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Phase II block after an intubating dose of succinylcholine Importance of neuromuscular blockade monitoring

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Summary

Case report. We present the case of a 65-year-old female patient admitted for urgent laparoscopic resection of gallbladder under general anaesthesia due to acute cholecystitis with prolonged apnoea (5 hr) and phase II block after an intubating dose of succinylcholine (1 $mg.kg^{-1}$) in a patient with unsuspected deficit of serum cholinesterase (1360 $U.L^{-1}$ (37 °C), normal value 4000-9900) and low number of dibucaine (47, normal value > 70). This case was diagnosed through the routine use of quantitative neuromuscular blockade monitoring (acceleromyography) and thus adopted appropriate measures avoiding unnecessary intubation period and erroneous decisions that could be deleterious in this patient. We emphasize that routine use of neuromuscular monitoring is advocated in all patients (especially during emergency surgery) and this case report illustrates perfectly the importance and how necessary is neuromuscular monitoring to evaluate the neuromuscular function, improving diagnosis and anaesthethic management. *Anestezjologia i Ratownictwo 2010; 4: 307-311.*

Keywords: neuromuscular blockade, neuromuscular blocking agents, neuromuscular monitoring, succinylcholine, Phase II blockade, anaesthesia

Introduction

Since the introduction of succinylcholine into clinical practice in 1951 [1], it is considered as a neuromuscular blocking agent of choice in the techniques of rapid sequence induction, started by Snow [2] in 1959 and subsequently by Step and Safar [3] in 1970.

Abnormal response to succinylcholine had been described previously, such as prolonged apnoea or phase II block (dual block). Phase II block has a confusing and controversial interpretation [4], characterized by the appearance of marked weakening of train of four stimuli (TOF), unlike the normal depolarizing neuromuscular block (Phase I block), that has a TOF-ratio (T4: T1 relationship) close to the unit.

Case report

A 65-yr-old female, (ASA II, weight 65 kg, height 146 cm) without medical history of previous diseases or anaesthesias was admitted for urgent laparoscopic resection of gallbladder under general anaesthesia due to acute cholecystitis. Her preoperative physical evaluation and investigations were completely normal

except the patient was considered to be at risk of difficulty with intubation (obesity with body mass index of 30,5 kg.m^{-2}), Mallampati classification grade 3, mild retrognathia, prominent teeth and moderate reduction in neck movement and mouth opening). The preoperative fasting period was only 3 hr, so she was considered as a "full-stomach" patient. She was also uncooperative ruling out awake fibreoptic intubation. After application of routine monitoring (ECG, pulse oximeter, non-invasive arterial pressure) and previously to drugs administration, neuromuscular monitoring was performed using train-of-four (TOF) nerve stimulation with acceleromyography (TOF-Watch SX$^{\rightarrow}$, Organon Teknika B.V., Boxtel, The Netherlands) at the *adductor pollicis* muscle, with prior calibration (mode Cal2) obtaining the supramaximal stimulus at 45 mA. The patient was preoxygenated by mask with 100% oxygen for several minutes and then, anaesthesia was induced with propofol, fentanyl and succinylcholine (1 mg.kg^{-1}). Intubation was performed with Sellick's manoeuvre without incidences (Cormack-Lehane classification grade II). The patient was ventilated with oxygen and air in a ratio of 1:1 (3 L.min^{-1}) and desflurane (1,3 MAC). She also received antibiotic (cefotaxime 1g and metronidazole 1,5 g), postoperative nausea and vomiting prophylaxis (dexamethasone 8 mg and ondansetron 4 mg), pantoprazole (40 mg), acetaminophen (1 g) and desketoprofen (50 mg). Active protection against hypothermia was used with heated fluid and a hot air blanket.

Depolarizing neuromuscular blockade reached 95% in 1 minute. We waited the recovery of succinylcholine to administer a no depolarizing neuromuscular blocking agent, but surgery finished in 97 min without recovery. A prolonged succinylcholine apnoea was diagnosed, so the patient was transferred intubated to the post anaesthetic care unit (PACU). A propofol infusion was administrated all the time the patient was respiratorily insufficient (II phase block) and remained in the post anesthesia care unit. Recovery started at 145 min and TOF fade was seen, indicating the presence of a phase II block (dual block). We allowed spontaneous recovery, with TOF-ratio of 70% in 4 hr 17,5 min, TOF-ratio of 80% in 4 hr 35,5 min, TOF-ratio 90% in 4 hr 59,25 min and finally TOF-ratio 100% in 5 hr 1,5 min. The patient was extubated without incidences 6 hr and 39 min after the injection of suxamethonium, when TOF-ratio 100% was observed to maintain stable for a while (figure 1).

The laboratory values of serum cholinesterase and dibucaine number were studied after surgery in the patient and her son (table 1). The definitive diagnosis was prolonged apnoea and phase II block after an intubating dose of succinylcholine in a patient with unsuspected deficit of serum cholinesterase and low number of dibucaine.

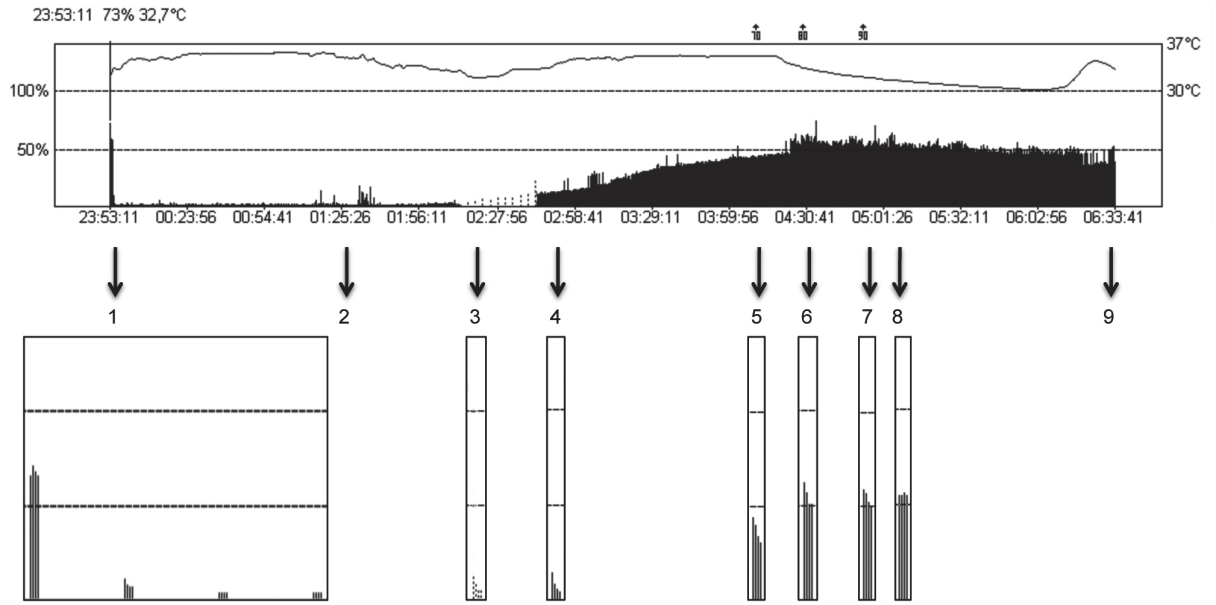

Figure 1. TOF-Watch SX$^{\rightarrow}$ neuromuscular blockade register

At the top, the graphic shows the complete evolution of the neuromuscular block. Amplitude stimuli scale is marked on the left vertical axis (%); skin temperature scale on the right one (°C) and time is exposed in the horizontal axis.

Special point means:

1. Initial depolarizing neuromuscular block. Observe the absence of fade to TOF stimulation (the same amplitudes for all stimuli).
2. Artefacts during the translation of the patient to the PACU.
3. Appearance of phase II block. Intense fade is present.
4. Progressive recovery of neuromuscular function.
5. TOF-ratio 70%.
6. TOF-ratio 80%.
7. TOF-ratio 90%.
8. TOF-ratio 100%.
9. Extubation.

Table 1. Laboratory values

	Normal value	Patient	Patient's son
Serum cholinesterase	4000-9900 $U.L^{-1}$ (37 °C)	1360	3813
Number of dibucaine	> 70	47	87

Number of dibucaine = [1 – (activity with dibucaine / activity dibucaine)] x 100

Discussion

The clinical situation described above is usual in many hospitals, with the needing of intubating a patient with high risk of regurgitation, possible difficult airway management and uncooperative for awake fibreoptic intubation. In such situation, we could use succinylcholine (1 $mg.kg^{-1}$), rocuronium (1,2 $mg.kg^{-1}$) or apply the timing or priming principles [5]. We decided to perform the classical rapid sequence intubation with Sellick's manoeuvre and succinylcholine.

After a usual intubating dose of succinylcholine (1 $mg.kg^{-1}$), in a patient with normal plasma cholinesterases, it is expected to observe a neuromuscular block lasting for 5-11 min (with 3-7 min of maximum block). When neuromuscular blockade last 10 to 30 min, a plasma cholinesterase deficit or an atypical enzyme in a heterozygous patient must be suspected, and in a patient with homozygous atypical enzyme the block will last up to 200 min, with up to 90 minutes of maximum block [6]. However, the appearance of a phase II block was an unforeseen event that could be diagnosed through the use of quantitative neuromuscular monitoring.

The routine use of neuromuscular monitoring is advocated in all patients [7], especially in emergency surgery, and this case report illustrates perfectly the importance and how necessary is neuromuscular monitoring to evaluate the neuromuscular blockade, sometimes with profound variation and influenced by a great number of factors. Without neuromuscular monitoring, the prolonged effect of suxamethonium could have been unnoticed, especially if we should administered no depolarizing neuromuscular blocking agents to facilitate surgery. Then, at the end of the surgery we should find a clinical situation with almost complete neuromuscular blockade, and differential diagnosis should be established [8] with postoperative curarization (and failure to reverse it).

Prolonged apnoea and phase II block, two rare events, are more frequent to appear after repeated doses of succinylcholine (i.e. in a difficult airway scenario) or with continuous infusion, rather than after a single bolus dose [9], although both had been described after only 20 mg in a patient with low serum cholinesterase (1900 u. L^{-1}) [10].

Without neuromuscular monitoring, after uncontrolled use of no depolarizing neuromuscular blocking agents, the first option considered in differential diagnosis would be surely residual curarization, and consequently neostigmine or sugammadex administered. The effect of sugammadex on a dual block remains unknown, but presumably there will be no interaction. However, neostigmine has been reported to induce prolonged neuromuscular blockade in a patient with atypical plasma cholinesterase [11] so the situation would have worsened.

Neuromuscular monitoring allowed us to measure the time from administration of succinylcholine to the initial recovery response to TOF stimulation (recovery started at 145 min), time that far exceeds the definition of Levano et al [12] of prolonged recovery, who establish the diagnosis of succinylcholine apnoea when it exceeds 10 minutes.

The visual evaluation of the TOF stimuli was correlated with the clinical situation, also compatible with prolonged effect of suxamethonium. In order to exclude malfunction of the TOF-Watch SX monitor, a simple peripheral nerve stimulator was also used to evaluate

the TOF response after facial nerve stimulation, with the same result as in the *adductor pollicis*. The TOF-Watch SX monitor performed normally both before and following this case.

Looking for other causes that could explain these findings: there were no ionic or pH alterations or any disease in this patient. She was neither a smoker nor drinker, and had no clinical, familial or personal features of myopathy or neuromuscular diseases. Finally, we don't really know the impact of the anaesthetic technique on the phase II block in this patient, because she did not receive other drugs that induce or enhance the blockade excepting desflurane. Isoflurane has been described to potentiate phase II block [13] but there are no references concerning the real effect of desflurane on a dual block.

If we examine now the figure 1, the neuromuscular block caused by succinylcholine can be divided into two phases, the first is a typical (excepting the prolonged duration) depolarizing blockade (phase I block), whereas in a second phase, a typical phase II block is manifested, with fade to TOF stimulation. In the first phase, depolarization of the endplate by suxamethonium causes the adjacent voltage-gated sodium channels to open, inducing a wave of depolarization to sweep along the muscle. If the depolarizing relaxant is not removed from the cleft, the sodium channels adjacent to the endplate remain in the inactivated state, resulting in muscle paralysis [14]. After initial depolarization, in addition to this sodium channel–dependent mechanism, the receptor itself, becomes desensitized to further depolarization [15]. Prolonged exposure of the endplate to succinylcholine will result in progressive desensitization to the depolarizing action of succinylcholine, as well as to the chemical transmitter acetylcholine; hence, the block will gradually change from a depolarizing endplate-muscular block (Phase I) into a desensitizing Phase II neuromuscular block, which is characterized by progressive tetanic fade and posttetanic facilitation [16]. Fade could be attributed to a prejunctional effect of succinylcholine. This assumption is based on evidence that succinylcholine reduce the presynaptic release of acetylcholine in muscular endplate [14].

Some authors postulate that the dual block may be antagonized by neostigmine, and the degree of reversal by neostigmine is proportional to the extent of fade and posttetanic facilitation [16], but there are also references describing neostigmine-induced prolonged neuromuscular blockade [11]. The rarity of dual block, with few cases properly monitored makes this point remains controversial.

In conclusion, we describe a prolonged apnoea and phase II block after an intubating dose of succinylcholine in a patient with unsuspected deficit of serum cholinesterase and low number of dibucaine. This case was diagnosed through the routine use of quantitative neuromuscular blockade monitoring and thus adopted appropriate measures avoiding unnecessary intubation period and erroneous decisions that could be deleterious in this patient.

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Konflikt interesów / Conflict of interest
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