Quantitative Neuromuscular Monitoring: "Love All, Trust a Few, Do Wrong to None"

Béla Fülesdi, MD, PhD, DSci,* and Sorin J. Brull, MD, FCARCSI (Hon)†

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GLOSSARY

BMI = body mass index; **COVID-19** = coronavirus disase 2019; **PTC** = post-tetanic count; **TOF** = train of four

Love all, trust a few, do wrong to none. – William Shakespeare (1564–1616); All's Well That Ends Well

In this issue of *Anesthesia & Analgesia*, Blobner et al[1] present an erudite debate about the value of quantitative neuromuscular monitoring in a modern clinical practice that includes the selective relaxant binding agent, sugammadex. The article provides an interesting and educational debate, clearly designed to expose the reasons behind clinicians' decisions to use quantitative neuromuscular monitors (Pro section) or to avoid their use (Con). The discussion is germane, well balanced, and covers most issues that anesthesiologists consider when making clinical decisions.

It is entirely possible, even likely, that the "con" section may further entrench some clinicians in their current practice, rather than facilitate learning of new knowledge or skills. This would not be unusual, particularly in medicine; the literature is replete with reasons why some physicians cling to their current ("that's the way I always do it") practice, rather than evolve to new ideas and applications. Perhaps the most difficult obstacle that prevents clinicians from adopting new technologies is not the ability to recognize their novel and improved functionality, or even the need to question their safety—it is the difficulty in unlearning ("deinnovating") their current, comfortable, and time-tried practice. It is perhaps this obstacle that is most important in the decision to transition to new (and demonstrably, safer) anesthesia practice that includes routine monitoring of neuromuscular function and away from antiquated (and demonstrably, less safe) practice of being guided by "experience" (ie, no monitoring) or by subjective assessment using a peripheral nerve stimulator.

To best understand and accept the authors' Pro-Con debate, we start by reviewing many obstacles (barriers) to deinnovation. These closely held beliefs likely prevent clinicians from embracing change.

1. Lack of recognition of variability in the clinical effects of neuromuscular blocking agents. Clinicians continue to be guided by the clock: wait 90 seconds before intubation; readminister a rocuronium "top-up" every 20 minutes; "patient is ready, pull the tube" 10 minutes after neostigmine (or 3 minutes after sugammadex) administration, etc. However, even after a single dose, spontaneous recovery from cisatracurium, rocuronium, or vecuronium block requires 33 to 137 minutes.[2] Similarly, the proportion of patients with residual paralysis, defined as a train-of-four (TOF) ratio <0.9, remains >95% for the first 60 minutes after administration of neostigmine for antagonizing deep block.[3] It is thus clear that making clinical decisions based solely on the pharmacokinetics and pharmacodynamics of neuromuscular blocking agents (or, in fact, any drug) is woefully inadequate. This individual patient variability cannot be excluded with a peripheral nerve stimulator or with clinical tests. Therefore, both appropriate operating room workflow and patient safety favor the use of quantitative neuromuscular monitoring regardless of the type of neuromuscular blocking agent used (aminosteroid or benzylisoquinolinium).

From the *Department of Anesthesiology and Intensive Care, University of Debrecen, Medical Advisory Board of the Ministry of Health, Debrecen, Hungary; and †Department of Anesthesiology and Perioperative Medicine, Mayo Clinic College of Medicine and Science, Jacksonville, Florida.

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Address correspondence to Sorin J. Brull, MD, FCARCSI (Hon), Department of Anesthesiology and Perioperative Medicine, Mayo Clinic College of Medicine and Science, 4500 San Pablo Rd S, Jacksonville, FL 32224. Address e-mail to sjbrull@me.com.

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2. Belief that routine administration of sugammadex supplants the need for monitoring. In the "con" section of the debate,[1] the authors stated that monitoring is not needed in the era of sugammadex, since its reversal is "fast and effective." However, sugammadex is 3× more selective for rocuronium than for vecuronium. In a recent randomized trial, after successful antagonism of vecuronium with 2 mg/kg sugammadex, reparalysis occurred in 2 of 13 (15%) patients when tested in the postanesthesia care unit.[4] When quantitative monitoring is not used, routine reversal of rocuronium block with sugammadex still results in residual neuromuscular block in 4% to 8% of patients.[5,6] A recent meta-analysis confirmed that sugammadex is more rapid and effective in antagonizing rocuronium or vecuronium compared with neostigmine.[3] However, atracurium and cisatracurium still make up a significant portion of the market, and sugammadex cannot be used for their antagonism.
3. Another common current barrier to adoption of quantitative monitoring is the erroneous belief that patients who receive depolarizing (succinylcholine) or short-acting nondepolarizing (mivacurium) neuromuscular blocking agents do not need to be monitored due to the rapid metabolism of the drugs by butyrylcholinesterases. However, without neuromuscular monitoring, prolonged paralysis occurs in patients with inherited or acquired butyrylcholinesterase deficiency and up to 50% of such patients report unwanted awareness of paralysis.[7] This is not an inconsequential complication since the incidence of butyrylcholinesterase deficiency is 1 in 500 patients (in heterozygotes for the abnormal gene) and 1 in 2500 patients in those with the homozygote gene. More than 86% of patients with intraoperative awareness report distress and are at high risk for posttraumatic stress disorder[7]; respiratory complications occur in 25% of unmonitored butyrylcholinesterase-deficient patients.
4. Because of its ubiquitous use as a sign of adequate recovery, a TOF ratio >0.90 may be considered by many clinicians a guarantee that spontaneous respiration would resume safely and that pulmonary complications would be avoided. We must remember that return of the TOF ratio to a value >0.90 (or even >1.00) signifies that only one-third of receptors are functioning normally[8]; this means that the other two-thirds of receptors are still blocked. It is fortuitous that this margin of safety[8] is sufficient, in most cases, to protect our patients.

As with almost anything in medicine, the "devil" is in the details. While moderate block (defined as the presence of a TOF count 1–3) and deep levels of neuromuscular block (defined as post-tetanic count [PTC] ≥1)[9] could be guided by tactile evaluation of "twitches," clinicians cannot discern the presence of a TOF ratio >0.40 (ie, fade) and might incorrectly assume there is sufficient neuromuscular recovery.

In high-risk patients, there is no alternative to neuromuscular monitoring-based management of intraoperative block and antagonism. This patient group may include obese patients who have altered neuromuscular blocking agent and sugammadex pharmacokinetics, sleep apnea patients who are prone to upper airway closure in the early postoperative setting due to residual effects of the muscle relaxant, and elderly patients who are at greater risk of developing postoperative pulmonary complications.

5. Clinicians rely on medical heuristics or decision-making shortcuts (rules of thumb). Such heuristics include concepts of cognitive bias (a systematic pattern of deviation from a norm or rationality), which is increasingly recognized as an important source of medical error.[10] The reliance on heuristics such as "the adequacy of the breathing pattern" based on observation of oscillations of the reservoir bag of the ventilator may lead to the erroneous interpretation that sufficient respiratory function for tracheal extubation exists.[11] The reservoir bag oscillations (breaths), however, represent diaphragmatic, not upper airway muscle function, rendering the patient at increased risk for postextubation airway obstruction. It is also noteworthy that clinicians rely more on such heuristics during times of stress, time pressure, and multiple distractions—that is, exactly the components experienced during emergence and extubation of surgical patients.

Other major barriers deal with clinicians' general psychological characteristics ("human nature"):

6. Overconfidence. Misdiagnosing "adequate recovery," especially when objective means are available but are not used, can and should be characterized as errors, particularly when they contribute to significant postoperative events. Anesthesiologists' overconfidence in their own ability to manage neuromuscular block and diagnose adequate recovery by subjective assessment was documented in a recent survey of international anesthesiologists;[12] such overconfidence is common to all physicians.
7. Departmental culture. Introduction of standards for neuromuscular monitoring and

antagonism can be very effective in gradually decreasing the incidence of residual neuromuscular block. However, this institutional educational effort requires a significant time investment, measured in years; it also requires a dedicated champion who can provide the needed ongoing educational support and who is in a position of authority to be able to effectively practice changes. A structured teaching program developed at a departmental or even institutional level can help clinicians acquire knowledge about occurrence of residual block and its consequences. Perhaps the most important and sustainable intervention is the introduction of a curriculum aimed to educate our next generation of trainees not only in the physiology and pharmacology of the neuromuscular junction, but most important, in the practical application of this knowledge to the operating rooms, postoperative care units, and intensive care units.

There are also several important technical barriers to broad acceptance and use of neuromuscular monitors:

8. Lack of neuromuscular monitoring equipment. This barrier should not exist in most modern hospitals since several anesthesia workstations already have built-in neuromuscular monitoring systems. A drawback of these built-in devices is their lack of portability, which prevents them from being used in non–operating room settings (postoperative care and intensive care units). In the past few years, perhaps because of increasing evidence of the utility of quantitative monitors and the publication of clinical guidelines mandating their availability, several new portable neuromuscular monitors have been introduced into routine clinical use.[13]
9. Complicated and time-consuming procedures that are necessary for application of the monitor and its calibration. Until recently, these difficulties were the most frequently mentioned barriers to routine neuromuscular monitoring. Last-generation acceleromyographic monitors needed proper preparation: immobilization of forearm and fingers and application of a hand adapter to ensure the thumb muscle had a preload and that it returned to its original position after each contraction. Thereafter, calibration had to be performed to ensure accuracy of measurements. This intricate and time-consuming requirement was a frequent complaint, along with the inability to use the motion-dependent acceleromyographic monitor in settings in which the patient's arms were placed under surgical drapes and away from the anesthesiologist's access. However, with new electromyography-based devices, problems of application, calibration, and intraoperative use appear to have been solved: "It takes a little over 18 seconds longer to apply a quantitative neuromuscular monitor than a peripheral nerve stimulator during clinical care."[14]
10. Price of monitors and recurring cost of disposables (electrodes) for quantitative monitors add to the total cost of surgery. However, this argument does not consider the potential cost savings from avoidance of reversal agent use or the need for lower doses of expensive antagonists such as sugammadex. A recent multimodal analysis of the potential impact of quantitative monitoring on clinical outcomes and total cost of care has found that the incidence of residual neuromuscular block was 60%; in fact, 18% of their patients had a TOF ratio <0.50.[15] The authors analyzed the marginal cost of a postoperative pulmonary complication, defined as postoperative pneumonia and/or unanticipated reintubation. A sensitivity analysis found that savings achieved from avoiding only 5 cases of pulmonary complications could finance the entire cost of monitors and electrodes for an entire year.[15]

We are grateful for the cogent and erudite debate[1] provided by the authors; they probably recognize that many of the "con" arguments appear contrived, as most of the "myths" or barriers have been debunked long ago. Yet, these arguments still exist and are used by many clinicians to justify their unwillingness to change practice, despite abundant evidence (Table).

Table. Key Reasons for Using Quantitative Neuromuscular Monitoring

Prevent residual neuromuscular block.
Lower the incidence of postoperative pulmonary complications, particularly in vulnerable populations (age >80 y; infants ≤1 y; BMI >40).
Prevent subjective symptoms of weakness.
Prevent unintended/accidental awareness and recall.
Optimize intraoperative dosing of neuromuscular blocking agents.
Optimize timing of antagonism of neuromuscular block.
Optimize dosing of antagonists of neuromuscular block.
Assure effectiveness of antagonism.
Lower neuromuscular blocking drug consumption and avoid overdosing intensive care unit patients.
Decrease length of postoperative care unit stay.
Lower medical costs of postoperative pulmonary complications.
Decrease length of hospital stay.
Optimize clinical decision-making during acute or expected periods of neuromuscular blocking agent shortages.
Help diagnose fixed dilated pupils in COVID-19 acute respiratory distress patients.
Manage iatrogenic extravasation of neuromuscular blocking agents.
Determine potency, duration, and effectiveness of neuromuscular blocking agents and their antagonists.

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019.

The responsibility is now squarely on the shoulders of our specialty organization to publish clinical guidelines for perioperative neuromuscular monitoring. ■

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