses (80 to 200 mg/kg) (3-5) and to induce NMB at clinical doses (20 mg/kg) after subthreshold doses of d-tubocarine (0,05 mg/kg) (3). Hashimoto *et al* documented interaction of amikacin with d-tubocarine in man, and showed significant potentiation of NMB at low doses (200 mg), but for a short time (a few minutes) (6). KRONENFELD *et al.* reported a recurrence of NMB after reversal of vecuronium NMB, to a patient who had undergone sternal irrigation with polymyxin and amikacin (7). However polymyxin could have played an important role in this recurrent NMB, as its powerful neuromuscular blocking properties have been well documented (8, 9). Hasfurth and Bailey reported the case of a patient who needed tracheal reintubation and overnight mechanical ventilation in the ICU probably due to rocuronium and neomycin interaction (10). However, their patient received several preoperative doses of neomycin and several boluses of rocuronium during the surgical procedure.

Based on her lean body weight (60 kg for Body Mass Index 25), our patient received a

0,6 mg/kg dose, which clinical duration is 31 minutes (15-85). The drug should then have been significantly eliminated at the time of starting amikacin, 55 minutes later. This shows how powerful can be the potentiation between these two drugs.

Amikacin-rocuronium interactions has never been reported to our knowledge. Although interactions between aminoglycoside and neuromuscular blockade are known to be possible, there are inconsistent. For instance, Dupuis *et al* found that gentamycin and tobramycin prolonged the neuromuscular actions of vecuronium but not that of atracurium (11). The long duration of NMB (4 hours) after a single doses of amikacin and rocuronium not given concomitantly, in a patient who did not have any precipitating factors, make this case even more interesting. Launois-Bensaude disease doesn't seem to be responsible of this, since no effect on neuromuscular junction has been described for this disease.

Although literature shows that neostigmine produce only a partial reversal of aminoglycoside-induced block, we were able to fully reverse it with this drug. Calcium (chloride or gluconate) has been shown even more effective than cholinesterase inhibitors for reversal of this type of NMB, but its use is not recommended because the antagonism that it produces is not sustained, and it may prevent the antibacterial effect of the antibiotic (1, 2). 4-aminopyridine has been used for research purpose but is not easily available for clinical use (2).

Recent data's show that there is a high incidence of residual NMB in clinical daily practice until 2 hours after a single intubating dose of non-depolarizing muscle relaxant with an intermediate duration of action (12). Our case emphasize the need to monitor every NMB, especially when potentiating drugs such as aminoglycoside antibiotics are administered concomitantly, which is frequently the case in daily practice.

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