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Neuromuscular monitoring: an update

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Abstract

This review makes an advocacy for neuromuscular blockade monitoring during anaesthesia care, by: (i) describing the fundamental principles of the methods currently available, at the same time emphasizing quantitative recording measurements; (ii) describing the different ways in which muscles respond to the effect of neuromuscular blockade and their use in clinical practice; (iii) presenting results of different studies on timing and agents of neuromuscular block reversal, including a recommendation for sugammadex use and experimental results with calabadion and (iv) in the end emphasizing the need for implementing neuromuscular monitoring as a practice that should be used every time a neuromuscular block is required.

Keywords: neuromuscular monitoring, residual neuromuscular blockade, peripheral nerve stimulator, quantitative monitoring, sugammadex, calabadion

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Introduction

Neuromuscular monitoring (NMT) is good guidance whenever there is a need to use neuromuscular blockade to significantly improve the quality of intubation and reduce airway injury [1]. Neuromuscular blocking agents (NMBAs) are usually administered during anaesthesia to facilitate endotracheal intubation and to improve surgical conditions.

Why monitor?

There is a great discrepancy between the literature's recommendations on NMT and clinical practice, as many anaesthetists do not monitor neuromuscular function, or do not know how to correctly interpret results. Studies revealed that about 20% of European anaesthesiologists and 10% of US, Australian and New Zeeland anaesthesiologists never use nerve stimulation for neuromuscular blockade's depth monitoring [2, 3]. Recent studies continue to emphasize that subjective assessment using nerve stimulators is performed in less than 40% of patients and objective monitoring in only used for 17% of patients [4, 5].

Residual neuromuscular block is defined by the presence of signs or symptoms of muscular weakness after administration of NMBAs, even when neuromuscular blockade is reversed in the operating room**.** Residual neuromuscular block is a frequent occurrence and is associated with serious complications such as: pharyngeal dysfunction, increased risk for aspiration and pneumonia, acute respiratory events (hypoxemia, airway obstruction), need of tracheal intubation, discomfort for patients and surgeons, increased length of stay in the Post Anaesthesia Care Unit (PACU), all of the above occurring at TOF ratios below 0.9 [6-8]. A quantification of neuromuscular blockade is essential for all stages of anaesthesia when NMBAs are used [9]. Even if anticholinesterase reversal agents are routinely used, the incidence of residual block is still high: 20-40% [10, 11].

NMT is also useful in choosing the antagonist strategy. When using anticholinesterases or sugammadex, the choice of the reversal agent must be guided by neuromuscular monitoring (NMT). Antagonism dosage and injection time can also be optimized by the proper monitoring of the neuromuscular blockade's depth.

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Methods of neuromuscular monitoring

Clinical tests consist of the evaluation of respiratory parameters and muscle function (5-s head lift, grip strength) [12]. Extensively used since the introduction of NMBAs in clinical practice, they are unreliable, none of them having a sensitivity of > 0.35 or a positive predictive value of > 0.52 [13]. At a level of neuromuscular recovery that allows normal ventilation in an intubated patient, airway patency may still be impaired [14], while the 5-s head lift can be performed at train of four ratio (TOFR) as low as 0.5 in more than 70% of patients [15]. In addition, they require a high degree of cooperation and wakefulness, often difficult to obtain in an emergent patient [16].

Qualitative evaluation employs peripheral nerve stimulators (PNSs) and assesses visually or tactilely the response of the stimulated muscle [12]. A standard PNS can provide several patterns of nerve stimulation such as train of four (TOF), double-burst (DBS), tetanic and post-tetanic count (PTC), allowing the evaluation of train-of-four count (TOFC) or the degree of fade. Although more reliable than clinical tests, qualitative evaluation does not eliminate the risk of postoperative residual curarization (PORC). When evaluating TOFC, clinicians usually overestimate it, especially at moderate levels of block [17]. As regards fading, it is to be noted that tetanic fade can only be detected subjectively at TOFR < 0.3, while TOF fade is detected subjectively even by experienced clinicians only when TOFR < 0.4 [18, 19]. Using DBS, the TOFR threshold to detect fade can reach 0.6-0.7, but that prevents clinicians from detecting residual paralysis at TOFRs between 0.6-0.9 [18, 20].

Quantitative monitoring uses neuromuscular monitors, devices that stimulate the peripheral nerve while also recording, quantifying and displaying numerically the evoked responses [21]. Multiple techniques are in use, for which we presented advantages and limitations in Table 1.

Choosing the right nerve-muscle unit to monitor

Different muscle groups have various sensitivities to NMBAs. Neuromuscular block has faster onset, shorter duration and faster recovery at laryngeal and diaphragmatic muscles than at the APM, although the

Table 1. Techniques used for quantitative neuromuscular monitoring

Monitoring technique	Description	Devices for clinical use	Advantages	Limitations
Mechanomyography (MMG)	Measurement of the evoked mechanical response of the APM following ulnar nerve stimulation.	None	Precise Reproducible Gold standard	Cumbersome setup [21]
Electromyography (EMG)	Measurement of the muscle action potential following nerve stimulation.	Datex-Ohmeda NMT ElectroSensor	Best indicator of pure neuromuscular function [22]. Comparable with MMG but more consistent in time [23, 24]. Available for many sites [25]. Free muscle movement not required.	Influenced by other electronic devices in the OR (diathermy) or local temperature [21, 24].
Acceleromyography (AMG) most widely used technique, the de facto standard of clinical care [16, 22].	Measurement of the acceleration of the stimulated muscle with a piezoelectric sensor.	**Classic AMG:** TOF-Watch InfinityTrident NMT Pod	Easy to handle Suitable for any free-moving muscle [10]	Not interchangeable with EMG/MMG TOFR overestimation by at least 0.15 [26, 27] Baseline TOFR > 1.0 [28].
		3D AMG: STIMPOD TOFscan [21]	3D transducer to measure more precisely the muscle movement [29]	
Kinemyography (KMG)	Measurement of the electrical signal generated by the bending of a piezoelectric sensor strip placed between the thumb and the index	Datex-Ohmeda NMT MechanoSensor	Easy to use	Available only for the ulnar nerve – APM group Free thumb movement required Good strip placement between the fingers required [22]
Phonomyography (PMG)	Measurement of the low-frequency sounds evoked by muscle contraction	None	Easy to apply Usable for many sites [21] Good correlation with AMG, EMG, MMG [30]	
Compressomyography (CMG)	Modified non-invasive blood pressure cuff measuring the block depth by brachial plexus stimulation through electrodes attached on its inner surface [31]	TOF-Cuff	No need for free arm movement	Not interchangeable with MMG, but a TOF-Cuff® TOFR > 0.9 correlates well with a MMG TOFR > 0.7 [32]

former are more resistant to NMBAs [22]. Therefore, during surgery, the absence of a twitch at the APM does not guarantee paralysis of the diaphragm [33]. Concerning facial nerve stimulation, the corrugator supercilious muscle (CSM) follows tightly the blockade kinetics of the laryngeal adductor muscles, while the orbicularis oculi muscle (OOM) behaves more like a limb muscle [34]. Facial muscles are still more resistant to NMBAs than APM, which may result in overdosing of NMBAs and overestimation of the degree of recovery [25, 33]. Consequently, Thilen et al. revealed a fivefold risk of postoperative residual curarization when using facial muscle monitoring [35].

The optimum monitoring site is the most accessible one during surgery and where response muscles can be clearly seen [36]. Some researchers state that it would be more appropriate to use the facial nerve (CSM) for monitoring the earliest time for optimal intubation (for rapid sequence induction) or blockade of the diaphragm and the abdominal wall muscles, whereas the ulnar nerve (APM) unit is best used when information about pharyngeal muscle recovery is needed, especially before extubation [37, 38].

The preferred nerve-muscle unit remains the ulnar nerve (APM), but we must be aware of the overestimation of time required for relaxation of laryngeal muscles when using this site in induction [36]. When the hand is inaccessible, the posterior tibial nerve-flexor hallucis brevis muscle evaluated subjectively or by AMG can be chosen, with similar values compared to APM [39]. Another option is facial muscle monitoring subjectively or by AMG, as long as the stimulator electrodes are moved on the ulnar nerve before extubation, to ensure adequate recovery [22].

When and how we should antagonize NMBA?

In the late 1970s, it was established that a TOF ratio > 0.7 signifies a satisfactory recovery of the neuromuscular function [40]. Subsequent studies have shown that signs and symptoms of the residual blockade (such as swallowing dysfunction, atelectasis, hypercarbia, and postoperative hypoxemia) were recorded at this TOF ratio [41]. The current TOF ratio at which extubation is recommended is above 0.9.

Two types of reversal agents are used: acetylcholinesterase antagonists (pyridostigmine, edrophonium andneostigmine) and selective reversal binding agents (sugammadex). But what is the right time to produce the reversibility of the block? To find an answer to this question, we must guide ourselves by the depth of the neuromuscular block. The profound block is the period of time when there is no response to TOF stimulation, PTC and measured TOF are 0. A deep block involves TOF of zero and PTC = 1. The time period between recurrence of TOFC 1 and TOFC 3 represents the moderate block. During this period it is not recommended to apply PTC and the measured TOF is 0. The superficial block is characterized by TOFC equal to 4 and TOF measured between 0.1 and 0.4. A minimal block involves a TOF > 0.4. [42]. For deep neuromuscular block the reversibility time using 0.07 mg/kg neostigmine is 49 minutes (with a range of 13-146 minutes) (TOF ratio > 0.9) for rocuronium and 44 minutes (TOF – 0.7) for atracurium [43, 44]. In 2015, Rodnei and his team demonstrated the efficacy of sugammadex (4 mg/kg) in the reversibility of the deep block following rocuronium [16]. For the moderate neuromuscular block using cisatracurium, Kirkegaard et al. concluded that a dose of 0.07 mg/kg neostigmine produces block reversibility (TOF = 0.9) in 20 minutes (7-71 minutes) [45]. Kim and his team established that the average time required to reverse moderate block with rocuronium, using the same dose of neostigmine, is 23 minutes (range 8-57) [46]. The recommended sugammadex dose for reversing moderate block is 2 mg/kg [16]. Antagonism of low degrees of atracurium-induced neuromuscular blockade was studied by Fuchs-Buder et al. and they found that for successful block's reversal within 10 min, as little as 20 μg/kg neostigmine may be sufficient [47]. Studying the required dose of sugammadex for smaller degrees of residual block, Schaller found out that sugammadex, 0.22 mg/kg, and neostigmine, 34 μg/kg, effectively and comparably reverse a rocuronium-induced shallow residual neuromuscular block at a TOF ratio of 0.5 in 2 minutes [48].

A third category of neuromuscular block antagonists is currently being studied, namely calabadion. This molecule is a broad spectrum agent with action on both steroidal and benzylquinolone molecules. Huffman and his team tested calabadion on 60 rats and showed a recovery of TOF > 0.9 neuromuscular function in both the rocuronium block and the atracurium neuromuscular block [49] and Haerter also demonstrated a much faster action of calabadion compared to sugammadex [50].

In conclusion, current recommendations suggest that in the case of profound neuromuscular block, acetylcholinesterase inhibitors should be avoided and sugammadex (4-16 mg/kg) should be used; in the moderate block, both sugammadex (2 mg/kg) and acetyl cholinesterase antagonists (0.07 mg/kg neostigmine) can be used, and for the reversibility of the superficial block, a dose of 0.02-0.03 mg/kg of neostigmine is sufficient.

What do the guidelines say?

In order to convince the members to introduce the objective monitoring of the level of neuromuscular blockade in the routine management of general anaesthesia, some professional societies established specific guidelines. In 2000, The French Society of Anaesthesiology and Intensive Care stated that the presence of four responses to TOF stimulation is not enough to assess recovery; therefore an instrumental monitoring is required [51]. From 2010, the homologous Czech Republic society has recommended the use of the quantitative evaluation of the blockade depth, along with the choice of the ulnar nerve as the most appropriate site for stimulation. Achieving TOF-ratio above 0.9 is considered an adequate sign of recovery from the effect of non-depolarizing muscle relaxants [52]. Guidelines issued by the Australian and New Zealand College of Anesthetists (ANZCA) consider that neuromuscular function monitoring, preferably quantitative, must be available for every patient who undergoes neuromuscular blockade and should be used whenever the anaesthesiologist is considering extubation following the use of non-depolarizing neuromuscular blockade [53].

The latest recommendations for standard monitoring during anaesthesia issued by The Association of Anaesthetists of Great Britain & Ireland in December 2015 state that the peripheral nerve stimulator is a mandatory device if neuromuscular blocking drugs are used. It should be used from induction time until recovery from blockade and consciousness return. A more reliable guarantee for the return of safe motor function is evidence of a train-of-four ratio > 0.9 made by a quantitative device. As a result, the anaesthetic departments are encouraged to use this kind of monitoring instead of qualitative devices [54].

Guidelines for the management of tracheal extubation released by the Difficult Airway Society emphasize the importance of the reversal of neuromuscular block and its monitoring. The use of a peripheral nerve stimulator to ensure a train-of-four ratio of 0.9 or above is recommended in order to reduce the incidence of postoperative airway complications [55].

Despite the use of nerve stimulating devices to monitor the depth of neuromuscular blockade for more than half a century and the existence of many studies that correlate the patient outcome to neuromuscular residual blockade, the American Society of Anesthesiologists (ASA) and the European Society of Anaesthesiology (ESA) have not yet published any guidelines or recommendations. The ASA standard of intraoperative monitoring does not include neuromuscular blockade monitoring [56]. An updated report by the ASA on Practice Guidelines for Postanesthetic Care added the next statements: *"assessment of neuromuscular function should be performed during emergence and recovery for patients who have received NMBAs or who have medical conditions associated with neuromuscular dysfunction"* and *"assessment of neuromuscular function primarily includes physical examination and, on occasion, may include NMBAs monitoring"*. As regards the reversal of NMBAs, the recommendation is to use anaesthetic regimens designed to avoid the need for antagonism in order to reduce adverse outcomes and improve patient comfort and satisfaction. The guidelines use also a vague formulation regarding the indication of block reversing: *"specific antagonists should be administered for reversal of residual neuromuscular blockade when indicated"* [57].

Conclusions

Neuromuscular block should be monitored for all patients who receive NMBAs during anaesthesia, to guide dosing of NMBAs and reversal agents, and to assess the degree of recovery.

Quantitative methods of measuring block's depth (such as acceleromyography or mechanomyography) are preferred. Onset and recovery from neuromuscular block occurs at different rates in different muscles. Satisfactory recovery from neuromuscular block has not occurred until the train-of-four ratio is > 0.9. By quickly and completely reversing any depth of neuromuscular block, sugammadex may reduce the rate of residual relaxation. There is a great need of global guidelines for neuromuscular monitoring during anaesthesia in order to reduce postoperative residual relaxation and improving patients' outcome.

Conflict of interest

Nothing to declare

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