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Editorial

Revisiting the Priming Principle for Neuromuscular Blockers: Usefulness for Rapid Sequence Inductions

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Post-operative residual neuromuscular blockade with non-depolarizing Neuromuscular Blocking Drugs (NMBD) has been an ongoing issue for decades [1,2]. The return to full neuromuscular function is even more critical for our patients with increasing acuity, co-morbidities and concomitant deconditioning that contraindicate the use of succinylcholine for Rapid Sequence Inductions (RSI) [3]. High-dose rocuronium (0.9 mg/kg or 1.2 mg/kg) [4] is often the first choice to secure an airway when succinylcholine cannot be used. However, the duration of paralysis may be problematic as described for the patient below.

The patient was a 50 year old female with an acute abdomen scheduled for an emergent exploratory laparotomy. Her history was pertinent for multiple intra-abdominal procedures including a Billroth II for a duodenal ulcer and arthritis that was treated with prednisone 5 mg daily. After an RSI with propofol and rocuronium (1.0 mg/kg), maintenance of anesthesia continued with oxygen/air/isoflurane. At the end of the surgery, 1.25 hours after induction, 1 weak twitch with Train-of-four (TOF) monitoring was present, and reversal of neuromuscular blockade was done with neostigmine/glycopyrrolate. After attaining four equal, strong, twitches, a respiratory rate of 14, tidal volumes of >500 ml, and the ability to follow commands, she was extubated and taken to the post operative care unit. Within a few minutes of arrival, she became tachypneic, had shallow respirations, and complained that she could not breathe. When the repeat TOF demonstrated significant fade and additional neostigmine/glycopyrrolate failed to improve her respiratory status, she was intubated. The patient regained four equal, strong, twitches 2.5 hours later, a total of 3.75 hours following the single dose of rocuronium.

A fundamental caveat of NMBD studies extrapolated to RSI is the variations in methodology. Most reports required the establishment of a quantitative baseline prior to the administration of a NMBD. The maintenance anesthesia was not standardized and the techniques used to assess the degree of neuromuscular blockade were varied. For example, the study that presented the efficacy of 0.9 mg/kg and 1.2 mg/kg rocuronium for intubation was not based on data for RSI. Rocuronium was given only after a steady-state anesthetic depth was maintained with incremental boluses of sodium thiopental prior to intubation attempts that were made at 90 seconds [4]. The depth of paralysis was assessed with TOF monitoring [4]. In a similar type of study, there were no differences found in the intubation conditions at 90 seconds when rocuronium was compared to divided-dose mivacurium (initial dose 0.15 mg/kg followed by a second dose of 0.1 mg/kg 30 seconds later [5]) monitored with mechanomyography after a steady state with propofol was achieved [6]. In the latter study, the spontaneous recovery of rocuronium was also varied and unpredictable.

The divided-dose using mivacurium is based upon the priming principle. In 1984, Foldes proposed that an initial "priming" dose of a NMBD could be administered to an awake patient in a sufficient amount to occupy a significant number of end plate receptors without resulting in significant neuromuscular blockade [7]. After induction of anesthesia, a second dose would rapidly optimize the occupancy of the remaining receptors and shorten the time to maximum blockade. This principle also reduces the dose-dependent side effects of a NMB, e.g. histamine release with mivacurium [5]. Using vecuronium, a priming dose of 0.05 mg/kg followed by an intubating dose of 0.05 mg/kg provided excellent intubation conditions at 61 ± 3 seconds [8]. Similar findings were found for atracurium [9], pancuronium [9] and cisatracurium [10]. In virtually all of these studies, however, the intubation dose was given 3-6 minutes after the first dose and established maintenance of anesthesia.

The organ-independent elimination of atracurium, cisatracurium and mivacurium is a major advantage for patients with multiple medical issues. In my hands, an RSI using a 0.05 mg/kg cisatracurium priming dose followed by an intubation dose of 0.1 mg/kg after induction with propofol provides excellent intubation conditions within 60 sec after administration. When mivacurium was available in the United States, for short procedures with contraindications to succinylcholine, I routinely performed RSI using an initial dose of 0.15 mg/kg mivacurium immediately before the administration of propofol that was followed by 0.1 mg/kg mivacurium without any delay. The time course of this RSI was virtually identical to what is used for divided dose mivacurium [5] with intubation conditions enhanced by a sufficient depth of anesthesia.

Sugammadex, a selective relaxant binding drug, is efficacious for the reversal of a dense neuromuscular blockade with rocuronium and other steroidal NMBD [11]. It is not available in the United States. If this drug does gain approval from the Food and Drug Administration, in the era of cost consciousness it is likely that many anesthesia practices will not advocate the addition of sugammadex to the formulary. A recent study demonstrated a marked increase in the cost of NMBD and reversal drugs (Australian $42 to $127 per case) with no differences in anesthesia time, operating time or time spent in the post anesthesia care unit [12].

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High-dose rocuronium for the RSI of patients for procedures of modest duration that do not require post operative mechanical ventilation is not often practical. Divided-dose administration of a non-depolarizing NMBD based on the priming principle should be considered as a viable alternative to rocuronium.

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