MYASTHENIA GRAVIS AND ATRACURIUM
A Case Report

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SUMMARY

The degree, duration of and recovery from neuromuscular blockade induced by atracurium in a patient with myasthenia gravis were monitored and recorded using the evoked compound muscle action potentials (EMG). The anaesthetic and perioperative management were simplified by the use of this technique. The significance of the behaviour of atracurium is discussed.

The perioperative management of patients with myasthenia gravis is complicated by their enhanced sensitivity to non-depolarizing neuromuscular blocking agents, and their relative resistance to depolarizing drugs (Wylie and Churchill Davidson, 1979).

Atracurium dibesylate is one of a new series of non-depolarizing agents and undergoes spontaneous degradation at physiological body temperature and pH. The metabolic products from this "Hofmann elimination" possess no significant neuromuscular blocking action (Hughes and Chaplin, 1981). In normal patients, more than 50% of an injected dose has been degraded within 30 min. There is also some enzymatic hydrolysis in vivo, but this has not been thought significant from the clinical viewpoint. To our knowledge, the response to atracurium in the myasthenic patient has not been studied previously, and it was thought that its rapid breakdown might find a place in the provision of neuromuscular blockade for such a patient.

CASE REPORT

A 37-yr-old patient, weighing 75 kg required an abdominal hysterectomy for menorrhagia. Myasthenia gravis had been diagnosed at the age of 13 yr, after a history of left-sided ptosis and generalized muscle fatigue. The diagnosis was confirmed by the patient's rapid improvement after edrophonium chloride i.v. and pyridostigmine bromide by mouth. Antibodies to acetylcholine receptors were weakly positive in the blood. The repetitive stimulation test (electromyography) was not performed at this time. Thymectomy was performed at the age of 19 yr and this resulted in considerable clinical improvement, enabling the patient's anticholinesterase therapy to be curtailed for 18 months. However, within 2 yr, steroid therapy was required in addition to anticholinesterase drugs and short courses have been required from time to time.

The patient had undergone abdominal surgery on three previous occasions, for two Caesarean sections and a cholecystectomy, and had required mechanical ventilation in the early postoperative periods after each procedure.

The patient's muscle fatigue was controlled up to the time of the present operation with pyridostigmine 60 mg 6-hourly, neostigmine 15 mg or 30 mg 4-hourly, and ephedrine 15 mg 6-hourly. She requested general anaesthesia for the procedure, as extradural anaesthesia performed previously for dilatation and curettage had proved unacceptable.

Anaesthesia

Premedication deliberately included anticholinesterase therapy, and consisted of pyridostigmine 60 mg and ephedrine 15 mg orally, given 3 h before operation, followed by nitraxepam 5 mg and droperidol 5 mg by mouth 90 min before the induction of anaesthesia.

An infusion of dextrose-saline was established at the right wrist and electrodes for the monitoring of neuromuscular transmission were placed on the opposite wrist. After induction of anaesthesia with thiopentone 350 mg, the patient breathed nitrous oxide in oxygen without a volatile adjuvant, through a Magill circuit and mask. Spontaneous breathing continued without the need for assisted or controlled ventilation, while control measurements of neuromuscular function were made. Atracurium (total dose 0.25 mg kg$^{-1}$) was given by a divided dose technique into the fast-running i.v. infusion. Ventil...
lation was assisted and then controlled as soon as spontaneous breathing, judged by clinical observation, had become inadequate. Tracheal intubation was carried out without the use of topical analgesia.

Anaesthesia was maintained with 70% nitrous oxide in oxygen plus increments of fentanyl (total dose 300 µg). Ventilation was controlled mechanically. Further increments of atracurium (0.05–0.1 mg kg\(^{-1}\)) were given as indicated, that is when the initial response (T\(_1\)) returned to 35% of its control height. The total dose of atracurium was 32.5 mg. No further increments of atracurium were given once the peritoneum had been sutured, and the patient was allowed to resume spontaneous ventilation.

Neostigmine was not used to reverse the blockade, to allow its natural "off-set" to be studied. Monitoring of neuromuscular transmission was continued in the recovery room for a further 40 min before the trachea was extubated, during which time the patient breathed 70% nitrous oxide through a Magill system. Before extubation, the patient could sustain a head-lift easily for 10 s, and indicated that her breathing was comfortable.

Following surgery, normal anticholinesterase therapy was restarted, and an increase in muscle fatigue was neither found, nor reported by the patient.

Heart rate and systolic arterial pressure were recorded at 5-min intervals throughout the period of monitoring neuromuscular transmission, and a sample of arterial blood for the analysis of blood-gas tensions and pH was taken 1 h after the induction of anaesthesia.

**Monitoring neuromuscular transmission**

Neuromuscular function was monitored continuously using train-of-four stimulation, and by detecting the evoked compound muscle action potentials (Datex ABM-1: Anaesthesia and Brain Activity Monitor). Conmed ECG electrodes were placed over the ulnar nerve and over the adductor pollicis muscle. Supramaximal stimuli at a frequency of 2 Hz and pulse duration of 0.1 ms were applied to the ulnar nerve, and the train-of-four stimuli repeated every 20 s. Automatic calculation of the ratio of the fourth to the first responses of the train-of-four stimuli (T\(_4\):T\(_1\)) was performed by the apparatus. This, together with the ratio of the first response to the patient's control response T\(_1\):T\(_0\) was displayed both graphically and digitally.

**RESULTS**

The record of the evoked train-of-four response during and after surgery is shown in figure 1. This is a photograph of the trace printed at the time by the Datex ABM-1 monitor. The light and the dark shading indicate the ratios T\(_4\):T\(_1\) and T\(_4\):T\(_0\) as described above. A "log %" scale is used by the monitor in order to enhance the interpretation of high levels of neuromuscular block.

After automatic calibration, and the recording of the control response (T\(_0\)), a total dose of atracurium of 0.25 mg kg\(^{-1}\) was required before spontaneous breathing ceased and intubation could be carried out. There was slight coughing on intubation. The diminution of responses to the train-of-four stimuli showed the "fade" pattern typical of that produced by non-depolarizing neuromuscular blocking drugs. T\(_1\) decreased to 10% of the control response.

**FIG. 1.** Evoked responses (EMG) after the administration of atracurium in a patient with myasthenia gravis. NMT = neuromuscular transmission; C = control; int. = intubation. *Applies to doses 2 and 3.
after atracurium 0.25 mg kg\(^{-1}\), given in divided doses. At no time did the T\(_1\) response disappear entirely; in fact the contraction responses to the first two stimuli of the train-of-four were always visible clinically.

The time intervals before T\(_1\) recovered to 35% of control height did not exceed the quoted range of 15–35 min (Payne and Hughes, 1981). Following the intubation dose and the first three increments, the times to 35% recovery of initial response were 21 min, 19 min, 11 min and 9 min, respectively (fig. 1). A double increment of 0.1 mg kg\(^{-1}\) was then given; the time to the same degree of recovery was extended to 16 min. This was followed by a dose equal to the previous increments (0.05 mg kg\(^{-1}\)), and the time to 35% recovery of the initial response was 8 min.

The time for T\(_4\):T\(_1\) to reach 75% of control was 20 min after the final increment (dotted line on fig. 1); the patient’s breathing was clinically normal by this time. Event “10” on figure 1 denotes the time at which 35% recovery was reached after the final increment of atracurium.

No clinically significant changes in heart rate or systolic arterial pressure were recorded. Arterial blood sampled during surgery showed a pH of 7.47 and a PaCO\(_2\) of 3.9 kPa.

DISCUSSION

Patients with myasthenia gravis are very sensitive to the non-depolarizing neuromuscular blocking drugs. Thus, the rapid elimination of atracurium by “Hofmann” degradation ought to be advantageous in these patients.

The monitoring of neuromuscular transmission in this myasthenic patient given atracurium showed some unexpected features which may have important clinical implications for other patients suffering from myasthenia gravis.

A surprising feature was the relatively high dose of atracurium required, amounting to 50% of the normal recommended requirements. Furthermore, 35% recovery of T\(_1\) always occurred within the normal expected time (Stenlake et al., 1981). Similarly, the time for T\(_4\):T\(_1\) to reach and remain at 75% of the control value following the last increment was 20 min, also within normal limits. It must be remembered that anticholinesterase therapy was maintained before operation.

The shortening of the time interval of 35% recovery of the initial response with successive increments of atracurium is also interesting. Previously only the non-cumulative property of atracurium has been noted (Payne and Hughes, 1981; Hunter, Jones and Utting, 1982). This makes the explanation of this finding difficult, particularly in a patient with myasthenia gravis. Enzyme induction is normally seen after more prolonged administration. One possibility is that esterase-dependent hydrolysis is taking place in these patients to a more significant degree than has been thought to occur hitherto (Payne and Hughes, 1981).

It appears that atracurium may be used to provide excellent surgical relaxation safely for patients with controlled myasthenia gravis whose normal therapy is not discontinued. Monitoring of neuromuscular transmission is of course mandatory for these patients, and facilities for full ventilatory support must be available.

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REFERENCES


MYASTHENIE ET ATRACURIUM

A propos d’un cas

RESUME

Nous avons surveillé et enregistré, grâce à la composante évoquée des potentiels d’action musculaire (EMG), l’intensité, la durée et la récupération du bloc neuromusculaire induit par l’atracurium chez une patiente myasthénique. Cette technique a permis de simplifier le protocole anesthésique et péri-opératoire. La signification du comportement de l’atracurium est discutée.
MYASTHENIA GRAVIS UND ATRACURIUM
Ein Fallbericht

ZUSAMMENFASSUNG


MIASENIA GRAVIS Y ATRACURIO
Informe de un caso

SUMARIO

Por medio de los potenciales de acción muscular compuestos evocados (EMG), se midieron y se registraron el grado, la duración y la recuperación de un bloqueo neuromuscular inducido por atracurio en un paciente con miastenia gravis. La gestión anestésica y perioperatoria se hallaron simplificadas por el uso de dicha técnica. El significado del comportamiento del atracurio se discute.