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Neuromuscular block management: evidence-based principles and practice

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Keywords: acceleromyography; electromyography; neostigmine; neuromuscular antagonists; neuromuscular blocking agents; quantitative neuromuscular monitoring; residual neuromuscular weakness; sugammadex

Learning objectives

By reading this article you should be able to:

- Explain the definitions of depth of neuromuscular block using post-tetanic count, train-of-four count and train-of-four ratio.
- Discuss the pharmacological variability of neuromuscular blocking and reversal drugs.
- Detail the consequences of residual block and its prevention.
- Describe the differences between acceleromyography and electromyography and their clinical use.

Key points

- Recent guidelines address monitoring of neuromuscular blocking drugs and antagonists.
- Residual neuromuscular block is common, unrecognised and causes harm to patients.
- Recovery from neuromuscular block requires a calibrated train-of-four ratio $\geq$0.9.
- Quantitative monitoring is essential to optimise surgical conditions and avoid residual neuromuscular block.
- Antagonism is more predictable with sugammadex than with neostigmine, but cannot guarantee recovery without quantitative monitoring.

Monitoring and reversal of neuromuscular block have been reviewed extensively, including in this journal.[1,2] Issues with management of neuromuscular block (NMB) and residual block persist, despite the introduction of the intermediate duration neuromuscular blocking drugs (NMBDs) in the 1980s, the reversal agent sugammadex in 2008, and availability of an increasing array of quantitative neuromuscular monitors for clinical practice. The most recent guidance from the Association of Anaesthetists (AoA), the American Society of Anesthesiologists (ASA) and the European Society of Anaesthesiology and Intensive Care (ESAIC) are reviewed, as will key aspects of neuromuscular physiology and pharmacology pertinent to clinical practice. A clinical practice strategy is described that uses quantitative neuromuscular monitoring for all patients receiving neuromuscular blocking drugs and offers guidance for neuromuscular block antagonism. The information is primarily intended to guide perioperative care of adult patients, but the principles are equally applicable to paediatric patients and critical care.

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Guidelines for managing neuromuscular block

Decades of evidence, expert opinion and editorial reviews have culminated in the publication of three landmark papers from the AoA, the ASA and the ESAIC.[3–8] The standout theme of these publications is the need for quantitative neuromuscular monitoring when patients receive neuromuscular blocking drugs. The 6th edition (2021) of the AoA's monitoring standards is a consensus document stating: "quantitative neuromuscular monitoring should be used whenever neuromuscular blocking drugs are given, throughout all phases of anaesthesia from before initiation of neuromuscular block until recovery of the train-of-four (TOF) ratio to >0.9 has been confirmed."[6] The guideline further calls for all locations where patients receive neuromuscular blocking drugs to be equipped with quantitative monitoring devices.

A task force of ASA members has produced clinical practice guidelines (2023) on the management of neuromuscular block.[7] Eight recommendations were produced according to the strength of available evidence. For optimal anaesthesia care, the panel strongly recommends quantitative monitoring over the use of clinical signs or a qualitative peripheral nerve stimulator (PNS), using the adductor pollicis muscle for neuromuscular monitoring, and recommends against monitoring the eye muscle responses to facial nerve stimulation.

An ESAIC task force (2023) simultaneously developed guidelines for the perioperative management of neuromuscular block based on three key topics: the need for neuromuscular blocking agents to facilitate tracheal intubation; the impact of deep block on outcomes from abdominal surgery; and strategies to best diagnose and treat residual neuromuscular block.[8] The key findings in relation to the risk of residual neuromuscular block and harm to patients exactly mirrored the ASA guidelines and called for "the use of ulnar nerve stimulation and quantitative neuromuscular monitoring at the adductor pollicis to exclude residual paralysis." Both documents provide guidance on antagonism and dosing recommendations for sugammadex and neostigmine, dependent on block level and underpinned by quantitative monitoring. However, neither guideline addresses neuromuscular management of the paediatric or critical care populations.

Review of key pharmacological principles

Definitions of levels of neuromuscular block

The depth of neuromuscular block can be defined based on the train-of-four (TOF) ratio, TOF count, and post-tetanic count (PTC) when using quantitative monitoring (Fig. 1).[4] This allows for consistency in understanding the applied pharmacology and its relevance to safe clinical care. Relaxation of the upper abdominal muscles, the larynx and the diaphragm requires *complete* (PTC=0) or *deep* (PTC≥1, TOF count=0) neuromuscular block. Deep neuromuscular block during laparoscopic surgery may improve outcomes, though evidence is conflicting. Surgical conditions are improved in many patients studied using deep block (PTC=0–5) but the clinical benefit is marginal and study shortcomings are evident.[8] There is insufficient evidence for reduced postoperative pain or decreased incidence of perioperative complications. Instead, individualised titration of depth of

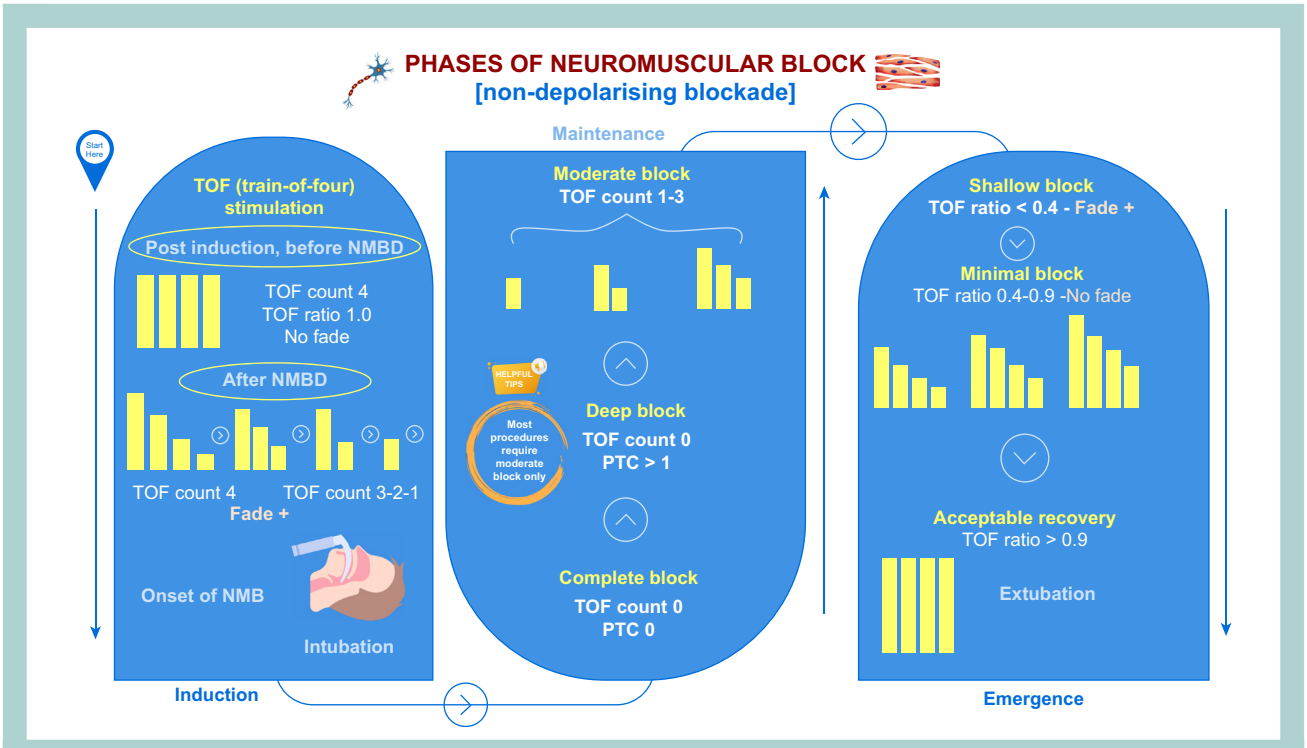

Fig 1 Phases of neuromuscular block. Adapted from Naguib and colleagues.[4] Complete (PTC=0), deep (PTC ≥1, TOF count=0), moderate (TOF count=1–3), shallow (TOF ratio <0.4), minimal (TOF ratio=0.4–0.9), recovery (TOF ratio >0.9). NMB, neuromuscular block; NMBD, neuromuscular blocking drug; PTC, post-tetanic count; TOF, train-of-four; TOF count, train-of-four count; TOF ratio, train-of-four ratio.

neuromuscular block is best guided by monitoring and surgical conditions.[8] *Moderate* block (TOFC=1–3) is likely to be sufficient to keep the patient immobile in most surgeries, provided adequate levels of anaesthesia are maintained. Coughing, respiratory efforts and other involuntary movements may be addressed by deepening the level of anaesthesia (with additional volatile anaesthetic, propofol or opioids). Adequacy of anaesthesia, including use of processed EEG, should be confirmed before giving additional neuromuscular blocking drugs. The need to ensure adequate anaesthesia during neuromuscular block was highlighted by the 5th National Audit Project (NAP5) study of accidental awareness under general anaesthesia.[9] On return of the 4th twitch of a TOF sequence, two levels of block can be defined: *shallow* block (TOF ratio <0.4); and *minimal* block (TOF ratio 0.4–0.9) (Fig. 1). There is a wide range of symptoms and signs, even at *minimal* block in the extubated patient, including reduced vital capacity and hand grip strength, impaired swallowing, increased pulmonary aspiration risk, upper airway obstruction, diplopia, subjective feelings of weakness, delayed recovery and reduced chemoreceptor-mediated response to hypoxia. Acceptable recovery is reached once the TOF ratio recovers to ≥0.9, but even when TOF ratio=1.0, most postsynaptic receptors are still occupied by the neuromuscular blocking agent; thus, forced vital capacity is only partially recovered, and the acute ventilatory response to hypoxia is depressed from normal.[10]

Differential muscle sensitivity (Fig. 2)

The larynx, diaphragm, upper abdominal, and corrugator supercilii muscles display relative resistance to neuromuscular block. Their rich blood supply ensures a rapid onset (wash-in) of non-depolarising neuromuscular block, but a limited peak effect and a rapid recovery (wash-out). By contrast, the most sensitive muscles (ocular, pharyngeal and genioglossus) are slowest to recover. Other factors, such as the number of postsynaptic receptors relative to fibre size, also contribute to the differential muscle sensitivity. Inadequate recovery signs include diplopia, swallowing difficulty, genioglossus muscle weakness and result in an increased risk of upper airway obstruction and pulmonary aspiration. The adductor pollicis and the orbicularis oculi muscle responses suggest similar sensitivity. The ulnar nerve/adductor pollicis muscle unit is recommended for quantitative neuromuscular block monitoring because of ease of access to the hand and close correlation with recovery of most sensitive muscles, providing an extra level of safety.

Variability in pharmacodynamics of neuromuscular blocking drugs

Onset of block and recovery times vary greatly. The predicted onset time for standard intubation doses of $2\times ED_{95}$ (ED_{95}=amount of drug required to reduce baseline twitch height by 95%) of rocuronium ranges from 2 to 3 min, but multiple factors affect it: young age, female sex, rapid injection rate, use of priming, coadministration of ephedrine, all shorten onset time; whereas esmolol increases it. The duration of neuromuscular block may be prolonged with increasing age, female sex, pregnancy, coexisting renal or hepatic disease and by drugs including magnesium, esmolol and aminoglycoside antibiotics. Notwithstanding any of these factors, there is wide variability in time-to-twitch and TOF ratio depression and achieving ideal conditions for intubation. Recovery time also varies greatly. Two hours after a single intubating dose of vecuronium, rocuronium or atracurium, 37% of patients had TOF ratios <0.9, and 11% had ratios <0.7.[11]

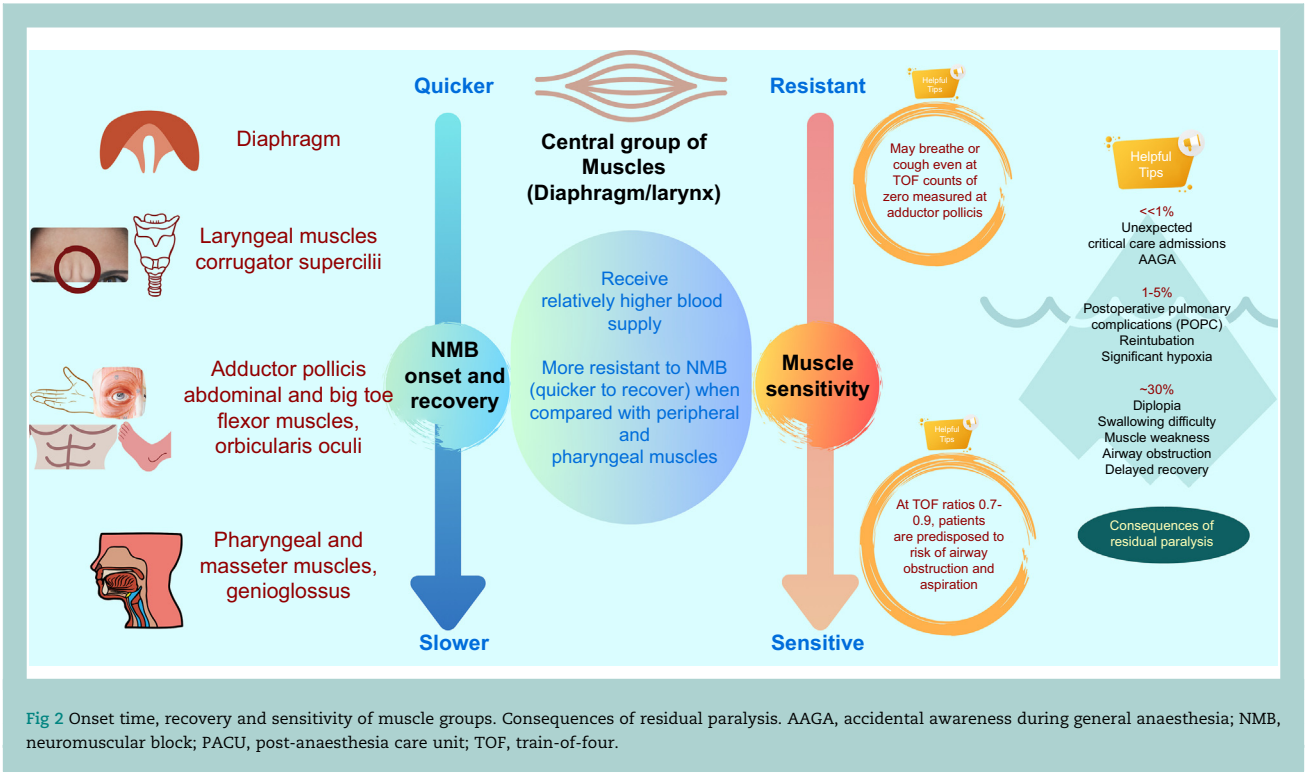

Fig 2 Onset time, recovery and sensitivity of muscle groups. Consequences of residual paralysis. AAGA, accidental awareness during general anaesthesia; NMB, neuromuscular block; PACU, post-anaesthesia care unit; TOF, train-of-four.

The median (range) duration of action of cisatracurium is 57 (37–81) min, rocuronium is 63 (33–119) min and vecuronium is 62 (35–137) min, revealing the variable and often prolonged duration of action of neuromuscular blocking drugs in some patients.[12] Even small doses of rocuronium (20–25 mg, or $1\times ED_{95}$) may result in incomplete spontaneous recovery in up to 20% of patients after 2 h.[13]

Appreciating the differences in muscle sensitivity explains why patients may still respond to laryngoscopy and intubation, why these responses may be present even when a measured adductor pollicis TOF ratio is reduced to zero and why 'time-based' decisions on readiness for intubation (or extubation) are flawed. Monitoring throughout anaesthesia allows variability between patients to be appreciated, based on individual neuromuscular responses.

Monitoring to optimise and prevent residual neuromuscular block

The current definition of residual neuromuscular block is a TOF ratio <0.9; its incidence ranges from 0% to 90.5% (median 30%).[14] The Canadian RECITE study (performed before the registration of sugammadex in Canada) revealed a residual neuromuscular block rate of 65% at tracheal extubation, with patients managed at the discretion of anaesthetists, using neostigmine and subjective (qualitative) evaluation of peripheral nerve stimulator (PNS) responses.[15] A meta-analysis of 53 studies and 12,664 patients over four decades, showed residual neuromuscular block rates of 33.1% with no neuromuscular monitoring (management guided by clinician experience and patient clinical signs) and 30.6% when using qualitative assessment.[16] Clinical tests of recovery (sustained head lift, sustained hand grip, tongue depressor tests) all fail to reliably detect residual neuromuscular block. With sensitivity rates of 10–30% and positive predictive values (precision) ~50%, residual neuromuscular block cannot be excluded unless TOF ratios are <0.4, exposing patients to considerable harm.[4] Use of a PNS allows subjective (tactile or visual) detection of TOF count and PTC, but only provides an unreliable estimate of recovery by evaluating fade of the fourth twitch compared with the first twitch (T4/T1) response. Whereas detection of moderate (TOF count 1–3) and deep (PTC >1) block is possible using a PNS, readiness for tracheal extubation (defined as TOF ratio $\geq$0.9) CANNOT be determined by subjective (non-quantitative) means. Statements such as 'four strong twitches are present' or 'there is no fade' are demonstrably false and do not guarantee adequate neuromuscular recovery. Fade assessed subjectively (visual or tactile means) cannot be detected reliably when the TOF ratio is >0.4, with a resultant wide gap (TOF ratio 0.4–0.9) when using subjective monitoring. This degree of block can only be appreciated when using quantitative measurement of the TOF ratio. When using double-burst stimulation (DBS), fade of the second of the two mini-tetanic responses cannot be detected reliably when the DBS (or TOF) ratio is >0.6. Although the gap using DBS is narrower (TOF ratio 0.6–0.9) than that of TOF (TOF ratio 0.4–0.9) when using subjective means, neither pattern can safely and reliably determine the adequacy of recovery, and their use should be abandoned (Figure 1 online video).

Quantitative monitoring

Acceleromyography (AMG) and electromyography (EMG) monitors are most applicable in clinical practice. Both freestanding portable devices and devices integrated to widely used patient monitoring systems are available.

Acceleromyography

Though no longer commercially available, the TOF-Watch (Organon, Cork, Ireland) was the first device used widely in clinical practice and has been evaluated against the 'gold standard' of mechanomyography (MMG). Acceleromyography devices utilise the principle of Newton's law: *force = mass×acceleration*. When a piezoelectric sensor is applied to the thumb (fixed mass) and stimulated, the acceleration in response to stimulation is directly proportional to the force of contraction. A resultant electrical signal is processed and displayed as a numerical value/ratio. There are some caveats with AMG use. Firstly, the thumb must be allowed to move unimpeded, otherwise readings are inaccurate—for example, when arms are tucked under surgical drapes and inaccessible during surgery. Two or three serial TOF measurements at 15-s intervals should always be taken, before deciding an action (need for top-up doses, determining block level, ensuring recovery after reversal) (Figure 2 online video). Secondly, unlike with MMG and EMG, the baseline TOF ratio often exceeds 1.0 (100%), with figures as high as 1.4 (140%). This 'reverse fade' is an idiosyncrasy of the technology, as supramaximal current (stimuli) should always induce maximal (therefore, equal) responses (Figure 3 online video). The mechanism is uncertain but is likely because of the elastic recoil of the thumb not returning to baseline after each TOF stimulus.[17] For this reason, AMG devices should be calibrated with a baseline (supramaximal) value, before neuromuscular block, and 'normalised' to determine a target ratio of 0.9 for recovery. For example, with a baseline value of 1.2, recovery to 0.9 requires a ratio of 1.08. Some AMG devices cap the ratio at 1.0 (100%) and calculate the TOF ratio as the fourth response (T4) compared with the second response (T2), or T4/T2 ratio, rather than the typical T4/T1 comparison. In clinical practice these manipulations may make relatively little difference, but they present a limitation of AMG-derived values. There is also evidence that AMG precedes EMG recovery,[18] that for AMG, recovery to 0.95 or above is required to avoid postoperative pulmonary complications[19] and the ESAIC guideline recommends recovery to 1.0 when raw (uncalibrated non-normalised) ratios are used.[8] A new generation of AMG devices enhances accuracy by using three-directional sensors, which account for the multidirectional movement of the adducting thumb in response to ulnar nerve stimulation. Some manufacturers claim that their products do not require calibration. In practical terms, the TOF ratio using AMG should be as close to 1.0 as possible, realising that even at this level of recovery, most (>75%) postsynaptic receptors are still blocked. Despite these caveats, AMG monitors are widely available, are simple to apply and use and an extensive evidence base shows their superiority over clinical and qualitative methods of recovery using peripheral nerve stimulation.[16]

Electromyography

Electromyography devices measure the peak-to-peak amplitude or area under the waveform curve of the evoked muscle action potential to measure the intensity of the response. Electromyography and MMG monitoring are closely matched. There are advantages to using electrical, rather than mechanical signals. Electromyography reflects more accurately the response at the neuromuscular junction (where all neuromuscular blocking agents work), is not affected by

changes in muscle contractility and responses are independent of hand position and thumb movement. Hypothermia does impact EMG responses (but less than AMG or MMG), as does interference from surgical electrocautery. The response to ulnar nerve stimulation can be measured at the adductor pollicis, abductor digiti minimi and at the first dorsal intraosseous muscles. Several EMG devices are now commercially available. These require proprietary stimulating-recording strip use and placement, are easily applied, speedily calibrated and provide accurate 'close to gold standard readings.' Target recovery is acceptable at TOF ratios >0.9. Electromyography monitoring is the 'ideal quantitative monitor' in the evidence-based consensus opinion of an expert group.[4]

Other monitoring modalities

Kinemyography (KMG) measures the distortion (proportional to the force of contraction) of a piezoelectric sensor placed between the thumb and index finger, in response to ulnar nerve stimulation. It is subject to a large bias, its limits of agreement are wide, and like AMG, it is position-dependant though there is no associated reverse fade.

The TOF-Cuff (RGB Medical Devices, Madrid, Spain) uses a form of compressomyography, with stimulating and recording sensors integrated within a blood pressure cuff; it measures upper arm muscle response to neurostimulation of nerves of the brachial plexus. Onset and recovery do not correlate with responses at the ulnar nerve using AMG and EMG and appear to reflect more closely the resistant central muscles, including the larynx and diaphragm.

Monitoring site

Recent guidelines have identified the ideal site for neuromuscular block monitoring in routine clinical practice; the adductor pollicis muscle response to ulnar nerve stimulation is best suited to perioperative monitoring.[7,8] This most closely approximates the sensitive muscle groups needing longer times to recovery. Posterior tibial nerve stimulation may be used, but the time course for recovery of the flexor hallucis brevis muscle may differ by several minutes from recovery of the adductor pollicis muscle. The facial nerve should not be used for monitoring. The ASA practice guide strongly recommends against using the eye muscles for neuromuscular monitoring.[7] If the facial muscles are monitored, lower stimulating currents are necessary to reduce the risk of direct muscle stimulation. In addition, the relative resistance of some eye muscles to neuromuscular blocking drugs may falsely indicate presence of neuromuscular transmission, resulting in excessive dosing. There may be an assumption of adequate recovery when this is not the case, leading to premature awakening and tracheal extubation. There is a fivefold greater risk of residual neuromuscular block with facial nerve compared with ulnar nerve monitoring.[20] If the facial nerve is monitored during anaesthesia, the ulnar nerve response should always be measured at the end of surgery, before waking the patient and tracheal extubation.

Agents for reversal of neuromuscular block

Neostigmine

Neostigmine is an anticholinesterase drug requiring coadministration of glycopyrrolate or atropine to counter its muscarinic effects. Neostigmine is characterised by a ceiling effect, a variable (and slow) antagonistic action, and by requiring high levels of spontaneous recovery to guarantee safe (complete) antagonism.[7,8] Dosing (for both aminosteroidal and benzylisoquinolinium agents) is dependent on the level of block at the time of reversal and should be based on patient's actual body weight. For antagonism of minimal block (TOF ratio >0.40), the recommended neostigmine dose is 30 μg kg^{-1}, and maximal antagonism may be reached within 10 min (Fig. 3). In the presence of moderate (TOF count 1–3) or shallow (TOF ratio <0.4) block, neostigmine reversal time may be prolonged and must be accompanied by quantitative monitoring to demonstrate adequate recovery. The maximum dose of neostigmine is 50 μg kg^{-1} and a variable period (up to 20–30 min) may be required for reversal. Investigators have compared reversal with neostigmine at tactile reappearance of twitches 1–4, measuring time to achieve TOF ratio of 0.9 using MMG.[21] At fourth twitch reappearance the mean time was 10 min, but the range was 5–26 min. Patients receiving i.v. anaesthesia all achieved recovery by 10 min; in contrast with only 60% of patients receiving sevoflurane.[21] Reversal is equally effective and predictable with neostigmine or sugammadex when antagonists are given at advanced levels of spontaneous recovery (TOF ratio ≥0.4).[7,8] Both the ASA and the ESAIC guidelines recommend reversal with neostigmine only after achieving recovery levels as high as possible, ideally from minimal block levels (TOF ratio >0.4) but at a minimum, once TOF ratio has recovered to 0.2.[7,8] Quantitative monitoring is essential to provide certainty of adequate recovery before awakening and extubation.

An interesting observation and concern with the use of neostigmine is the risk of a depolarising type of block when neostigmine is given at high levels of recovery. This has been demonstrated in awake volunteers, with unpleasant sensations of weakness lasting 20–30 min. The impact of neostigmine reversal (40 μg kg^{-1}) compared with placebo for patients spontaneously recovered to TOF ratio >0.9 after 1×ED95 doses of rocuronium has been reported.[13] There was no effect on muscle strength; in fact, general muscle weakness in recovery was improved. This may reflect the fact that at TOF ratio 0.9, up to 75% of receptors at the neuromuscular junction may still be occupied by a non-depolarising neuromuscular blocking drug (Fig. 3). Using small doses of neostigmine will increase acetylcholine receptor occupancy; by contrast, the awake 'unparalysed' patient may experience a cholinergic-type weakness caused by unopposed acetylcholine receptor activity.

Sugammadex

Sugammadex is a selective aminosteroid-binding agent, allows dose-dependent reversal of rocuronium- and vecuronium-induced block, but does not antagonise isoquinolinium (atracurium, cisatracurium) neuromuscular blocking drugs. Its features are well described.[1] Sugammadex provides a faster reversal than neostigmine: 2 *vs* 12.9 min for moderate block, 2.9 *vs* 48 min for deep block. The manufacturer's recommended reversal doses are: 16 mg kg^{-1} when PTC=0 (rescue reversal), 4 mg kg^{-1} from deep block (PTC 1–2) and 2 mg kg^{-1} from moderate block (TOF count ≥2). Dose finding studies have examined sugammadex requirements for reversal from minimal block (TOF ratio >0.5)[22] and shallow block (TOF ratio 0.2).[23] The sugammadex dosage needed to achieve TOF ratio >0.9 within 5 min was, respectively, 0.22 mg kg^{-1} and 0.49 mg kg^{-1}. Despite providing speedier and more

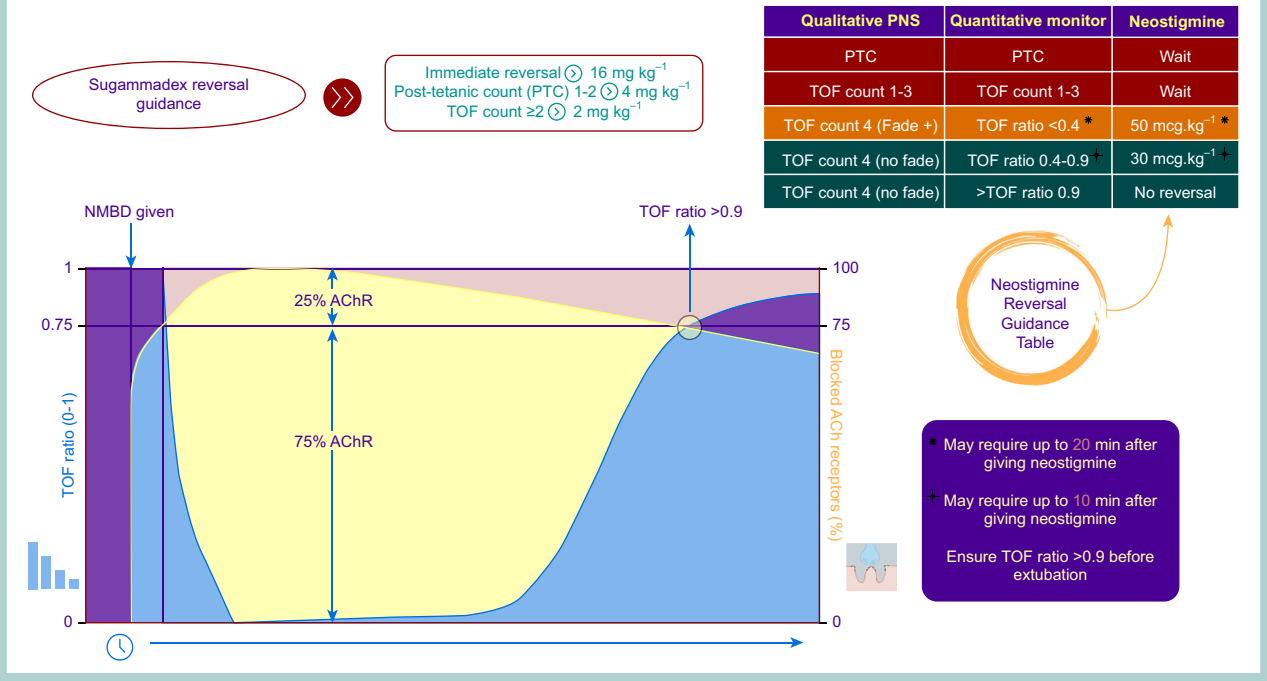

Fig 3 Acetylcholine receptor occupancy and train-of-four ratio. Reversal guidance for neostigmine and sugammadex. Blue, TOF ratio. Yellow, acetylcholine receptor occupancy. The graph demonstrates that up to 75% of acetylcholine receptors may remain occupied when the TOF ratio is 0.9, indicating a large margin of safety with respect to neuromuscular transmission. Adapted from Fink and colleagues. Anaesthetic Pharmacology: Basic Principles and Clinical Practice. Cambridge University Press 2011; 608–32. AChR, acetylcholine receptor; NMBD, neuromuscular blocking drug; PTC, post-tetanic count; TOF, train-of-four.

predictable responses, sugammadex administration in the absence of quantitative monitoring does not guarantee adequate recovery. An incidence of TOF ratio <0.9 of 4.3% (confidence interval 1.7–9.4%) has been reported when sugammadex dosing was based on 'clinical evaluation'.[24] Other investigators examined the incidence of postoperative pulmonary complications in older patients managed intraoperatively with peripheral nerve stimulation and found residual neuromuscular block rates of 10% with sugammadex use; indeed, a significant proportion (3.2%) had a TOF ratio <0.7.[25] Though the incidence of residual neuromuscular block with sugammadex compared with neostigmine is lower, reversal without quantitative monitoring guidance does not guarantee avoidance of residual neuromuscular block.

Adverse drug events with sugammadex and neostigmine

Data from serious adverse cardiac event reporting to the FDA showed an increase in reported cases of bradycardia and asystole after the introduction of sugammadex in 2015.[26] However, a large retrospective cohort study of 89,753 cases (18% received sugammadex; 82% neostigmine), found no clinically significant difference in major adverse effects (bradycardia, cardiac arrest, bronchospasm, anaphylaxis).[27] Volunteer studies reveal a high incidence of hypersensitivity responses, especially at larger doses. Japanese experience with widespread sugammadex use has resulted in concerns about the risks of anaphylaxis. An incidence of 1:5000 was reported with the combination 'rocuronium-sugammadex'.[28] There is concern about the risk of anaphylaxis with increasing use of sugammadex, particularly after patent expiry, with subsequent reductions in cost and more widespread use. Vigilance is required, given that the onset of these major complications occurs at the end of surgery, with challenges around awakening and extubation. Sugammadex dosing should be limited and based on quantitative monitoring, along with continued ECG monitoring after it is given because of its effects on heart rate. Sugammadex is not recommended for reversal of suspected rocuronium-induced anaphylaxis. There are reports of other complications including bronchospasm, laryngospasm, 'lightening of anaesthesia', and known drug interactions including progestogen capture, with an impact on those using progestogen-containing contraception.[1] These reinforce the fact that no drug is free of adverse effects and complications, and should be given only when required and in the correct dose.

Residual neuromuscular block and postoperative complications

The link between residual neuromuscular block and its impact on postoperative recovery is well established. Large cohort studies have shown that the use of neuromuscular blocking drugs is linked to harmful outcomes.[29] Quantitative monitoring reduces the incidence of residual neuromuscular block, hypoxic episodes, need for airway support, tracheal reintubation, and recovery room and hospital length of stay. There is also evidence for a reduction in postoperative pulmonary complications such as pneumonia, respiratory failure and unplanned re-intubation if residual neuromuscular block is avoided.[30] Initial data from the observational POPULAR

Clinical practice strategy

Incorporate NMB drugs into a clinical care plan and manage neuromuscular block based on quantitative monitoring throughout all phases of anaesthesia, to facilitate optimal airway management, decrease vocal cord injury, optimise surgical conditions, and eliminate residual neuromuscular block and its harmful consequences.

Pre-induction

Pre-list briefing allows discussion and planning: Surgical operating requirements, level of block, patient positioning, and access for monitoring

Induction

Use the ulnar nerve – adductor pollicis muscle combination
Activate & calibrate (if needed) the device with TOF stimulation at 12-20 s intervals, after induction but before giving NMBDs:
- Confirms monitor function.
- Confirms correct electrode positioning.
- Provides insight to inter-patient variation in onset time and depth of block.
- Allows dosing of NMBD and hypnotics / opioids to facilitate optimal timing and quality of airway management and intubation.

Helpful Tips

Clean and dry the skin before applying stimulating electrodes ***[negative (black) electrode distal]***

Maintenance

Helpful Tips

Hand not accessible
All monitors can be used at induction and recovery.
EMG-based monitor suitable for all phases.
AMG-based and facial nerve/muscles monitoring not reliable.
Before awakening and extubation,revert to ulnar nerve /adductor pollicis muscle unit.

Ongoing monitoring with PTC and TOF count depending on block depth, facilitates NMBD top up dosing (if required).

Top-up dosing should be given based on surgical requirement and measured responses and not by rote.

Moderate block (TOF count 1-3) is sufficient for most surgical procedures focusing on patient immobility and not muscle paralysis.

Laparoscopic / body cavity procedures may benefit from deeper levels of block(?).

Planning for reversal and recovery should take place based on duration of surgery, depth of block needed, and choice / availability of reversal agent.

Emergence and Extubation

Helpful Tips

A TOF ratio >0.9 (>0.95 when using AMG) must be achieved before awakening and extubation, by spontaneous recovery or by drug reversal.

Neostigmine reversal (Fig. 3)
At advanced spontaneous recovery of minimal block (TOF ratio >0.4), reversal is predictable and timely (within 10 min).

Shallow block (TOF count 4, TOF ratio <0.4) may be reversed provided sufficient dose given and time allowed.

Deeper block levels are not reliably reversed with neostigmine.

Sugammadex reversal (Fig. 3).

USING PNS? (Fig. 3)
Not recommended
TOF ratio cannot be determined.
Guaranteed recovery (TOF ratio >0.9) not possible.
Absence of fade ≠ ready for extubation.

Fig 4 Clinical practice strategy. A practical strategy with tips on effective planning and management of neuromuscular block. AMG, acceleromyography; EMG, electromyography; NMB, neuromuscular block; NMBD, neuromuscular blocking drugs; PNS, peripheral nerve stimulator; PTC, post-tetanic count; TOF, train-of-four.

study demonstrated that, as neuromuscular block is currently practiced, the use of neuromuscular blocking agents was associated with an increased incidence of postoperative pulmonary complications.[31] The authors were initially unable to associate the use of neuromuscular monitoring (using AMG or peripheral nerve stimulation) with a lowering of the risk of pulmonary complications.[31] However, reanalysis of their data showed that in patients who received quantitative AMG monitoring, the risk of postoperative pulmonary complications was reduced when a TOF ratio >0.95 was achieved before tracheal extubation. This suggests that when quantitative monitoring is used appropriately, a beneficial effect on postoperative pulmonary complications is present.[19]

Other beneficial effects of ensuring complete recovery before tracheal extubation include avoidance of postoperative muscle weakness. Adults who undergo intraoperative quantitative monitoring have significantly less overall weakness and rate their quality of recovery as superior to patients who are monitored subjectively.[32] Paediatric surgical patients also have been reported to experience residual neuromuscular block (28% incidence of TOF ratio <0.9), while severe residual block (TOF ratio <0.7) was reported in 6.5% of patients.[33] The feasibility and ease of intraoperative electromyographic monitoring in children has been reported.[34]

Antagonism of neuromuscular block and postoperative complications

Several large retrospective cohort studies have examined whether using sugammadex reduces the risk of postoperative pulmonary complications compared with neostigmine. The STRONGER study comparing 22,856 patients receiving sugammadex with a matched cohort receiving neostigmine, showed a 30% lower rate of composite pulmonary complications (3.5% *vs* 4.8%).[35] In contrast, other studies found no difference in the pulmonary complication rate, including observational cohort studies following the introduction of sugammadex.[36] Potential confounding factors that may explain the differences in outcome are that the definition of postoperative pulmonary complications varies between studies, and the application of quantitative neuromuscular monitoring has not been consistent. These retrospective studies were performed over a period when various safety measures were introduced: lung-protective ventilation, preoperative identification of high-risk patients and institution of early mobilisation and enhanced recovery programmes. Definitive prospective studies are unlikely to be performed given the large patient numbers that would be required. However, there is cumulated evidence for appropriate quantitative neuromuscular monitoring use and targeted antagonism, whatever the agent used, to avoid residual neuromuscular block and its harmful clinical impact.[19]

Clinical practice guide

A pragmatic approach to the management of neuromuscular block requires an understanding of the pharmacology and physiology reviewed, the use of a quantitative neuromuscular monitor whenever patients receive neuromuscular blocking drugs, an appreciation of the attributes of differing monitoring modalities, and a flexible individualised approach accounting for variable patient and surgical factors (Fig. 4, Figures 4 and 5 online videos). Communication and planning are necessary with the surgical team about access to and site for monitoring. An approach to neuromuscular block should target drug dosing, including top-up dosing requirements, based on objective monitoring, and not by rote or by the clock.

Conclusions

Residual neuromuscular block is widespread and often unmeasured and unseen. A strategy is required for managing neuromuscular block as part of a balanced anaesthesia technique, with neuromuscular block and its reversal underpinned by quantitative monitoring.[37] This strategy will depend on patient-related and surgical factors and on drug availability—for example, whether sugammadex is available. The implementation of such a strategy requires a willingness to change practice, to accept the evidence in the literature and the investment of time by individual practitioners. Change of current (inadequate) practice needs anaesthesia departmental champions and leadership.[4] Ongoing training, education, audit and quality initiatives are required. And although the recent national and international guidelines will be helpful in guiding future neuromuscular monitoring and management practice in the adult patient, similar guidelines are sorely missing in other patient groups at significant risk of postoperative complications: paediatric and ICU patients. The goal of elimination of residual neuromuscular block is achievable and will have major patient quality and safety benefits.

Declaration of interests

SJB has intellectual property assigned to Mayo Clinic (Rochester, MN); is a consultant for Merck & Co., Inc. (Kenilworth, NJ); is a principal, shareholder and Chief Medical Officer in Senzime AB (publ) (Uppsala, Sweden); and an unpaid member of the Scientific/Clinical Advisory Boards for The Doctors Company (Napa, CA, USA); Coala Life Inc. (Irvine, CA, USA); NMD Pharma (Aarhus, Denmark); and Takeda Pharmaceuticals (Cambridge, MA, USA). GR and PR declare that they have no conflicts of interest.

MCQs

The associated MCQs (to support CME/CPD activity) will be accessible at www.bjaed.org/cme/home by subscribers to *BJA Education*.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bjae.2023.10.005.

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