Mivacurium is a recently released short-acting nondepolarizing muscle relaxant with a benzylisoquinolium structure. It is known to be metabolized by plasma cholinesterase. The short duration of action makes mivacurium an increasingly popular choice for muscle relaxation in ambulatory surgery procedures. Individuals with abnormalities of plasma cholinesterase, however, may have longer than expected duration of action of mivacurium, requiring prolonged mechanical ventilation. We present two cases where this occurred.

Key words: Mivacurium, cholinesterase, neuromuscular blockade

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Mivacurium is a recently released short-acting nondepolarizing muscle relaxant with a benzylisoquinolium structure. It is known to be metabolized by plasma cholinesterase. As such, its duration of action would be expected to be prolonged in patients with reduced plasma cholinesterase activity. It is also known to be easily antagonized by anticholinesterase drugs.

We report two cases, occurring within 10 days of each other at our institution, where prolonged neuromuscular blockade occurred after mivacurium administration. Both of these patients were subsequently determined to have reduced plasma cholinesterase activity. Contrary to European reports, however, the blockade was very difficult to reverse, and these patients required prolonged ventilatory support.

Case I

A 68-year-old 84-kg white male presented to the outpatient surgical facility for elective microlaryngoscopy and vocal cord stripping. Past medical history was significant for atherosclerotic heart disease and past surgical history was significant for uncomplicated coronary artery bypass grafting in 1985. Current medications included oral nitrates and angiotensin-converting enzyme inhibitors. There was no other systemic disease noted.

Induction with propofol (1.5 mg kg⁻¹), fentanyl (2 μg kg⁻¹), and mivacurium (0.15 mg kg⁻¹) intravenously was uneventful. Anaesthesia was maintained with nitrous oxide (0.3–0.6 minimum alveolar concentration (MAC)) and isoflurane (0.5 MAC). At the conclusion of a 45-min surgical procedure, the patient had minimal respiratory activity with 2/4 twitches on train-of-four stimulation. The patient was noted to be responding appropriately to questions with eye movement. Reversal was attempted with neostigmine (0.08 mg kg⁻¹) and glycopyrrolate (0.03 mg kg⁻¹) intravenously. No change in clinical status was noted after 10 min. The reversal drugs were repeated in the same dosage. Again, no change in clinical status was noted. The patient remained responsive with 2/4 twitches on train-of-four stimulation. The situation was explained to the patient and he was transferred to the postanaesthesia care unit with mechanical ventilation.

The patient remained ventilated for approximately 5 h. Spontaneous activity returned very slowly, until the patient was able to make slight purposeful movements with his upper extremities. The patient remained responsive. Respiratory mechanics, however, remained far below minimal criteria for spontaneous ventilation. At this time, reversal was again attempted with neostigmine (0.075 mg kg⁻¹) and glycopyrrolate (0.03 mg kg⁻¹). Within 3 min, the patient exhibited significant improvement in muscular activity, and was able to sustain head lift for greater than 10 s. He was extubated at that time and was subsequently uneventfully discharged home.
Follow-up evaluation revealed a plasma cholinesterase level of 242 μU ml⁻¹ (normal 1900–3800 μU ml⁻¹). Dibucaine number was not available.

Case 2

A 49-year-old 75-kg white female presented for mastectomy due to localized carcinoma of the breast. She had previously undergone two surgical procedures without complications, although it is known that no muscle relaxant was used in at least one of these operations. Induction with propofol (1.5 mg kg⁻¹), midazolam (0.025 mg kg⁻¹), fentanyl (1.5 μg kg⁻¹) and mivacurium (0.15 mg kg⁻¹) was uneventful. Anaesthesia was maintained with nitrous oxide (0.5 MAC) and propofol infusion (0.15 mg kg⁻¹) was uneventful. Anaesthesia was maintained with nitrous oxide (0.5 MAC) and propofol infusion (120 mg kg⁻¹ min⁻¹). Subsequently, no muscle twitch was detectable with a previously functioning nerve stimulator for 3 h. At that time, she developed a neuromuscular stimulation pattern typical of a dense nondepolarizing blockade. Reversal was attempted with edrophonium (0.5 mg kg⁻¹). There was no change in clinical status. One hour later (4 h after mivacurium administration), the reversal was re-attempted with edrophonium (0.5 mg kg⁻¹). The patient developed a train-of-four response of 4 twitches with a 25% ratio, but was unable to maintain spontaneous ventilation. One hour later (5 h after mivacurium administration) the patient was again administered edrophonium (0.5 mg kg⁻¹) and was able to be successfully extubated.

Follow-up evaluations revealed a normal dibucaine number, but a plasma cholinesterase level of 544 μU ml⁻¹ (normal 1900–3800 μU ml⁻¹).

Discussion

Mivacurium is a short-acting, nondepolarizing muscle relaxant which is hydrolyzed by plasma cholinesterase. It is also reversible with anticholinesterase agents. The rate of hydrolysis has been found to be 70–80% of that of succinylcholine. Mivacurium duration of action would be expected to be prolonged in patients with cholinesterase deficiencies. These two case reports confirm that this is indeed true.

The manufacturer states that clinical trials including patients with plasma cholinesterase activities as low as 20% below the lower limit of normal did not reveal significant effects on the mivacurium-induced motor blockade. Our two patients, however, had activity levels more than 70% below the lower normal limit. Many conditions may cause these reductions and these patients will not always be recognized preoperatively.

Whittaker identified a number of causes of decreased plasma cholinesterase activity, including: inherited deficiencies; physiologic variances (pregnancy, newborn infants); acquired causes (liver disease, malignancies, collagen diseases, infections, anaemia, uraemia, myocardial infarction, fever, myxoedema, burns); iatrogenic causes (contraceptive pills, MAO inhibitors, cholinesterase inhibitors, chemotherapy).

Ostergaard et al. gave patients homozygous for the atypical plasma cholinesterase gene mivacurium doses of 0.3 mg kg⁻¹. He reported that once recovery from neuromuscular blockade had begun, reversal of residual blockade with neostigmine was effective and safe. He also reported that a correlation was found between cholinesterase activity and duration of mivacurium block in genotypically normal patients.

Basta reported that patients homozygous for the atypical cholinesterase gene given 0.2 mg kg⁻¹ mivacurium had 'a markedly prolonged blockade that is readily reversible'.

We report that contrary to these findings, when an intubating dose (0.15 mg kg⁻¹) of mivacurium is given to patients with low plasma cholinesterase activity, reversal is very difficult and clinically ineffective until significant spontaneous recovery had already occurred.

In conclusion, we report two cases of prolonged neuromuscular blockade following mivacurium administration in patients with reduced plasma cholinesterase activity (70–80% below normal lower limits). Contrary to previous reports, this neuromuscular blockade was difficult to reverse with anticholinesterase agents. It was necessary to wait for almost total spontaneous recovery before reversal and extubation were safely accomplished. We believe that this type of patient will be seen with increased frequency as mivacurium usage becomes more common.

References