Mivacurium chloride and late onset congenital myopathy

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Summary
We describe the successful use of the short-acting, non-depolarizing neuromuscular blocking agent, mivacurium, in a 53-yr-old female patient with late onset congenital myopathy, undergoing elective submucous resection of the inferior turbinates. She was unable to climb stairs and walking was limited to periods of 15 min because of generalized weakness, fatigue and shortness of breath. A Datex Relaxograph was used to monitor the train-of-four count. No increase in sensitivity to mivacurium was demonstrated. A dose of 12 mg (three times the recommended ED95) resulted in 88 % reduction of the first of the train-of-four count (T1) compared with control (TC). Spontaneous recovery of T1/TC to 100 % took 11 min 20 s from the time maximum block was first achieved. The recovery index (25–75 % T1/TC) was 4 min 40 s. (Br. J. Anaesth. 1996; 76: 160–162)

Key words
Neuromuscular block, mivacurium. Complications, myopathy.

Abnormal responses to neuromuscular block are well recognized in several muscle disorders [1–4]. Late onset congenital myopathy presents in adulthood with a gradual generalized weakness of not only the limb muscles but also the respiratory muscles. Little is known about the effect of neuromuscular block in patients with congenital myopathy. The few cases that are reported describe the use, without complications, of normal doses of the long-acting neuromuscular blocking agent, pancuronium, in patients who presented in childhood with this condition [5, 6]. We are unaware of any previously reported use of the short acting neuromuscular blocking drug, mivacurium, in patients with adult onset congenital myopathy.

Case report

MEDICAL HISTORY
A 53-yr-old female patient, weighing 50 kg, height 177 cm, presented for elective submucous resection of the inferior turbinates. She had a long history of muscle weakness dating back to adolescence when she found that she had difficulty keeping her arms above her head for any period of time. In her late twenties she had difficulty climbing stairs and more recently was unable to do so. She used crutches to walk but was limited to periods of 15 min because of generalized weakness, fatigue and shortness of breath. She wore a neck collar continuously as the weakness in her neck caused her head to droop. There was no specific difficulty with swallowing and no diplopia. She had no muscle weakness during childhood.

Her other past medical history revealed that she had developed osteoporosis in her forties and had been receiving hormone replacement therapy. She also suffered from dyspepsia for which she received omeprazole and cisapride. There was no family history of muscle disorders and she was a non-smoker.

CLINICAL EXAMINATION
She was a thin lady with no signs of cardiac or respiratory failure. There was wasting of the deltoid, glutei and to a lesser extent the quadriceps muscles. She was unable to abduct her arms beyond 90° offering only mild resistance to forced adduction. There was mild weakness of hip flexion and leg extension such that movement against gravity and mild resistance to force were possible but not sustained. Reflexes were symmetrical with a negative plantar reflex. Cranial nerve examination was normal.

INVESTIGATIONS
Full blood count, urea, creatinine and other electrolyte concentrations were normal, including serum creatine kinase. Electrocardiography and chest x-ray were normal. Lung function tests performed before operation showed a peak expiratory flow rate of 380 litre min⁻¹ (80 % of predicted). Forced vital capacity (FVC) was 1.88 litre (52 % of predicted). FEV1 was 1.85 litre (60 % of predicted) with FEV1/FVC 98 %. Maximal pressures generated at the mouth, after full inspiration and full expiration, that is maximal expiratory and maximal inspiratory pressures, were measured using a mouth pressure meter (Precision Medical, Pickering, Yorks, UK). These were 26 % and 36 % of predicted, respectively, reflecting global respiratory muscle weakness. Carbon monoxide transfer tests were within normal limits. Nerve conduction studies were normal and a previous electromyograph showed myopathic changes. A
quadriceps muscle biopsy showed generalized widespread mild degenerative changes with selective type 2B fibre atrophy and a predominance of type 1 fibres. These changes were indicative of a non-specific congenital myopathy.

ANAESTHESIA

We were concerned that the patient would experience difficulty in breathing and prove to be a weaning problem after operation as a consequence of her generalized respiratory muscle weakness. Initial anaesthetic management therefore included pre-operative chest physiotherapy and breathing exercises and we ensured the availability of an intensive care bed.

Anaesthesia was induced with propofol 2 mg kg⁻¹ and fentanyl 1 μg kg⁻¹. Anaesthesia was maintained initially with incremental doses of propofol with 66 % nitrous oxide in 34 % oxygen and the patient’s breathing was assisted with a face mask at this stage.

Monitoring comprised electrocardiography, non-invasive arterial pressure, pulse oximetry, capnography and vapour analysis. The skin over the non-dominant forearm and hand was degreased using an alcoholic 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 from the adductor pollicis was recorded. A normal TOF trace was obtained. The size of the gain setting, supra-maximal stimulus and the stimulus artefact were noted.

As the patient had muscle weakness, only a small dose (1 × ED₉₀) of mivacurium was administered. No effect on the TOF was seen after 4 min and therefore an additional dose of 4 mg was given. This resulted in a gradual reduction in the first twitch of the TOF (T₁) which stabilized to a T₁ response of 50 % compared with control (TC). Intubation was attempted with a cuffed tracheal tube size 8 mm at this stage but was unsuccessful because of difficulty in seeing the vocal cords. Another dose of mivacurium 4 mg was therefore administered 8 min after the first dose, which resulted in a decrease in T₁/TC to 12 %. At this point the intubating conditions were much improved and the trachea was intubated. Maximum block of 88 % was achieved 12 min after the first dose of mivacurium had been given. The patient was taken into theatre and her lungs ventilated with 66 % nitrous oxide and 0.5 % enflurane in oxygen.

The cardiovascular system was stable and she remained normothermic throughout surgery. Additional mivacurium was not required and neuromuscular block was allowed to recover spontaneously. Recovery of T₁/TC to 100 % took 11 min 20 s from the time maximum block was first achieved, with a recovery index (25–75 % T₁/TC) of 4 min 40 s. Antagonism of neuromuscular block was not deemed necessary as the TOF ratio had recovered spontaneously to 1.0. The patient emerged from anaesthesia breathing spontaneously and the trachea was extubated uneventfully. Before extubation, the patient demonstrated good hand grip strength. In view of her myopathy, head lift testing was inappropriate. The postoperative period was unremarkable.

Discussion

The congenital myopathies are a rare and complex group of inherited muscle disorders which are associated with enzyme defects and structural abnormalities in the muscle fibres. Mitochondrial oxidative enzyme activity is reduced or absent in central core and multicore congenital myopathies [7–9]. The presence of abnormal muscle cell organelles such as rods and nemaline bodies characterize nemaline myopathy while abnormal nuclei are found in centronuclear myopathy [10]. In addition to the enzyme defects there is also heterogeneity of muscle fibre sizes, and atrophy or predominance of certain muscle fibres. In some patients it may be difficult to assign a specific diagnostic group as the muscle biopsy exhibits only non-specific changes and it must be noted that the cytoarchitectural changes and clinical severity may not correlate.

Most patients with congenital myopathy present in childhood. Generalized hypotonia may be detected as early as the neonatal period and delayed motor milestones are common. The child thus has difficulty in getting up from the floor, walking and later running and climbing stairs. There may be associated skeletal abnormalities such as scoliosis, pes cavus, clubbed feet or congenital hip dislocation [11]. Most cases are non or very slowly progressive; indeed, there may be early improvement in childhood but with varying degrees of subsequent deterioration [12]. The involvement of the respiratory muscles may cause respiratory failure which represents a common cause of death [5, 13].

Late onset congenital myopathies present in adulthood with gradual onset of mild muscle weakness involving proximal or distal muscle groups but eventually becoming generalized [14, 15]. As with the childhood disease, they are generally non or very slowly progressive and respiratory muscle paresis causing respiratory failure may be a contributory factor to death [16].

Our patient had a slow, progressive, disabling condition for which there was objective evidence of generalized muscle weakness. Of particular concern was the global respiratory muscle weakness, as suggested by assessment of peak inspiratory and peak expiratory mouth pressures. Failure to ventilate adequately and cough in the postoperative period may cause sputum retention and areas of lung collapse. Infection and hypoxia may supervene causing prolonged recovery and possibly even death. Fortunately our patient suffered none of these complications.

There is a predisposition to malignant hyperthermia during general anaesthesia in patients with
central core congenital myopathy, particularly if associated with a raised creatine kinase concentration [17]. Muscle biopsy showed none of the features diagnostic of this type of congenital myopathy and our patient did not have a raised serum creatine kinase concentration. We therefore felt justified at the time in using a volatile agent. The importance of excluding risk factors must however be stressed before using known triggering agents of malignant hyperpyrexia in patients with muscle weakness.

Mivacurium chloride is a bis-benzylisoquinol- onium diester neuromuscular blocking drug. It was selected because of its relative short duration of action. This characteristic seemed desirable as there was concern that this patient may exhibit particular sensitivity to neuromuscular block. After a single dose of $1 \times \text{ED}_{95}$, a greater than 90 % reduction in T1 compared with TC would be expected after 4 min [18]. Satisfactory intubating conditions, however, were not achieved in our patient until a total of $3 \times \text{ED}_{95}$ had been administered over 12 min. Recovery to 95 % T1/TC would be expected to take 30 min, with a recovery index of 7 min after a single bolus dose of $3 \times \text{ED}_{95}$ [18]. In our patient, recovery of T1/TC to 100 % took 23 min 20 s from the end of the first dose with a recovery index of 4 min 40 s. No unusual sensitivity to neuromuscular block with mivacurium was therefore demonstrated in our patient. Indeed, it could be argued that the patient showed some resistance to block but as the drug was given cumulatively it is more likely that some hydrolysis of the agent had occurred between increments.

Patients with neuromuscular disorders have a very variable response to neuromuscular blocking drugs. It is thus important to monitor neuromuscular function accurately in all such patients. We have described the safe and satisfactory use of mivacurium chloride in a patient with late onset congenital myopathy. However, we cannot on the basis of one patient suggest that all similar cases will necessarily have no complications, nor can we advocate an advantage in the use of mivacurium compared with other intermediate neuromuscular blocking agents.

References