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Recommendations for standards of neuromuscular monitoring during anaesthesia

Dear Editor,

We presented recommendations for neuromuscular monitoring during anaesthesia, which were approved by the Council of the College of Anaesthesiologists, Singapore in September 2019 and the Council of the Academy of Medicine, Singapore in May 2021. Neuromuscular blocking drugs (NMBDs) are used to facilitate tracheal intubation and mechanical ventilation; provide good surgical field; and in the management of raised intracranial pressure.[1] However, the use of NMBDs has been associated with a high incidence (40–60%) of postoperative residual neuromuscular block (PRNB).[2,3] PRNB is associated with increased morbidity: upper airway obstruction, impaired coughing and swallowing, pulmonary atelectasis, aspiration pneumonitis, hypoxia, weakness, diplopia, and awareness (with unintended paralysis after extubation).[2,3] It can also potentially lead to increased hospital lengths of stay and costs of hospital admission.[2] Contributory factors to PRNB include: wide variation in the duration of action of NMBDs; lack of or inappropriate neuromuscular monitoring practices; and poor understanding and training regarding PRNB and neuromuscular monitoring. Education and training on the use of neuromuscular monitoring has been shown to decrease the incidence of PRNB and post-operative adverse respiratory events.[2,3]

Neuromuscular blockade facilitates tracheal intubation and ventilation, and continued intraoperative monitoring may be considered crucial in abolishing intraoperative movements due to poor relaxation in certain circumstances. It can be monitored through clinical tests, and qualitative and quantitative methods using a peripheral nerve stimulator (PNS). However, a study in a teaching hospital in Singapore found that the majority of anaesthetists (98.7%) did not routinely use PNS monitoring, and that PNS monitoring was only used in 17.9% of patients.[4] The prevalence of PRNB detected in the post anaesthetic care unit was 33.4%. Factors associated with this include a lack of knowledge and education on neuromuscular monitoring.[4] The study's survey questionnaire revealed an underestimation of PRNB and incorrect answers by up to 69% of respondents, including those for the definition of PRNB, and the timing and use of reversal agents.[4]

Our recommendations aim to promote appropriate use of neuromuscular blockade and its monitoring, and so improve the safety of anaesthesia care in Singapore. Our recommendations are best practices in the opinion of our members and are not mandatory.

Monitoring of neuromuscular block. Clinicals tests are not reliable and are not recommended to assess adequacy of recovery.[2,3,5] Qualitative methods include clinical tests or electrically evoked motor responses such as the train-of-four (TOF) that delivers 4 single-twitch (T) electrical stimuli (T1, T2, T3 and T4) at supramaximal current at 2Hz. It is most often applied to the ulnar nerve at the wrist, which causes contraction of the thumb (adductor pollicis) muscles. Qualitative TOF information includes: the number of detected muscle responses known as the TOF count (TOFC) of 0–4, the amplitude of the twitches, and the presence (if any) of visual or tactile fade (decreasing amplitude of successive twitches). These qualitative TOF details provide information about the depth of neuromuscular blockade and limited information about the level of recovery.

Quantitative methods utilise contemporary PNS devices that calculate the TOF ratio (TOFR), i.e. the ratio of the fourth twitch height to first twitch height (T4/T1), most commonly measured by acceleromyography. Adequate recovery from neuromuscular block is defined as a TOFR $\geq$0.9 at the ulnar nerve/adductor pollicis. Residual block occurs if the TOFR is <0.9. Only quantitative methods can objectively determine adequate recovery. Literature suggests that a TOFR >0.95 before extubation should be used to reduce postoperative complications.[6] Anaesthetic departments are encouraged to replace existing qualitative nerve stimulators with quantitative devices.[2,3]

Post-tetanic count (PTC) is used to monitor deeper levels of neuromuscular blockade. PTC consists of 5 seconds of a 50Hz tetanus stimulation, a 3-second pause followed by single twitches at 1Hz. It allows the clinician to titrate maintenance doses (NMDs) to maintain a deep block, and also to calculate the correct dose of sugammadex if reversal of intense or deep block is needed.

When and how to monitor neuromuscular block. Monitoring neuromuscular blockade with a PNS device is recommended for all stages of anaesthesia when NMBDs are administered.[2,3] It allows optimal management of neuromuscular blockade through accurate assessment of the onset, duration and effects

of NMBDs; appropriate titration of NMBD top-ups; and safe reversal.

It is recommended that a baseline reading of TOF twitches be measured after anaesthetic induction and before NMBDs have been administered. This confirms correct electrode placement and functioning of the PNS device, and allows mathematical correction of subsequent TOFR readings (normalisation).[2] During induction, TOF twitch ablation indicates optimal readiness for laryngoscopy. Intraoperative PNS monitoring guides NMBD administration, as the duration of action of NMBD can be extremely variable. Spontaneous recovery to a TOFR ≥0.9 may take 2–6 hours.[7] Many factors prolong the usual duration of neuromuscular blockade: increasing age; cardiac, liver and renal dysfunction; hypothermia; and use of halogenated volatile anaesthetic agents and intravenous infusions of NMBD. Spontaneous recovery from the short-acting depolarising NMBD, succinylcholine may also be markedly prolonged due to congenital (plasma cholinesterase deficiency) or acquired causes.

Common sites of monitoring neuromuscular block. The commonest site of neuromuscular monitoring is the ulnar nerve at the distal forearm to monitor the contraction of adductor pollicis. Other sites include the posterior tibial nerves (causing twitching of the big toe) and facial nerve (orbicularis oculi and corrugator supercilii muscles). The site of PNS monitoring affects its application and interpretation. Different muscle groups have different sensitivities to NMBD, affecting twitch height depression. The diaphragm is the most resistant to NMBDs and therefore recover faster from NMBDs. TOF monitoring of the facial nerve/corrugator supercilii may be used as a surrogate marker of diaphragmatic paralysis. The greater resistance of the diaphragm has 2 important clinical implications. First, there may be diaphragmatic breathing (impairing conditions for abdominal surgery) despite a TOFC=0 at the hand. Second, using the facial nerve and eye muscles (both of which recover earlier from NMBD) to determine recovery, leads to increased PRNB as the more sensitive muscles may still be partially paralysed. The adductor pollicis is more sensitive to and therefore recover slower from neuromuscular blockade. Therefore, it is the recommended muscle for assessing recovery.

Depth of neuromuscular block. The various degrees of neuromuscular block, their definitions and clinical relevance are summarised in Table 1. Intense block (TOFC=0, PTC=0) occurs soon after the administration of NMBD. Reversal at this stage may be required after failed airway management that requires "rescue" resumption of spontaneous ventilation. Deep block (TOFC=0, PTC=2) ensures patient immobility, for example, in open eye surgery or neurosurgery. Moderate "surgical" block (TOFC=2) is appropriate for most abdominal surgery, although this may be obtained by other methods such as using a remifentanil infusion. Shallow block (TOFC=4, with fade) indicates the earliest time for safe neostigmine reversal. Minimal block (TOFC=4, with minimal fade undetectable by visual or tactile assessment) still requires reversal.

Neuromuscular monitoring to guide dose and timing of reversal agent. Recovery of neuromuscular function after NMBD administration occurs either spontaneously (metabolism or elimination), or pharmacologically (neostigmine or sugammadex).

Neostigmine is an anticholinesterase inhibitor and should be given only after a TOFC has spontaneously reached 4.[5] In one study, during sevoflurane anaesthesia, after neostigmine administration at a TOFC of 1, 2, 3, and 4, the percentage of patients reaching TOFR ≥0.9 after 10 minutes were 5%, 10%, 20% and 55%, respectively.[8] If only qualitative PNS monitoring is available, and TOFC=4, the dose of neostigmine can be titrated depending on the presence or absence of fade.[2,5] In the presence or absence of fade, 40mcg/kg or 20–30mcg/kg of neostigmine should be given, respectively. The rationale for this is as follows. Clinicians are not able to detect fade at a TOFR >0.4.[9] Therefore, in the absence of clinically detectable fade, 2 possible scenarios are possible. One is "minimal" fade, i.e. partial neuromuscular block is present (but clinically undetectable) and needs reversing. This is also called the "zone of blind paralysis" (TOFR 0.5–0.8).[1] The other is that there is "truly" no fade, i.e. neuromuscular function has adequately recovered (TOFR ≥0.9). The lower dose of neostigmine effectively reverses the "minimal" neuromuscular blockade, but does not cause side effects in patients who have adequately recovered, including paradoxical muscle weakness and fade although this is controversial. If a baseline reading cannot be obtained (e.g. during rapid sequence induction) then reversal may be guided by the TOF count and the subjective detection of fade (albeit less sensitive than objective methods), and administration of reversal per Table 1.

The peak effect time for neostigmine is 10–15 minutes, and patients should only be woken up and extubated after this period. Only if there is quantitative measurement of TOFR ≥0.9 can the patient be diagnosed as adequately recovered and not requiring a reversal agent.

Table 1. Definitions of levels of neuromuscular block and associated clinical relevance, and dosing regimen for reversal agents

	Intense	Deep	Moderate	Shallow	Minimal	Recovered
Clinical scenario	Soon after NMBDs administered	Ensure immobility during surgery	"Surgical block"	Reversible (can administer neostigmine)	Clinically undetectable fade but still not adequately recovered	Adequately recovered
TOF count	0	0	2	4 (Obvious fade)	4 (Clinically undetectable fade)	4 (Truly no fade)
TOF ratio				0.1–0.4	0.5–0.8	≥0.9
PTC	0	2				
Neostigmine, mcg/kg	WAIT[a]	WAIT[a]	WAIT[a]	40	20–30	No need (side effects)
Sugammadex, mg/kg[b]	16	4	2	1–2	1–2	No need (costs and side effects)

NMBDs: neuromuscular blocking drugs; PTC: post-tetanic count stimulation; TOF: train-of-four stimulation
[a] It is recommended to wait until TOF=4
[b] For reversal of rocuronium and vecuronium

Sugammadex is a cyclodextrin that encapsulates aminosteroid NMBDs such as rocuronium and to a lesser extent, vecuronium in a 1:1 ratio. Unlike neostigmine, it can reverse intense, deep and moderate block reliably when administered at appropriate doses (see Table 1). A meta-analysis of randomised controlled trials comparing sugammadex versus neostigmine suggested that sugammadex reverses NMBD faster and more reliably, with lower risk of adverse events.[10] Appropriate dosing is related to the depth of neuromuscular block and necessitates careful PNS monitoring. Sugammadex has been used during "cannot intubate, cannot oxygenate" scenarios but it does not guarantee upper airway patency or control, and there have been cases of airway adverse events (e.g. laryngospasm and negative pressure pulmonary oedema).[11]

Conclusion. Adequate monitoring of neuromuscular blockade under anaesthesia contributes to patient safety. There is poor use of neuromuscular monitoring and a significant incidence of PRNB in Singapore. This letter, along with our approved recommendations by the Council of College of Anaesthesiologists, Singapore, and the Council of the Academy of Medicine, Singapore, aims to encourage clinicians to monitor and adequately reverse neuromuscular blockade, to reduce PRNB and its attendant risks.

Declaration

None of the authors have affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed.

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Patrick Wong [1]*FRCA*, Edwin Seet [2]*MMed (Anaes)*, Chandra Mohan Kumar [2]*FRCA*, Kwong Fah Koh [3]*MMed (Anaes)*, Terry Ling Te Pan [4]*FANZCA*, Terence Quah [5]*MMed (Anaes)*, Nelson Ping-Ping Chua [6]*MMed (Anaes)*

[1] Department of Anaesthesia, Waikato District Health Board, Hamilton, New Zealand
[2] Department of Anaesthesia, Khoo Teck Puat Hospital, Singapore
[3] Department of Anaesthesia, Woodlands Health Campus, Singapore
[4] Department of Anaesthesia, National University Hospital, Singapore
[5] Anaesthesiology, Gleneagles Hospital, Singapore
[6] Department of Anaesthesiology, Intensive Care & Pain Management, Tan Tock Seng Hospital, Singapore

Correspondence: Dr Patrick Wong, Department of Anaesthesia, Waikato District Health Board, 183 Pembroke Street, Hamilton 3204, New Zealand.
Email: patrick.wong@waikatodhb.health.nz