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CORRESPONDENCE

Ephedrine delays rocuronium recovery

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To the Editor,

Ephedrine is a sympathomimetic amine used to treat hypotension.[1] The onset time of neuromuscular blocking agents (NMBA) is influenced by muscle blood flow and cardiac output,[2] and ephedrine can reduce the onset time of NMBAs by increasing these variables.[3] Moreover, ephedrine seems to increase acetylcholine release[1] and is used to treat congenital myasthenic syndromes.[4] We report an unexpected case of reparalysis following ephedrine administration. This report is written with the patient's signed consent.

A 63-yr-old male (83 kg, 174 cm) underwent anterior resection for rectal cancer. After anesthesia induction with propofol and remifentanil, muscle relaxation was achieved with rocuronium 50 mg. Anesthesia was maintained with desflurane and epidural 0.375% ropivacaine. Neuromuscular function was monitored by acceleromyography (AMG) at the adductor pollicis muscle using a train-of-four (TOF)-Watch® SX monitor interfaced with a computer using the TOF-Watch SX monitor software (Organon, Ireland, now Merck & Co., USA). The acceleration transducer was placed with the hand adapter (Hand-Adapter®; Organon, Ireland, now Merck & Co., USA). Surgery lasted 152 min, and rocuronium 10 mg was administered throughout the procedure every time the second twitch (T_2) in the train-of-four reappeared; the total rocuronium dose was 70 mg. At the end of surgery, a hypotensive episode occurred (mean arterial pressure < 50 mmHg); ephedrine 5 mg *iv* was administered and blood pressure was restored rapidly. At the time of the ephedrine injection, which was 68 min following the previous rocuronium bolus, the first twitch (T_1) was 25% and the train-of-four ratio was (TOFR) 38%. Two minutes later, the T_1 had decreased to 19% and the TOFR had decreased to 0% (Figure). The fourth twitch reappeared four minutes after ephedrine administration, and almost nine minutes elapsed before the TOFR reached its pre-ephedrine administration value. Ten minutes later, the TOFR was 55% and, therefore, sugammadex (100 mg) was administered. Two minutes later, the patient's trachea was extubated and he was returned to the surgical ward one hour later.

In this case, ephedrine was administered when the patient was recovering spontaneously from neuromuscular blockade ($T_1 = 25\%$ and TOFR $= 38\%$). After ephedrine administration, we expected the patient's blood pressure to increase without any neuromuscular effect. Instead, two minutes after ephedrine administration, T_1 decreased to 19% and the TOFR was 0%.

A strict AMG monitoring was performed throughout the entire operation to reduce NMBA accumulation in peripheral compartments. Nevertheless, we observed more intense blockade after ephedrine. The onset time of NMBAs is influenced by different hemodynamic factors,[3] and since rocuronium is a drug with a fast onset of effect, the blood effect-site equilibration constant is correlated with cardiac output.[2] Therefore, by increasing cardiac output and tissue perfusion, we assumed that ephedrine could have enhanced inter-compartmental clearance of rocuronium[5] which flowed back into blood circulation to be redistributed to the neuromuscular junction. We did not observe a reversal effect driven by ephedrine-related

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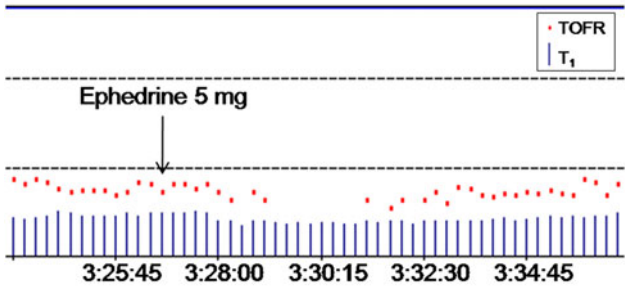

Figure The effect of ephedrine on rocuronium recovery. Neuromuscular monitoring with TOF-Watch® SX shows a gradual increase of first twitch (T_1 - vertical lines) and train-of-four ratio (TOFR - ●) values. After ephedrine administration (three hours, 26 min and 45 sec after induction) a decrease of T_1 and TOFR values can be observed. A few minutes later the T_1 starts to increase and the TOFR reappears (three hours, 31 min and 15 sec after induction)

acetylcholine release, probably because of the low dose of ephedrine administered. We exclude the possibility that residual rocuronium from a previous administration at the injection site could have been flushed into the circulation by ephedrine because fluids were delivered by a volumetric pump. Strangely, we never obtained TOFR values between 0 and 30%, suggesting that our monitoring was not optimal. Nevertheless, we performed six train-of-four stimulations prior to calibration, and no changes in the patient's arm position occurred during the procedure.

During general anesthesia with NMBA, monitoring of neuromuscular function is highly recommended, and anesthesiologists should keep in mind that ephedrine can delay recovery from rocuronium. This could be an important issue, especially in order to prevent residual neuromuscular blockade. A prospective observational study could be designed to test our hypothesis.

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