CASE REPORT

Mivacurium chloride and myasthenia gravis

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SUMMARY

We describe the successful use of the short-acting, non-depolarizing neuromuscular blocking agent, mivacurium, in a patient with myasthenia gravis taking pyridostigmine 120 mg four times daily. Increased sensitivity to mivacurium was demonstrated using train-of-four monitoring. A dose of 0.5 times the recommended ED$_{50}$ (3.0 mg) resulted in 93% block of T1. Spontaneous recovery was prolonged with a recovery index (25%-75% T1) of 20.5 min. Residual block was antagonized without difficulty using neostigmine 2.5 mg. We discuss the relationship between plasma cholinesterase, acetylcholinesterase and anticholinesterase drugs. (Br. J. Anaesth. 1994; 72: 468-469)

KEY WORDS

Patients with myasthenia gravis have a variable response to non-depolarizing neuromuscular blocking agents [1], although more often they exhibit increased sensitivity [2, 3]. Their response to suxamethonium may also be unusual; both resistance and early phase 2 block have been described [4].

Mivacurium chloride is a benzylisoquinolinium diester that is hydrolysed rapidly to inactive metabolites by plasma cholinesterase. Hepatic metabolism, if it occurs, is not clinically significant [5]. Mivacurium is the only short-acting non-depolarizing neuromuscular blocker. This characteristic could make it a suitable choice in a myasthenic patient requiring neuromuscular block. We are unaware of any previously reported use of mivacurium in a patient with myasthenia gravis undergoing major surgery.

CASE REPORT

A 76-yr-old woman, weighing 84 kg, height 167 cm, presented for elective colposuspension. She had a 30-yr history of myasthenia gravis, recognized initially by an optician, but not diagnosed formally until 2 yr later with a positive edrophonium test. She was managed initially with pyridostigmine 360 mg orally, four times daily but over the years the dose had been reduced to 120 mg four times daily. She had not had a thymectomy and had not been treated with either steroids or plasmapheresis. She had mild generalized weakness but no bulbar symptoms (Osserman grade 2A).

The patient's medical history included dependent oedema and chronic obstructive airway disease. She smoked 30 cigarettes per day. Her exercise tolerance was limited mostly by her myasthenia gravis to a slow 100 m. She denied other cardiopulmonary symptoms. Her medications on admission included pyridostigmine 120 mg four times daily, bendrofluazide 2.5 mg once daily and a salbutamol inhaler, 2 puffs as required. On examination she was obese and on auscultation bilateral expiratory wheeze was evident. There were no signs of heart failure. Full blood count, plasma urea, creatinine and electrolyte concentrations were all within normal laboratory ranges. Electrocardiogram was normal. Lung function tests before operation showed: peak expiratory flow rate 185 litre min$^{-1}$; forced vital capacity 2 litre; FEV$_1$/FVC 0.65; arterial blood-gas tensions (in room air): $P_{\text{a}O_2}$ 12.9 kPa; $P_{\text{a}CO_2}$ 6.11 kPa; pH 7.45; $HCO_3^-$ 31.2 mmol litre$^{-1}$; BE +7.3 mmol litre$^{-1}$; $S_{\text{p}O_2}$ 98%.

Preoperative management consisted of allowing her to take her usual oral dose of pyridostigmine 120 mg on the evening before and on the morning of surgery (at 06:00 with a cup of tea); 2 puffs of salbutamol were administered on leaving the ward at 10:00.

Anaesthesia commenced at 10:15. The patient was monitored using electrocardiography, non-invasive arterial pressure, pulse oximetry, capnography, vapour analysis and a nasopharyngeal temperature probe. Anaesthesia was induced with propofol 180 mg and fentanyl 100 $\mu$g i.v. after which the cords were sprayed with 4% lignocaine and the trachea intubated without the aid of neuromuscular block. Anaesthesia was maintained with 66% nitrous oxide and 1% enflurane (end-tidal) in oxygen, with the patient ventilated to normocapnia. An extradural catheter was inserted at L2-3 and, after a test dose of 0.5% plain bupivacaine 3 ml, a total of 0.25% plain bupivacaine 8 ml was injected.

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. The size of the gain setting, supranormal stimulus and the stimulus artefact were noted. The ulnar nerve was stimulated for 13 min during a period of stable anaesthesia and then the EMG was recalibrated to minimize baseline drift [6] before administration of the neuromuscular blocker.

Neuromuscular block was found to be inadequate and therefore a dose of 0.1 times the recommended ED$_{95}$ of mivacurium was given (0.6 mg, 0.007 mg kg$^{-1}$) to test for extreme sensitivity. No effect on the TOF was seen and therefore after 4 min a further bolus dose of mivacurium 2.4 mg was administered to give a total of 3.0 mg (0.035 mg kg$^{-1}$, 0.5 times the recommended ED$_{95}$). This resulted in a rapid onset block of 93% of T1 height. Forty minutes later the twitch height had recovered to 93% of control (TOF ratio of 90%). On completion of surgery the patient was given neostigmine 2.5 mg and glycopyrrolate 0.6 mg i.v. for antagonism of residual fade. There was no evidence of a depolarizing block subsequently. The patient was extubated 5 min later having demonstrated good clinical reversal, as assessed by hand grip strength, 5-s head lift and eye opening to command. An extradural infusion of 0.125% bupivacaine and fentanyl 8.33 μg ml$^{-1}$ was commenced and the patient was discharged to the ward uneventfully.

DISCUSSION

In this patient, mivacurium appeared to be more potent than anticipated with a block of 93% of control T1 after a dose of only half the recommended ED$_{95}$ dose (obtained during narcotic anaesthesia). In addition, the duration (7-93% T1) and recovery index (25-75% T1) were prolonged to 40 min and 20.5 min, respectively. In a previous study [5], one of the authors had noted mean 5-95% and 25-75% recovery times of T1 to be 18.6 and 6.9 min, respectively. Even allowing for the use of enflurane, which decreases the ED$_{95}$ of mivacurium to 0.05 mg kg$^{-1}$ [7] and for the patient’s obesity, the variables observed in our patient would seem to be prolonged.

While the altered pharmacodynamics may be attributed to the myasthenia gravis there are further considerations relating to the administration of pyridostigmine. One study demonstrated that recovery time from mivacurium-induced neuromuscular block was related inversely to plasma cholinesterase activity [8]. Anticholinesterase drugs are known to reduce the activity of plasma cholinesterase, in addition to acetylcholinesterase [9, 10] in non-myasthenic patients. This finding also seems to occur in myasthenic patients and reduces with time from the last dose [11]. Measurement of plasma cholinesterase activity was not considered to be useful in this patient. Studies to date suggest that neostigmine still facilitates antagonism of mivacurium-induced block [5]. In this study, neostigmine was administered only when T1 had almost recovered and the TOF ratio was 90%; this did seem to antagonize residual fade. Although the TOF ratio had recovered to 90%, recent evidence [12] suggests that a TOF ratio greater than 0.9 is required to maximize ventilatory variables. Achievement of the above seemed particularly important in this patient with myasthenia gravis and respiratory disease. While the duration of mivacurium was more prolonged than anticipated, it was perfectly adequate for the duration of surgery.

We have described the safe and satisfactory use of mivacurium chloride in this particular patient. The complexity of the pharmacology in such patients highlights the need for accurate monitoring of neuromuscular function in all patients. We cannot, however, on the basis of a single case report, advocate an advantage in the use of mivacurium compared with other intermediate neuromuscular blocking agents.

REFERENCES