Prolonged Recovery of Neuromuscular Transmission during General Anaesthesia after Mivacurium Administration - Case Report

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Abstract

Introduction: Mivacurium is the shortest-acting non-depolarizing relaxant, used for brief procedures, such as those performed in the ambulatory setting. The recommended intubating dose of 0.2 mg/kg usually provides a clinically effective neuromuscular block for approximately 15 to 20 minutes and spontaneous recovery is 95% complete within about 25 to 30 minutes.

Case presentation: 71-years-old woman was admitted for an elective laparotomy surgery with an intraoperative examination. Standard monitoring and TOF Scan (both the adductor pollicis muscle and the orbicularis oculi) were used. 8 mg dexamethasone, 0.1 mg fentanyl, 150 mg propofol, and 18 mg mivacurium were administered for induction. At the end of the procedure, there was no response from TOF. The return of neuromuscular transmission was achieved only after 75 minutes from the induction.

Discussion: Mivacurium as a short-acting non-depolarizing muscle relaxant is well suited for short-term operations and operations of unpredictable duration. However, previous studies have shown that an extended neuromuscular block is likely in patients with significantly reduced plasma cholinesterase activity (especially in patients who are homozygous for the atypical plasma cholinesterase gene) as well as when administering some drugs and during other clinical situations.

Conclusions: Extensively prolonged apnoea during general anaesthesia is a dangerous incident. Therefore, we still need systematic reviews to determine the prevalence of incidents of extended neuromuscular block after mivacurium.

In case of prolonged muscle relaxation, we should think about possible reversible causes of this phenomenon since it is not always related to genetic causes. Furthermore, mechanical ventilation and close clinical monitoring are required during administering mivacurium. All of this to achieve the best possible patient outcomes.

Keywords

Mivacurium, Prolonged duration of action, Plasma cholinesterase, Neuromuscular block, TOF, Non-depolarizing

Introduction

Mivacurium is a mixture of three stereoisomers that competitively block cholinergic receptors within the motor plate, resulting in skeletal muscle relaxation. It is a potent non-depolarising neuromuscular blocking agent that has a short-acting duration because of its rapid elimination by plasma cholinesterase. Therefore, it’s the drug of choice for short procedures where we want relaxation to resolve before the end of the procedure (e.g., for laryngeal microsurgery or thyroidectomy with intraoperative neuromonitoring). The recommended intubating dose (2 × ED95) usually provides a clinically effective neuromuscular block for approximately 15 to 20 minutes and spontaneous recovery is 95% complete within about 25 to 30 minutes [1,2]. Consequently, in case of long procedures, where mivacurium was used...
for intubation, and long-term relaxation is needed, 
the appropriate approach would be to extend it with 
a non-depolarizing drug, most often rocuronium. 
However, previous studies have shown that an extended 
neuromuscular block is likely in patients with significantly 
reduced plasma cholinesterase activity (especially 
in patients who are homozygous for the atypical 
plasma cholinesterase gene) [3]. The second observed 
adverse effect was linked to mivacurium-induced 
histamine release, causing cardiovascular effects such 
as hypotension and cutaneous flushing. The following 
clinical case report provides information on what to be 
aware of when administering the relaxant mivacurium.

Case Presentation

On 19/05/2021 a 71-year-old woman was admitted 
to the Gynecology Department of The Regional 
Specialist Hospital in Olsztyn, Poland. She was referred 
to the hospital for an elective laparotomy due to the 
diagnosis of a tumor of the right appendages and 
endometrial hyperplasia. This patient had obesity 
(height = 165 cm, weight = 93 kg, BMI = 34.16 kg/m²), 
suffered from persistent atrial fibrillation and had a 
history of cholecystolithiasis. She received a score of 2 in 
the ASA classification. She had no history of genetically 
determined abnormalities of plasma cholinesterase 
or muscle disorder. On a daily basis, she only takes 
Neoparin (Enoxaparin sodium) 40 mg 1 × 1 and Concor 
(Bisoprolol) 1.25 mg 1 × 1. She was rated 1 on the 
Mallampati scale. She didn’t receive any premedication.

The next day the patient arrived at the operating 
room. The patient was also in a clinical trial 
comparing the TOF Scans, therefore we measured the 
neuromuscular transmission with this device through 
the electrodes placed above the ulnar nerve (the 
adductor pollicis muscle -TOFapb + standard method) 
and on the forehead (the corrugator supercilius muscle - 
TOFcsm). After securing the perioperative monitoring: 
EKG, NIBP, SaO₂, ventilation parameters, an epidural 
blockade L3-L4 was performed with 10 ml Bupivacaine 
Hydrochloricum 0.5%, 6 ml Fentanyl (0.1 mg/2 ml) and 
34 ml NaCl at 6 milliliters per hour. Dexamethasone 8 mg 
as an antiemetic, 0.1 mg fentanyl, 150 mg propofol, and 
18 mg mivacurium were used for induction. The patient 
was intubated after 135 seconds with a 7.0 tube using 
a bougie guide (Cormack grade 2). Anaesthesia was 
maintained with a mixture of sevoflurane (MAC 0.9) and 
air with FiO₂ = 0.5, FGF = 1l/min. Ventilation was carried 
out in SIMV-PC mode with PEEP = 5 m bar, without 
pressure support. An intravenous infusion of 1000 
ml of Optilyte was administered. The neuromuscular 
transmission was measured every 15 seconds during 
the first 10 minutes and then every 5 minutes till 
etubation. After 30 minutes, TOFapb-Scan still showed 
0%. TOFapb > 90% was obtained only after 75 minutes 
after the administration of a single dose of mivacurium 
(Figure 1). The patient was extubated without any 
complications after 80 minutes with TOFapb = 96% and 
received 10 points in Aldrete score.

Discussion

Mivacurium belongs to the group of non-depolarizing, 
highly specific, short-acting muscle relaxants. However, 
we have to keep in mind that significantly reduced 
plasma cholinesterase activity (especially in patients who 
are homozygous for the atypical plasma cholinesterase 
gene) and mutations in the butyrylcholinesterase enzyme 
(BChE) may prolong the effect of the neuromuscular 
blocking agents such as mivacurium and succinylcholine. 
Heterozygotes can have a muscular paralysis of

![Figure 1: Degree of neuromuscular blockage.](image-url)
moderate duration, while homozygotes can experience muscular block longer than 2 hours [4]. This is due to the fact that succinylcholine is also degraded by plasma pseudocholinesterase (pChe). Previous studies have shown several mutations in the BChE (I373T, G467S, W518R, L184S, V421A, M462I, and R577H) that can cause extensively prolonged apnoea during general anaesthesia when mivacurium or succinylcholine are used [5]. Injection of human cholinesterase increases pChe activity and may help to shorten the duration of action of mivacurium three to four times. Another medicine that can be of some use is neostigmine. When administering after cholinesterase it increases the rate of recovery further, albeit full recovery may be slow [6,7]. When diagnosing the causes of prolonged neuromuscular block, it should also be remembered that the intensification of the mivacurium effect may be caused by: inhalation anaesthetics (apart from nitrous oxide), antibiotics (including aminoglycoside antibiotics, polymyxins, tetracyclines, lincomycin, clindamycin), antiarrhythmic drugs (propranolol, calcium antagonists, lidocaine, procainamide, quinidine), diuretics (furosemide, possibly thiazide diuretics, mannitol, acetazolamide), magnesium salts, lithium salts, ketamine, ganglion blockers. Drugs that reduce the effect of plasma cholinesterase may increase the effect of mivacurium - these include antimiotic drugs, pancuronium, organophosphorus compounds, some hormones, MAO inhibitors, and plasma cholinesterase inhibitors. Some drugs may worsen or induce latent myasthenia gravis, increasing the sensitivity to the effects of mivacurium, including various types of antibiotics, β-blockers, and anti-arrhythmic drugs (procainamide, quinidine), chlorpromazine, anti-rheumatic drugs (chloroquine, D-penicillamine), steroids, phenytoin, lithium salts. Hypothermia may also prolong the duration of action [8]. Additionally, the clinically effective duration of block may be about 1.5 times longer in patients with end-stage kidney disease and about 3 times longer in patients with end-stage liver disease than in patients with normal renal and hepatic function. Severe acid-base and/or electrolyte abnormalities may also potentiate or cause resistance to the neuromuscular blocking action of mivacurium [9]. However, none of the causes mentioned above was the reason for prolonged neuromuscular blockade in our patient since she had no hypothermia, electrolyte abnormalities, renal or hepatic disease, etc. It is also important that even if the TOF ratio is 0%, it is possible to observe the patient’s respiratory movements because the diaphragm and respiratory muscles are the least susceptible to relaxation of the skeletal muscles [10]. This means that the indications of the ventilator, or even the patient’s respiratory movements, are not a good prognostic factor for the receding relaxation.

**Conclusion**

Extensively prolonged awakening during general anaesthesia is a dangerous incident. The drug should be administered in individually selected doses under the supervision of an experienced physician who knows the effects of the drug and possible complications associated with its use. We should not administer mivacurium if the conditions for resuscitation, oxygen therapy, and mechanical ventilation are not provided, or if drug antagonists are not within immediate reach. Mechanical ventilation and close clinical monitoring are required during administering this drug. In case of prolonged muscle relaxation, we should think about possible reversible causes of this phenomenon since it is not always related to genetic causes. Furthermore, we still need systematic reviews to determine the prevalence of incidents of extended neuromuscular block after mivacurium. All of this to achieve the best possible patient outcomes.

**Conflict of Interest**

None.

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**Authors’ Contributions**

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