Patient Safety and Quantitative Neuromuscular Transmission Monitoring in 2022

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Historically, intermediate-acting neuromuscular blockade has been accomplished by population-based dosing accompanied by clinical signs and/or subjective (qualitative) electrical stimulus-based twitch monitoring. Somewhat surprisingly, neuromuscular transmission (NMT) monitoring is still not a formally articulated basic anesthesia monitoring standard of care when an intermediate-acting neuromuscular blocker (NMB) is administered.[1] Recently, the Anesthesia Patient Safety Foundation (APSF) Committee on Technology advocated for NMT monitoring when an intermediate-acting muscle relaxant is used.[2] The recommendation for NMT monitoring arises from accumulated experiences of residual neuromuscular blockade in postoperative patients, which is not a rare phenomenon. Such patients are subjected to the postoperative physiologic and psychologic risks associated with chemically induced weakness. The psychologic risk is obvious, whereas the physiologic ones can be obvious or subtler, but include hypoxemia, respiratory distress, need for supplemental oxygen, impaired upper airway protection, and longer recovery room stay.[3] Residual neuromuscular blockade is most prevalent when a patient is assessed as being "clinically strong" before or after neuromuscular blockade reversal by using only clinical indicators (e.g., adequate tidal volume, grip strength, and/or five-second head lift). The practice of using only clinical monitoring for neuromuscular blockade and assessment of recovery persists despite ample documentation that residual neuromuscular blockade happens in approximately one in five patients on postanesthesia care unit arrival.[4] Residual neuromuscular blockade is defined as when the ratio of the fourth to the first twitch height/excursion (T4/T1) is < 0.9 after intermediate-acting muscle relaxant administration.[5]

With the growing ubiquity of nerve stimulators, there has been a steady move toward titration of NMBs against a motor response to an electrical stimulus. The stimulus is applied most commonly over the ulnar nerve to enable stimulation and assessment of a hypothenar response or periorbitally to assess the orbicularis oculi or levator palpebri response. Actually, monitoring the motor response to an electrical stimulus is a significant step forward over only dosing and reversing NMBs based on elapsed time, clinical response, and patient weight. Moving from clinical monitoring to train-of-four (TOF) NMT monitoring represents the initial next step in advancing the sophistication of NMT monitoring. TOF monitoring has been extensively studied; thus, we know that with no twitch response, there is nearly 100% neuromuscular receptor blockade (NMRB), with 1 twitch 90% NMRB, 2 twitches 80% NMRB, 3 twitches 75% NMRB, and still 0–75% NMRB with 4 twitches.[6]

To obtain a more nuanced assessment, the medical professional assesses the T4/T1 ratio. The target ratio is at least 0.9 for typical adequate clinical reversal.[7] Although the T4/T1 ratio can be assessed by visual inspection, palpation, or electronically, it is well described that visual and tactile assessment of the T4/T1 ratio is remarkably imprecise and unable to reliably discriminate between a ratio of 0.4 and >0.9.[8] This is of clinical consequence and explains the advocacy for implementing quantitative T4/T1 NMT monitoring (QNMT). In QNMT, the device reports a twitch count and then an objective T4/T1 ratio once there are at least 4 twitches. This allows objective verification that a ratio of at least 0.9 has been reestablished after spontaneous or pharmacologically reversed recovery. As a small aside, it is noteworthy that a baseline T4/T1 ratio is actually greater than 1. This is because the release of acetylcholine into the neuromuscular junction is not completely cleared between the TOF twitches; therefore, there is some potentiation. If a QNMT monitoring device is not available, then achieving sustained 5-s tetanus at 100 Hz approximates a T4/T1 ratio of roughly 0.9. Conversely, using 50-Hz tetanus is inadequate to assess adequate recovery/reversal, and it may be no better than using qualitative TOF.[9]

Over the last 6 years, a new molecule, sugammadex, has become available to reverse neuromuscular blockade. Sugammadex encapsulates several of the intermediate-action NMBs (i.e., rocuronium and vecuronium). Unlike neostigmine, which creates a competitive antagonism by increasing acetylcholine in the neuromuscular junction, sugammadex does not have a ceiling effect. Despite the rapid and largely reliable pharmacodynamics of sugammadex, NMT still plays an important role to verify that the target T4/T1 ratio is >0.9 or that a sustained tetanus at 100 Hz has been achieved after sugammadex administration, as advised in the package insert.[10] Skipping this step unnecessarily puts our patients in harm's way. As one of our mentors used to say, the operating room is no place for optimism.

In fall of 2022, the APSF has included a QNMT module in the Technology Education Initiative to help provide clinicians with a better understanding and mental model for NMT monitoring and QNMT monitoring, NMB dosing, redosing, pharmacodynamics, interaction of volatile anesthetics with neuromuscular blockade, and reversal of neuromuscular blockade.

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REFERENCES

1. American Society of Anesthesiologists. Committee on Standards and Practice Parameters. Standards for basic anesthetic monitoring. Last affirmed: December 13, 2020. https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring. Accessed April 12, 2022.
2. The APSF Committee on Technology. APSF endorsed statement on revising recommendations for patient monitoring during anesthesia. *APSF Newsletter.* 2022;37:7–8. https://www.apsf.org/article/apsf-endorsed-statement-on-revising-recommendations-for-patient-monitoring-during-anesthesia/. Accessed April 22, 2022.
3. Raval AD, Uyei J, Karabis A, et al. Incidence of residual neuromuscular blockade and use of neuromuscular blocking agents with or without antagonists: a systematic review and meta-analysis of randomized controlled trials. *J Clin Anesth.* 2020;64:109818. 32304958. Accessed April 22, 2022.
4. Grabitz SD, Rajaratnam N, Chhagani K, et al. The effects of postoperative residual neuromuscular blockade on hospital costs and intensive care unit admission: a population-based cohort study. *Anesth Analg.* 2019;128:1129–1136. 31094777. Accessed April 22, 2022.
5. Brull SJ, Naguib M, Miller RD. Residual neuromuscular block: rediscovering the obvious. *Anesth Analg.* 2008;107:11–14. 18635461. Accessed April 22, 2022.
6. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg.* 2010;111:120–128. 20442260. Accessed April 22, 2022.
7. Naguib M, Brull SJ, Kopman AF, et al. Consensus statement on perioperative use of neuromuscular monitoring. *Anesth Analg.* 2018;127:71–80. 29200077. Accessed April 22, 2022.
8. Viby-Mogensen J, Jensen NH, Engbaek J, et al. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology.* 1985;63:440–443. 4037404. Accessed April 22, 2022.
9. Capron F, Fortier LP, Racine S, et al. Tactile fade detection with hand or wrist stimulation using train-of-four, double-burst stimulation, 50-Hertz tetanus, 100-Hertz tetanus, and acceleromyography. *Anesth Analg.* 2006;102:1578–1584. 16632846. Accessed April 22, 2022.
10. Bridion (sugammadex). Prescribing information. Merck; 2015. https://www.merck.com/product/usa/pi_circulars/b/bridion/bridion_pi.pdf. Accessed April 12, 2022.