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Incidence and Risk Factors for Postoperative Residual Neuromuscular Blockade

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Abstract
Purpose of Review To define the incidence of residual neuromuscular blockade (rNMB) and identify patients at risk.
Recent Findings Incidence of rNMB continues to be high, and risk factors are complex and difficult to predict. Sequelae of rNMB, however, are significant.
Summary Despite literature describing the significance of rNMB on patient safety, the incidence continues to be high, and risk factors are difficult to predict. Patient, anesthetic, and surgical risk factors all contribute, and an understanding of the unique risks for each individual patient is required to properly prevent rNMB.

Keywords Paralysis · Neuromuscular blockade · Neostigmine · Residual paralysis · Postoperative residual curarization

Introduction

Neuromuscular blocking agents have been used to provide paralysis during anesthesia for more than half a century. Paralytics improve intubating conditions, reduce the risk of movement during operative procedures, and provide optimal surgical conditions, especially during procedures where even the slightest movement could prove catastrophic. As anesthesia providers, we must understand not only the pharmacokinetics and pharmacodynamics of these medications but also how they should optimally be used in the setting of an ever-expanding variety of surgical procedures and patient types.

In this article, we will review the literature outlining the incidence of residual neuromuscular blockade, briefly describe the adverse outcomes associated with residual blockade, and describe which patients are at increased risk.

Incidence

It is clear that residual neuromuscular blockade (rNMB) following extubation is inadvisable. Multiple investigators have studied the incidence using a variety of definitions (train of four, or TOF, ratios > 0.9 vs > 0.7) and measurements (using quantitative neuromuscular monitoring). Regardless of definition or technique, the incidence has consistently been found to be significant. During the late 1990s and 2000s, a variety of manuscripts described incidence as low as 16% and as high as 88% [1–3]. Despite a better understanding of the risks and improved description of the importance of monitoring over the past decade, the incidence continues to be high, with adult and pediatric, and national and international data continuing to demonstrate an incidence between 20 and 58% [4–7, 8••].

A recently published prospective, multicenter, observational trial found that the incidence of rNMB, as defined by a TOF ratio of < 0.9, was 64.7%, with 31% of studied subjects having a TOF ratio < 0.6. [9••]. While consistent with other studies, this finding was especially significant given the facts that all patients received neostigmine reversal and all were monitored with qualitative devices by the anesthesia providers (quantitative data was blinded to the provider). Furthermore, the providers were aware that they were participating in a study, and one would suspect that these providers were being more careful than normal in dosing and reversal of paralytics.

A variety of investigators have attempted to elucidate the impact of rNMB. While beyond the scope of this particular manuscript, rNMB has been shown to increase the incidence of postoperative respiratory complications, reduce quality of recovery, prolong length of stay in the postoperative care unit (PACU), and increase likelihood of ICU admission [8••, 10, 11].

This article is part of the Topical Collection on *Neuromuscular Blockade*

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Given the well-documented morbidities associated with rNMB, it is unclear why the incidence continues to be high (if not increasing). A variety of factors may be contributory:

Procedure Length With the advent of new surgical techniques, procedures have become shorter. Procedures lasting less than an hour are commonplace, and while many can be performed without paralysis, many do still require neuromuscular blockers. Following an intubating dose of rocuronium, cisatracurium, or vecuronium, recovery of first twitch can take 20–40 min [12, 13]. Reversal of these agents from one twitch with neostigmine can take up to 30 min itself (to achieve TOF ratio > 0.9) with some patients taking over an hour to reach this threshold [14], easily placing patients in a vulnerable situation during short case duration. Even under ideal circumstances (with a TOF count of 4), it can take 10–15 min to achieve a TOF ratio > 0.9. Furthermore, in these scenarios, production pressures may result in providers rushing patients to extubation and room exit before they are truly clinically ready.

Minimally Invasive Procedures Anesthetic teaching in the 1980s and 1990s frequently included the admonition to "reverse the paralytic when the surgeon is halfway done with the fascial closure." With the advent of minimally invasive (including robotic) procedures over the past two decades, paralysis is now needed for nearly the entirety of the surgical case, and closure frequently only takes minutes (especially with sutures being replaced with skin adhesives/glues). This allows for less time for reversal agents to achieve maximum efficacy and potentially a higher incidence of deep paralysis at the end of the case (that is, a lack of return of any spontaneous recovery).

Monitoring Accessibility In the not-so-distant past, most cases were done in the standard supine position, and anesthesia providers had access to the wrist for easy qualitative (or quantitative) monitoring. Again, with the advent of new techniques, this is frequently no longer possible. Arms are frequently tucked, tables are turned 180° from the anesthesia provider, or patients are prone/lateral, allowing no access to the ulnar nerve. Facial/tibial nerve monitoring yields different onset and recovery times compared with ulnar monitoring, and care must be taken when extrapolating this data to assessments of full recovery. Thilen, for instance, demonstrated that risk of rNMB was five times higher in patients monitored at the face vs wrist [15].

Total Intravenous Anesthetics Many providers choose to administer total intravenous anesthetics (TIVA) from time to time based on patient factors (e.g., high risk of nausea) or surgical factors (e.g., evoked potential monitoring). Volatile anesthetics are potent potentiators of neuromuscular blocking agents. Recovery times during TIVA can be markedly shorter than during volatile anesthetics, and dosing/reversal of paralytics can be confounded by these factors if not accounted for or measured with appropriate monitors [16].

Patient Variables Advanced age results in predictable hepatic, renal, and volume-of-distribution alterations in recovery from neuromuscular blocking agents. Variability in recovery profile increases as does potential duration of paralysis [12, 17]. This leads to unpredictability in dosing/reversal, again increasing the risk of rNMB. Weight also confounds dosing/reversal, with total body weight dosing leading to an overdose (with prolonged effect) and ideal body weight dosing leading to an underdose (with shortened effect) [13]. Finally, a number of unique studies have been published clouding the picture even further: Maidatsi demonstrated that the time to recovery following rocuronium administration in patients receiving desflurane was longer than in those receiving sevoflurane, and Dahaba demonstrated that American patients had longer recovery times than Chinese, who in turn had longer recovery times than Austrians [18, 19].

With this constellation of variables in mind, it is not surprising that dosing of paralytics and reversal timing can be complex and recovery can vary from case to case (or patient to patient). Regardless of the cause, the incidence of rNMB persists, as do the sequelae.

Risk Factors

Studies examining the incidence of rNMB have also yielded interesting results regarding risk factors. Saager and colleagues determined that male gender, higher BMI, and surgery at a community hospital were independent risks [9••]. Interestingly in the Canadian version of the same study, no differences were noted based on gender, age, BMI, type of surgery, or comorbidities [20]. Additional risks noted in the literature include short case duration (as described above), repeated doses of paralytic, and lack of reversal [21], as well as advanced patient age (> 70 years old) [22].

Rudolph and colleagues used a database of 2144 patients to determine which risk factors could be used in a scoring system to predict rNMB [23•]. Of these patients, 432 (20%) experienced rNMB. Risk factors most associated with rNMB in this cohort (further described in their manuscript as an rNMB prediction score) included hepatic failure, neurologic disease, total neostigmine dose, metastatic solid tumor surgery, and female sex. The difference in detected risks between studies is almost certainly a factor of patient and procedural heterogeneity as well as small sample size. The best lesson to be learned from this frequently conflicting literature is that the incidence is high and risk factors are complex and not entirely predictable.

Synthesizing the literature becomes more complex when investigating the impact of rNMB in patients with a variety of independent risk factors. Men, for instance, with sleep apnea who also had rNMB were found to have a high likelihood of depressed hypoxic ventilatory responsiveness [24], leading one to take extra care in reversal of paralysis in this subgroup.

Finally, it should be noted that it is clear that quantitative monitoring is superior to qualitative monitoring or subjective assessments of neuromuscular block. In a study comparing quantitative monitoring with no monitoring, incidence of rNMB was 1.6% vs 32% [7]. Exclusion of rNMB cannot predictably be performed with subjective or qualitative measures, with sensitivity of detection decreasing as TOF ratio rises above 0.4 [25]. Qualitative monitors, however, are frequently unavailable in many settings, adding yet another risk to patients developing rNMB.

Conclusions

It is clear that rNMB adversely impacts patient safety. It is also clear that the incidence continues to be high, and that risk factors are multifactorial. In an ideal setting, all patients would be young, thin, and healthy and would be monitored at the wrist with a quantitative device, while the surgical procedure would allow for early reversal of paralysis. Of course, this does not reflect reality, and we must remain cognizant of the complex risk factors that increase the risk for rNMB, and individualize our care depending on patient, anesthetic, and surgical risks.

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