Mivacurium chloride and myotonic dystrophy

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Summary
We describe the successful use of the short-acting, non-depolarizing neuromuscular blocking agent, mivacurium, in a patient with myotonic dystrophy. Increased sensitivity to mivacurium was demonstrated using train-of-four monitoring, with a single dose of mivacurium providing adequate block for 90 min of surgery. Spontaneous recovery appeared prolonged with a recovery index (25–75 % T1) of 10 min and a recovery time (5–95 % T1) of 30 min. The use of reversal agents and anticholinergic agents was avoided.

Key words
Neuromuscular block, mivacurium. Complications, myotonic dystrophy.

Myotonic dystrophy is the commonest of the myotonic syndromes. It is an autosomal dominant inherited muscle disorder characterized by failure of muscle relaxation (myotonia), muscle atrophy and several clinically significant ophthalmic, endocrine and cardiac manifestations. Patients may show abnormal responses to various anaesthetic agents with increased sensitivity to suxamethonium [1], propofol [2] and thiopentone [3].

Respiratory complications are common in the postoperative period and may be augmented by several anaesthetic and analgesic drugs. As anticholinesterase drugs can precipitate myotonia or may result in inadequate antagonism of neuromuscular block [4], the use of the intermediate duration drugs vecuronium and atracurium has been advocated to avoid the need for reversal agents [5, 6].

Mivacurium chloride is a benzylisoquinolium diester that is hydrolysed rapidly by plasma cholinesterase and atracurium has been advocated to avoid the need for reversal agents [5, 6].

Case report
A 32-yr-old man, weighing 63 kg, presented for laparoscopic cholecystectomy. He had a strong family history of myotonic dystrophy and for this reason had been investigated and diagnosed positive for the disease at 11 yr of age, although at this time he was asymptomatic. He had been reviewed by a neurologist in 1992 some 18 yr later at which time he was found to exhibit myotonia of his hands, marked wasting of the sternocleidomastoids and frontal balding. He described only very mild and occasional difficulty with swallowing. Despite this he was graded “more severe than average” by the neurologist reviewing him at that time.

The patient’s medical history included an uneventful tonsillectomy and adenoidectomy at 7 yr of age. He had presented with abdominal pain in June 1994 when he underwent a negative gastroscopy. An ultrasound scan was abnormal and showed small calculi within the gallbladder; cholecystokinin i.v. confirmed the diagnosis by positive reproduction of the symptoms. Preoperative assessment revealed a man with the characteristic facies of dystrophia myotonica together with demonstrable myotonia of the hands on firm handshake. The patient however felt that his symptoms had improved in the last few years and denied any current difficult in swallowing or dyspnoea on exercise. He had a healthy and normal exercise tolerance and denied any other cardiorespiratory symptoms. He was not receiving medication and denied any other hospital admissions. On examination he had normal heart sounds and vesicular breath sounds with no evidence of heart failure. Full blood count, plasma urea, creatinine and electrolyte concentrations were within normal laboratory ranges. The electrocardiogram revealed a sinus rate of 80 beat min⁻¹ with borderline first-degree heart block.

Preoperative lung function tests showed peak expiratory flow rate of 250 litre min⁻¹ and forced expiratory volume in 1 s of 2.5 litre. In view of his normal exercise tolerance it was deemed unnecessary to perform arterial blood-gas analysis. \( S_{\text{PO}} \), was, however, noted to be 100 % on room air. He was not premedicated.

The patient was monitored using electrocardiography, non-invasive arterial pressure, pulse oximetry, capnography, and a nasopharyngeal temperature probe. After preoxygenation with 100 % oxygen, anaesthesia was induced with propofol 3 mg kg⁻¹. Ventilation was assisted with a face mask using a Lack system. Anaesthesia was maintained with 66 % nitrous oxide and 1–2 % enflurane (end-tidal) in oxygen.

The skin over the non-dominant forearm and hand was degreased using an alcohol solution. Five silver–silver chloride electrodes were placed: two over the ulnar nerve, one over the mid-point of the
distal skin crease at the wrist, one over the palmar aspect of the head of the first metacarpal and one over the belly of the adductor pollicis muscle. These were connected to a Datex Relaxograph. Neuromuscular monitoring was commenced using train-of-four (TOF) stimuli (2 Hz at 20-s intervals) to the ulnar nerve and the gated, rectified and integrated electromyograph (EMG) from the adductor pollicis was recorded. A normal TOF trace was obtained. Mivacurium was then administered in a dose of 0.08 mg kg\(^{-1}\) (the ED\(_{95}\) dose) and the trachea was subsequently intubated at 100 % block of the TOF.

Intermittent positive pressure ventilation was applied by a Blease Manley ventilator. Anaesthesia was maintained with 1–2 % enflurane, as assessed by an agent analyser on a Datex AS3 monitor, and the patient remained normocapnic throughout the procedure.

Body temperature was maintained by the use of a warming blanket, HME humidifier and warmed i.v. fluids, and the patient remained normothermic throughout.

Neuromuscular function was allowed to recover spontaneously. T1 recovered to 100 % at 42 min at which time the TOF ratio was 0.5. Interestingly, however, fade persisted for a further 40 min, only achieving a ratio of 0.7 at 80 min. The TOF ratio was greater than 0.9 after another 10 min by which time the procedure was completed.

On completion of surgery, neuromuscular function was also assessed as clinically reversed by performance of a successful 5-s head lift, and despite being slower than most patients to awaken, the trachea was extubated without incident. The use of reversal agents and anticholinergics was avoided and subsequent recovery was uneventful. The patient continued to do well and was discharged from hospital 48 h later.

Discussion

In this patient, mivacurium appeared to have a more prolonged action than anticipated with the recovery time (5–95 % T1) and recovery index (25–75 % T1) being prolonged to 30 and 10 min, respectively. Previous studies [7] have noted mean 5–95 % and 25–75 % recovery times of T1 to be 18.6 and 6.9 min, respectively, independent of dosage group (0.1–0.3 mg kg\(^{-1}\) range). In addition, reports have demonstrated that both enflurane and isoflurane [8, 9] alter the dose–response relationship to mivacurium, with a possible decrease in the ED\(_{95}\) of mivacurium to 0.05 mg kg\(^{-1}\) during enflurane anaesthesia. An increased duration of action of mivacurium (22.2 min) independent of this enhancement of neuromuscular block has also been demonstrated with enflurane anaesthesia [8]. Despite consideration of the variation in recovery times under different anaesthetic conditions, the variables measured in our patient appeared to be prolonged.

The possibility of a rare cholinesterase variant causing the demonstrated prolongation of action of mivacurium cannot be excluded. However, other studies have not shown predictable responses to mivacurium in the presence of abnormal cholinesterase [8] and so this was not investigated further.

Respiratory complications are more common in myotonic patients for a variety of reasons. Weakness of the respiratory muscles may cause hypoventilation and decreased cough reflexes and the residual somnolent effect of anaesthetic agents may make sputum retention more likely. Under such circumstances a recovery TOF ratio of greater than 0.9 is important to maximize ventilatory variables [10]. While the action of mivacurium was prolonged in this patient it provided a perfectly adequate block for the duration of surgery (90 min) and avoided the need for anticholinesterase and anticholinergic agent administration.

We have described the safe and satisfactory use of mivacurium chloride in this patient; however, the sensitivity of the patient’s response to neuromuscular block illustrates the requirement for accurate monitoring of neuromuscular function in these patients. While it would seem sensible to use a short-acting neuromuscular blocker, we cannot suggest on the basis of a single case report any advantages in the use of mivacurium compared with other neuromuscular blocking agents in patients with myotonic dystrophy.

References