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CASE REPORT

Neuromuscular blockade in myasthenia gravis with atracurium besylate

S. WARD AND D. J. WRIGHT

Summary

The use of atracurium besylate, in small incremental doses, with continuous monitoring of neuromuscular function, is described during upper abdominal surgery in a patient with myasthenia gravis.

Key words

Neuromuscular relaxants; Atracurium besylate.
Complications; myasthenia gravis.

Myasthenia gravis is an autoimmune disease with a decrease in functional acetycholine receptors at neuromuscular junctions,[1] characterised by an increased sensitivity to the non-depolarising neuromuscular blocking agents.[2] Anaesthesia for patients with this rare disease, especially for unrelated conditions requiring surgical relaxation can prove difficult particularly in the early postoperative period.[3]

We describe the anaesthetic management of a patient with myasthenia gravis having a cholecystectomy using the new neuromuscular blocking agent atracurium besylate[4] with continuous monitoring of neuromuscular function.

Case history

A 37-year-old woman with myasthenia gravis (first diagnosed in 1976) presented for cholecystectomy. Her symptoms were of variable fatigue, difficulty in chewing and swallowing and inability to walk more than short distances because of increasing weakness. Medication was neostigmine 15 mg and pyridostigmine 60 mg, 2 hourly. Prior to anaesthesia there was no other system pathology.

At 0630 on the day of operation she received a single oral dose of neostigmine 15 mg and pyridostigmine 60 mg. At 1100 premedication of lorazepam 1 mg and metoclopramide 10 mg was administered orally. At 1300 she was brought to theatre when she complained of slight weakness. Surface electrodes were applied to the ulnar nerve at the wrist and the force of thumb adduction measured using a force displacement transducer incorporated in a hand grip.[5] Supramaximal single twitches were applied every 30 seconds immediately following induction of anaesthesia and continuously until the patient left the operating theatre.

Anaesthesia was induced with thiopentone (300 mg) and the trachea intubated under deep halothane after spraying the cords with 4% lignocaine. The lungs were ventilated with N_2O, O_2 and halothane. Physiological tensions of carbon dioxide were maintained throughout the pro-

S. Ward, FFARCS, Senior Registrar, Deborah J. Wright, BSc, Medical Physics Technician, King's College Hospital, Denmark Hill, London SE5 9RS.

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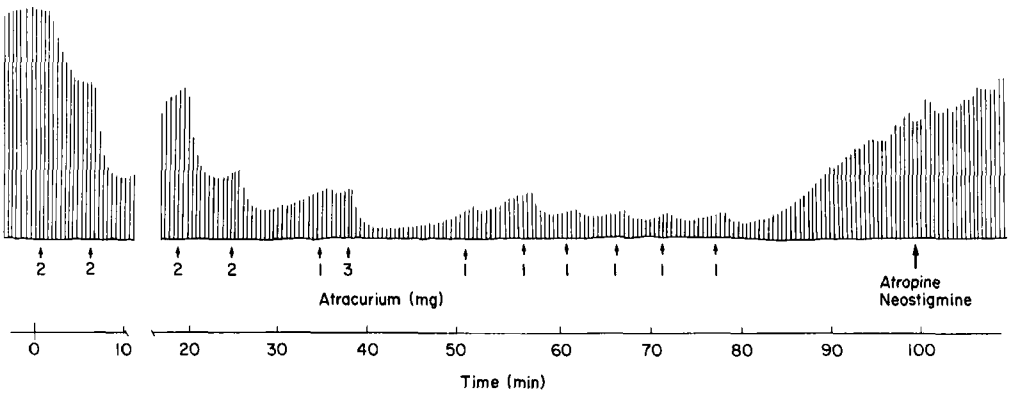

Fig. 1. Pharmacodynamic trace of patient with myasthenia gravis receiving multiple doses of atracurium besylate. Supramaximal single twitches to the ulnar nerve applied every 30 seconds with measurement of force displacement of adductor pollicis.

cedure using an end-tidal carbon dioxide analyser.

Despite high halothane concentrations (3%) the degree of abdominal relaxation was deemed insufficient for an upper abdominal operation by the surgeons. The halothane concentration was reduced (to 1.5%) and a small dose of atracurium (2 mg) was given. The depression of twitch height was observed and the rates of recovery were examined after further small increments (Fig. 1) of atracurium. At 25 minutes the surgeons found the conditions satisfactory and this degree of neuromuscular blockade was maintained from 40 minutes onward by giving 1 mg increments of atracurium at regular intervals. This timing was possible because of the observed constant predictable recovery of neuromuscular dynamics with each small dose. A total dose of 18 mg of atracurium was given. When surgical relaxation was no longer necessary, neuromuscular function was observed to recover (82 minutes). At 95 minutes spontaneous ventilation returned and the halothane was discontinued. Three minutes later atropine 0.6 mg followed by neostigmine 1.2 mg was administered intravenously. At 70% recovery of twitch height (105 minutes) the patient was extubated and returned to the intensive therapy unit for observation where she remained for 24 hours.

Muscle weakness in the next 24 hours was assessed by observing her ability to raise her arms above her head, and hourly measurement of her tidal volume. Two doses of pyridostigmine (0.5 mg intravenously) were given during the first 12 hours.

On the ward she was re-established on neostigmine 15 mg and pyridostigmine 60 mg, 3 hourly and discharged on the seventh day postoperatively after an uneventful recovery.

Discussion

The reduction in the number of acetycholine receptors at the neuromuscular junction in myasthenia gravis is due to autoimmune attack with both accelerated degradation and blockade of these integral membrane proteins.[6] This reduced receptor population, which is also more labile, significantly reduces both the EC_{50} (the plasma concentration of the drug at which the twitch height is reduced to 50% of its original level) and ED_{50} (the dose of the drug required to reduce the twitch height to 50% of its original level) of any non-depolarising neuromuscular blocker employed. Receptor blockade by antibody[7] making each patient appear partially curarised potentiates this effect. With the normal 'safety margin' of neuromuscular transmission absent (i.e., excess ligand with excess receptors) the dose-response curves in myasthenia gravis are moved to the left. So neuromuscular blockade will be possible with very small doses of non-depolarisers and their effect should be monitored by observing neuromuscular dynamics.[2]

In our patient surgical relaxation was not adequate under halothane anaesthesia and this was confirmed by examination of single twitch dynamics. Neuromuscular relaxation was obtained by incremental doses of atracurium

besylate. This novel neuromuscular blocker is broken down in the plasma by Hofmann elimination[8] which gives it very reproducible pharmacokinetics[9] and pharmacodynamics[10] in normal subjects. A dose of 0.3 mg/kg will give complete abolition of the single twitch with 50% recovery in 36 minutes and 90% recovery in about 40 minutes.[10] Our patient was given an initial dose of 0.03 mg/kg (2 mg). Assuming that pharmacokinetics are not significantly altered in myasthenia gravis, an agent with a short half-life ($T_{\frac{1}{2}}^{\beta}$, the elimination half-life in a two compartment pharmacokinetic model, = 20 min), small total distribution volume (V_d Area, the total distribution volume as determined using the area under the curve from an exponential drug decay curve, = 160 ml/kg) and a high clearance (*Cl*, the total body clearance from the area under the curve, = 5.5 ml/min/kg) would be preferable in this condition. Many patients receiving atracurium do not need reversal of neuromuscular block (unpublished data) and this was true in this patient who breathed spontaneously and was only given a small dose of atropine (0.6 mg) followed by neostigmine (1.2 mg) to aid this recovery and to eliminate the risk of recurarisation.

In the intensive care unit recovery was uneventful with only two further doses of anticholinesterases being required. She was back on the ward 24 hours later where her pre-operative therapy was reduced to every 3 hours.

Atracurium besylate whose clearance from the body is not dependent on renal or hepatic function, which has a relatively short half-life would appear the neuromuscular blocker of choice in myasthenia gravis at, of course, significantly reduced doses.

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