

Study Title: Best Practice With Rocuronium, Neostigmine, Sugammadex, and Subjective Monitoring

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## Protocol

The protocol recommended tactile assessments of the adductor pollicis TOF count, if feasible, and intraoperative muscle relaxation according to surgical requirement.

All rocuronium doses were calculated using ideal body weight (IBW). Previous studies indicate that NMBDs are more appropriately dosed based on IBW than on

actual body weight,<sup>12</sup> and high BMI has been identified as a risk factor for PRNB.<sup>13</sup> IBW was calculated by using the Devine formula as  $50.0 + 0.9 \text{ kg cm}^{-1}$  over 152 cm for males and  $45.5 + 0.9 \text{ kg cm}^{-1}$  over 152 cm for females, with intubation dose calculated as  $0.6 \text{ mg kg}^{-1}$  (IBW).

Doses for women were reduced by 15%, as the ED<sub>95</sub> is lower for females, leading to prolonged effects if given the same dose of rocuronium as males.<sup>14,15</sup> We calculated an additional 1% dose reduction per year over 55 of age because of previous studies indicating a prolonged effect in older patients,<sup>15</sup> with age being a known risk factor for PRNB.<sup>16</sup> The protocol recommended avoiding deep block (complete absence of the TOF response) because there is conflicting evidence that deep block is of benefit.<sup>17</sup> If there was a continued need for muscle relaxation, maintenance doses were recommended when the TOF count reached 3; each maintenance dose was calculated as 25% of the intubation dose rounded up to the next higher 5 mg, except during the last hour of the case when it was rounded down to the next lower 5 mg. At the end of the procedure, a tactile pre-reversal assessment of the thumb response to ulnar nerve stimulation was mandatory. If facial nerve stimulation and evaluation of eye-muscle twitches had been used intraoperatively, a change of monitoring site to ulnar nerve stimulation was conducted at the end of the procedure<sup>18</sup> to mitigate against eye-muscle monitoring as a significant risk factor for PRNB. <sup>13</sup> Reversal dose of neostigmine was calculated using ideal body weight (IBW) while the sugammadex dose was based on actual body weight. The protocol calls for a minimum of 10 minutes after neostigmine administration and minimum 3 minutes after sugammadex administration before tracheal extubation (Table 1).

Providers were trained regarding the implementation of the new protocol and instructed to follow the practice suggestions. The research staff assisted the providers with protocol reminders and dose calculations.

## Study procedures

We had originally planned to use either acceleromyography (Stimpod 450, Xavant, Pretoria, South Africa) or electromyography for research measurements in this study. After trying electromyographic measurements for four patients in this study we observed that the new electromyographic monitors at our institutions had inconsistent performance. We therefore decided to exclusively use a Stimpod 450 acceleromyograph for all patients. This is a tri-axial acceleromyograph, and subsequently all measurements were obtained in the same manner for all patients. All measurements were normalized, as this is recommended when using acceleromyography.<sup>19</sup> Two ECG surface electrodes were placed over the ulnar nerve at the wrist, with the positive electrode 3-4 cm proximal to the negative electrode. Immediately after induction of general anesthesia, and before any muscle relaxant had been administered, research staff obtained baseline TOFR measurements. The baseline and all other quantitative TOFR measurements were obtained by averaging two measurements separated by at least 15 s. If the initial two measurements were not within 10% agreement, additional measurements (up to four total) separated by at least 15 s were made and the two closest TOF ratios averaged. Anesthesia providers were blinded to all quantitative measurements. After baseline measurements, the research staff disconnected the Stimpod 450, but left the surface electrodes in place to be used for subsequent study measurements. Additional measurements were obtained in duplicate immediately before reversal when the anesthesia provider made the tactile pre-reversal assessment, immediately before tracheal extubation, and a final set of measurements were obtained within 5 min of arrival to the post anesthesia care unit (PACU).

Baseline measurements were used to normalize all subsequent measurements. This was done to correct for the inflated TOFR values that are usually obtained by acceleromyography.<sup>20,21</sup> As an example, if the baseline TOFR is 1.15 and the raw postoperative TOFR is 0.95, then the nTOFR is  $0.95/1.15 = 0.83$ . Normalization usually yields lower TOF ratios, and it is more likely to classify observations as positive for PRNB. Therefore, the incidence of PRNB is typically higher when comparing normalized to non-normalized (also referred to as “raw”) measurements. PRNB was defined as a nTOFR <0.9 on arrival to the PACU.