Prolonged neuromuscular block associated with mivacurium

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Summary
Mivacurium is a relatively new short-acting non-depolarizing neuromuscular blocker. A recommended dose of 0.15–0.2 mg kg⁻¹ provides tracheal intubating conditions within 2.5 min and duration of action of 15–30 min, making it a possible alternative to suxamethonium for short procedures requiring tracheal intubation. However, in common with suxamethonium its metabolism depends primarily on plasma cholinesterase and its duration of action is prolonged in patients with reduced plasma cholinesterase activity. We present a case of unexpected prolonged neuromuscular block in a child with previously undiagnosed plasma cholinesterase deficiency. (Br. J. Anaesth. 1995; 74: 237–238)

Key words
Neuromuscular block, mivacurium. Enzymes, cholinesterase.

Case report
A 6-yr-old boy was admitted for elective adenotonsillectomy. He was healthy and apart from recurrent throat infections had no other significant medical history. He had not been anaesthetized previously and there was no family history of anaesthetic problems. He was not taking any medication and had no known allergies. Physical examination revealed a normal male child weighing 22 kg.

EMLA cream was applied topically 1 h before surgery. General anaesthesia was induced with fentanyl 25 μg and propofol 50 mg i.v. Mivacurium was given as a single dose of 4 mg (0.18 mg kg⁻¹) and the trachea was intubated 1 min later. Anaesthesia was maintained with 1% isoflurane and 60% nitrous oxide in oxygen. An additional dose of fentanyl 25 μg was given as surgery commenced. Ventilation of the lungs was controlled with Penlon Nuffield 200 ventilator.

The operation was uneventful and was completed 25 min after induction of anaesthesia. At this stage there was no response to peripheral nerve stimulation with either train-of-four (TOF) or 50-Hz tetanic stimulation of the ulnar or facial nerves. Anaesthesia was continued in the operating theatre for an additional 20 min with no change in neuromuscular function. Neostigmine 1.25 mg and glycopyrronium 0.25 mg were given with no effect on neuromuscular transmission and so the patient was transferred to the high dependency unit where ventilation was continued and a propofol infusion commenced.

Neuromuscular block was monitored by transcutaneous stimulation of the ulnar nerve at the wrist. A single post-tetanic twitch was first observed 60 min after administration of mivacurium. Full neuromuscular function with normal TOF response returned 180 min after administration of mivacurium and the trachea was extubated uneventfully.

Serum cholinesterase activity was measured colorimetrically using benzoylcholine as substrate at the Cholinesterase Research Unit, Hammersmith Hospital, London. The patient had a cholinesterase activity of 27 iu, a dibucaine number of 23 and a fluoride number of 25. He therefore has one atypical and one silent gene (E₁E₂) and no genes for normal plasma cholinesterase.

Discussion
Four patients who were known to have atypical plasma cholinesterase activity caused by a homozygous atypical genotype have been studied previously after receiving mivacurium [1]. One adult patient received a dose of mivacurium 0.18 mg kg⁻¹ (as did the patient in this report) and 6 h elapsed before all four responses to TOF stimulation returned. The other three patients were given a smaller dose (0.03 mg kg⁻¹) and had complete neuromuscular block for 26–128 min and neuromuscular block was antagonized successfully with neostigmine when spontaneous recovery had begun.

There are two reported cases of unexpected prolonged neuromuscular block after mivacurium that occurred in previously undiagnosed patients with homozygous pseudocholinesterase deficiency. One occurred in a healthy adult undergoing wisdom teeth extraction and 4 h elapsed until recovery of neuromuscular function [2]. He had a plasma cholinesterase activity of 29 iu, dibucaine number of 20 and a fluoride number of 29 (measured colorimetrically at the Cholinesterase Research Unit, Hammersmith Hospital). The other [3] was a 12-yr-old girl undergoing muscle biopsy for investigation of proximal muscle weakness and suspected dermatomyositis. A period of 6 h 10 min elapsed before she could sustain head lift for 5 s, allowing safe tracheal extubation. It is not certain how much her underlying muscle pathology contributed to delay in the return of full neuromuscular function. She had a plasma cholinesterase activity of 712 iu (measured by kinetic assay; normal value 2900–7100 iu).

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In the case presented here, our patient was given the recommended dose of mivacurium for a child. He was healthy with no underlying pathology that could contribute to the response to mivacurium. Neostigmine was certainly instituted too early to be of use and was not given later after some spontaneous neuromuscular recovery because it was felt safer to await full spontaneous recovery than risk recurarization later.

The small number of reported cases of prolonged neuromuscular block after administration of the recommended dose of mivacurium to patients with abnormal or absent plasma cholinesterase suggests a recovery time to full neuromuscular function of 6–8 h in adults. The patient presented here is the only documented case occurring in a healthy child and the only individual with a heterozygous atypical/silent plasma cholinesterase genotype. Recovery time was 3 h.

Individuals with homozygote atypical plasma cholinesterase activity (E\textsuperscript{A}E\textsuperscript{A}) and with one or both silent genes (E\textsuperscript{i}E\textsuperscript{A}) take at least 3 h to recover neuromuscular function after being given suxamethonium [4] which appears to be similar to the time for recovery from mivacurium.

References