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Clinical Investigation

CLINICAL INVESTIGATION

Feasibility of a 'reversed' isolated forearm technique by regional antagonization of rocuronium-induced neuromuscular block: a pilot study

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Abstract

Background: The isolated forearm technique is used to monitor intraoperative awareness. However, this technique cannot be applied to patients who must be kept deeply paralysed for >1 h, because the tourniquet preventing the neuromuscular blocking agent from paralysing the forearm must be deflated from time to time. To overcome this problem, we tested the feasibility of a 'reversed' isolated forearm technique.

Methods: Patients received rocuronium 0.6 mg kg^{-1} i.v. to achieve muscle paralysis. A tourniquet was then inflated around one upper arm to prevent further blood supply to the forearm. Sugammadex was injected into a vein of this isolated forearm to antagonize muscle paralysis regionally. A dose titration of sugammadex to antagonize muscle paralysis in the isolated forearm was performed in 10 patients, and the effects of the selected dose were observed in 10 additional patients.

Results: The sugammadex dose required to antagonize muscle paralysis in the isolated forearm was 0.03 mg kg^{-1} in 30 ml of 0.9% saline. Muscle paralysis was antagonized in the isolated forearm within 3.2 min in nine of 10 patients; the rest of the patients' bodies remained paralysed. Releasing the tourniquet 15 min later did not affect the train-of-four count in the isolated forearm but significantly increased the train-of-four count in the other arm by 7%.

Conclusions: Regional antagonization of rocuronium-induced muscle paralysis using a sugammadex dose of 0.03 mg kg^{-1} injected into an isolated forearm was feasible and did not have relevant systemic effects.

Clinical trial registration: The trial was registered at EudraCT (ref. no. 2013-002164-53) before patient enrolment began.

Key words: blood supply; consciousness; gamma-cyclodextrins; intraoperative awareness, prevention & control; sugammadex

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Editor's key points

- The isolated forearm test is used to detect responsiveness in patients receiving neuromuscular blocking agents.
- It involves isolation of an arm before systemic administration of neuromuscular blocking agents.
- Given that isolation involves ischaemia, the technique cannot be continued for more than an hour.
- The authors propose a technique to keep one arm unparalysed for longer but without prolonged ischaemia.

The 'isolated forearm technique' (IFT) has been used for more than 35 yr to detect intraoperative awareness in patients receiving neuromuscular blocking agents during general anaesthesia.[1 2] The IFT enables patients to move parts of their body (i.e. the forearm), while the rest of the body remains paralysed. First, a tourniquet around the upper arm is inflated after the induction of anaesthesia but before any neuromuscular blocking agent is given. This tourniquet prevents the neuromuscular blocking agent from reaching the 'isolated forearm', and the patient remains able to communicate by moving one hand in response to a verbal command, while the rest of the body remains paralysed. Monitoring awareness with IFT during longer operations is feasible if the tourniquet is deflated from time to time to avoid pressure-induced nerve block.[3] However, application of this technique to patients for longer periods is not possible because deflation of the tourniquet might lead to paralysis of the arm if longer-acting neuromuscular blocking agents are used at high doses.

To overcome this problem, a modified, 'reversed' IFT might be feasible, in which muscle paralysis is not prevented in the isolated forearm but rather is antagonized regionally by injection of a small dose of sugammadex into the isolated forearm. This technique would be applicable to patients who are already paralysed and could also be repeated during longer procedures. Therefore, the aim of the present study was to evaluate the feasibility of regionally antagonizing neuromuscular block in an isolated forearm.

Methods

The trial was designed as a prospective, sequential, interventional, single-centre pilot study and was conducted at the Medical University of Vienna, Austria. The Institutional Ethics Committee approved the study (Ethics Committee of the Medical University of Vienna, ref. no. 1567/2013, EudraCT ref. no. 2013-002164-53), and written informed consent was obtained from the patients before study enrolment. The sugammadex dose was determined in the first 10 patients (Dose-finding Group), and the effects of the sugammadex dose were observed in the next 10 patients (Dose-effect Group).

According to the 'Good clinical research practice in pharmacodynamics studies of neuromuscular blocking agents', the following inclusion criteria were applied: adults (18–65 yr of age) who required minor elective surgery under general anaesthesia and were classified as ASA class I–II, with a BMI between 18.5 and 24.9 kg m^{-2}.[4] Patients were included only if free access to both arms was possible during the surgical procedure to ensure the correct application of the study medication and exact neuromuscular monitoring of both arms. Patients with a known neuromuscular disease or an allergy to one of the drugs used in the trial were not included. In addition, patients taking medications that were likely to interact with the study medication (e.g. hormonal contraceptives) or who were pregnant or breastfeeding were excluded.

Dose-finding Group

To determine the sugammadex dose needed to antagonize rocuronium-induced neuromuscular block regionally, a dose titration was performed in the first 10 patients. After the patients arrived in the operating theatre, standard monitoring (pulse oximetry, ECG, and non-invasive blood pressure) was applied. The regional antagonism of rocuronium-induced muscle paralysis was applied to one arm (interventional limb), whereas the other arm (control limb) was used to determine the state of neuromuscular block of the rest of the body. A pulse oximeter and a blood pressure cuff were attached to the control limb. Additionally, the patients were connected to a bispectral index monitor (BIS Vista Monitoring; Aspect Medical Systems, Norwood, MA, USA), and neuromuscular monitoring was conducted on both arms (TOF-watchSX; Organon Ltd, Swords, Dublin, Ireland). For neuromuscular monitoring, the skin was cleansed, and surface electrodes (Swaromed Ag/AgCl Electrodes; Nessler Medizintechnik GmbH, Innsbruck, Tirol, Austria) were placed above the presumed position of the ulnar nerve at the distal forearm, ensuring a distance of 3–6 cm between the electrodes, with the negative electrode located more distally. An accelerometer, which was used to detect the response signal of the adductor pollicis muscle, was placed on the thumb; the hand was fixed to the armrest, and no preload was applied to the effector muscle. A forced air blanket was used to maintain the core temperature >35°C and the skin temperature in the arms >32°C. Anaesthesia was induced with fentanyl (2–3 μg kg^{-1}) and propofol (1.5–2.5 mg kg^{-1}). After loss of consciousness, calibration of the train-of-four (TOF) watches was performed using the calibration program provided by the manufacturer. From this point onwards, the TOF count (200 μs, square wave, 2 Hz for 1.5 s) was measured every 15 s in both arms simultaneously. After this calibration, rocuronium 0.6 mg kg^{-1} was administered, and intubation was performed when the TOF count decreased to ≤1. Anaesthesia was then maintained with continuous propofol infusion, aiming for a BIS value of 40–60, and a small-bore i.v. line (Vasofix Safety, 22 gauge; B. Braun Melsungen AG, Melsungen, Germany) was inserted into the back of the hand of the interventional limb. When the TOF count returned to 1, blood was forced out of the veins of the interventional limb by elevating the arm. Further blood entry into the interventional limb was blocked by a padded tourniquet, which was inflated to 100 mm Hg above the patient's systolic arterial blood pressure, around the middle of the upper arm. The arm was placed back into the initial position, and the first sugammadex dose diluted in 30 ml normal saline was injected over a period of 30 s through the i.v. line at the back of the hand of the interventional limb.

The dose-titration process was designed as follows. The initial dose in the first patient was set to be sugammadex 0.5 mg kg^{-1} diluted in 30 ml normal saline. If the TOF ratio remained below 0.9 for the next 5 min, a top-up dose of one-quarter of this dose (e.g. sugammadex 0.125 mg kg^{-1} in Patient 1) diluted in 10 ml of 0.9% saline was administered. This procedure was repeated until a stable TOF ratio ≥0.9 (three consecutive measurements ≥0.9) was reached in the interventional limb or until a total of four injections were given. If a TOF ratio ≥0.9 was achieved with this titration, the initial and top-up sugammadex doses in the next patient were reduced to one-quarter of the initial dose given to the previous patient but were still diluted in 30 ml saline (10 ml for top-up doses). For example, if the muscle paralysis of Patient 1 was antagonized after the initial dose of sugammadex 0.5 mg kg^{-1}, the initial and the top-up doses would be reduced to 1.25 mg kg^{-1} in Patient 2.