Examining the Concept of Rescue Reversal by Sugammadex

Background: An unanticipated difficult airway during induction of anesthesia can be a vexing problem. In the setting of can't intubate, can't ventilate (CICV), rapid recovery of spontaneous ventilation is a reasonable goal. The urgency of restoring ventilation is a function of how quickly a patient's hemoglobin oxygen saturation falls *versus* how much time is required for the effects of induction drugs to dissipate, namely the duration of unresponsiveness, ventilatory depression, and neuromuscular blockade. It has been suggested that prompt reversal of rocuronium-induced neuromuscular blockade with sugammadex will allow respiratory activity to recover prior to significant arterial desaturation. Using pharmacologic simulation, we compared the duration of unresponsiveness, ventilatory depression, and neuromuscular blockade in normal, obese, and morbidly obese body sizes in this life threatening CICV scenario. We hypothesized that although neuromuscular function could be rapidly restored with sugammadex, significant arterial desaturation will occur prior to the recovery from unresponsiveness and/or central ventilatory depression in obese and morbidly obese body sizes.

Methods: We used published models to simulate the duration of unresponsiveness and ventilatory depression using common induction techniques with predicted rates of oxygen desaturation in various size patients and explored to what degree rapid reversal of rocuronium-induced neuromuscular blockade with sugammadex might improve the return of spontaneous ventilation in CICV situations.

Results: Our simulations (Figure 1) showed that the duration of neuromuscular blockade was longer with 1.0 mg/kg succinylcholine than with 1.2 mg/kg rocuronium followed 3 minutes later by 16 mg/kg sugammadex (10.0 *versus* 4.5 minutes). Once rocuronium neuromuscular blockade was completely reversed with sugammadex, the duration of hemoglobin oxygen saturation above 90%, loss of responsiveness and intolerable ventilatory depression were dependent on the body habitus, duration of preoxygenation, and induction dosing regimen. There is a high probability of intolerable ventilatory depression that extends well beyond the time when oxygen saturation falls below 90%, especially in obese and morbidly obese patients. If ventilatory rescue is inadequate, oxygen desaturation will persist in later groups, despite full reversal of neuromuscular blockade. Depending on body habitus and the opioid dosed, the duration of intolerable ventilatory depression following sugammadex reversal may be as long as 15 min in 5% of individuals.

Conclusions: The clinical management of CICV should primarily focus on restoration of airway patency, oxygenation, and ventilation consistent with the American Society of Anesthesiologist's Practice guidelines for management of the difficult airway. Pharmacologic intervention cannot be relied upon to rescue patients in a CICV crisis.

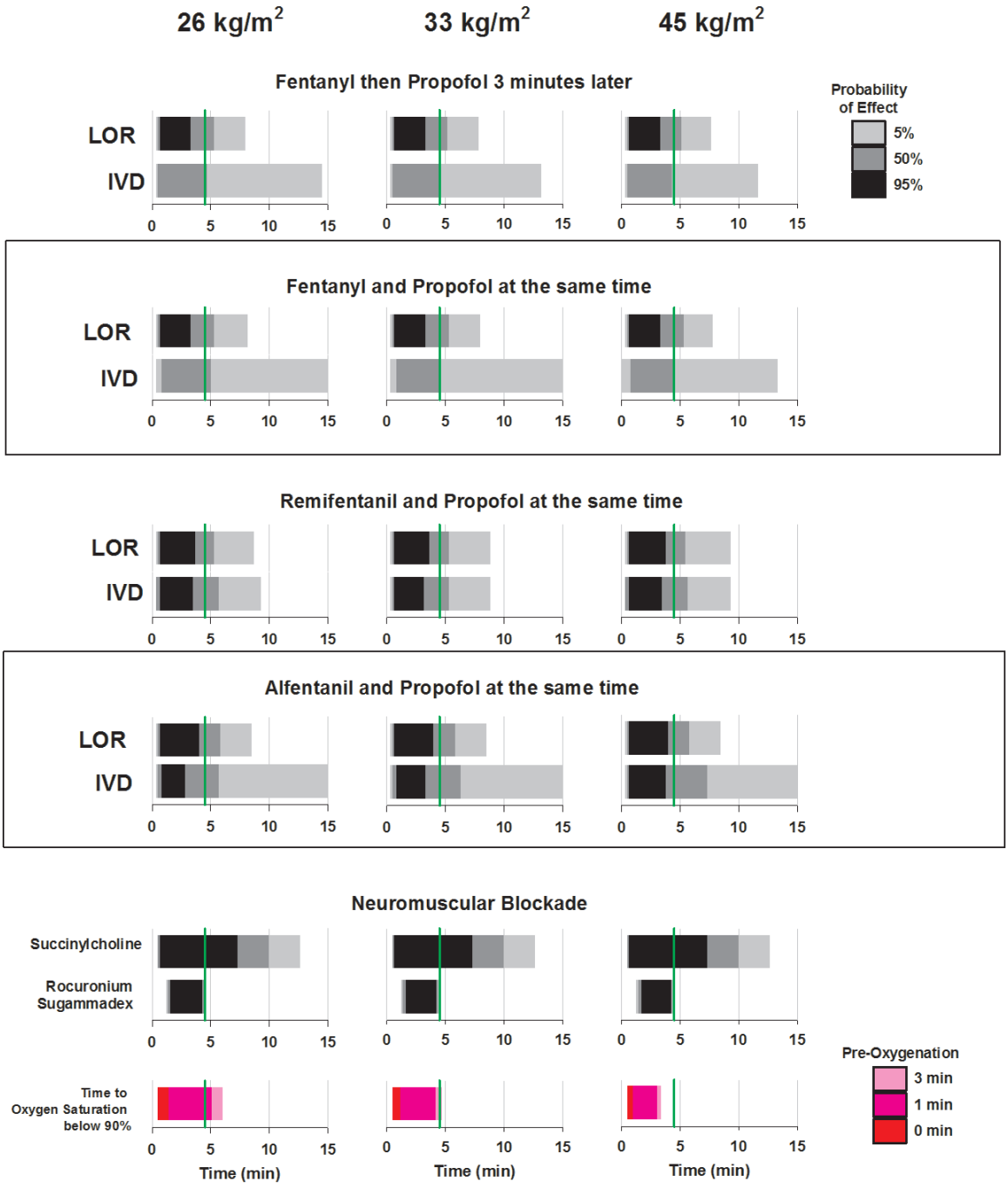

Figure 1. Predicted onset and duration of selected drug effects for various combinations of induction drug sequences administered to people of different sizes. Predicted effects include loss of responsiveness (LOR) defined as a loss of response to verbal and tactile stimuli, intolerable ventilatory depression (IVD) defined as a respiratory rate of 4 breaths or less per minute in an un-stimulated state, neuromuscular blockade is defined as percent of the first twitch depression (T1%) in patients who received succinylcholine or rocuronium/sugammadex paradigm, and duration of oxygen saturation above 90% in the presence of apnea. Induction drug sequences included (1) fentanyl followed 3 minutes later by propofol, (2) fentanyl simultaneously administered with propofol, (3) remifentanil simultaneously administered with propofol, and (4) alfentanil simultaneously administered with propofol followed by either succinylcholine or rocuronium. Rocuronium was reversed 3 minutes later with sugammadex. Doses of each drug are presented in Table 2.

Predictions for each induction sequence were performed for a normal (Body Mass Index, BMI = 26 kg/m^2), obese (BMI = 33 kg/m^2), and morbidly obese (BMI = 45 kg/m^2) individual. The duration of each effect is estimated as a probability greater than 5% (light grey), 50% (dark grey), and 95% (black). The time to oxygen saturation below 90% is presented as a function of the duration of preoxygenation prior to drug induced apnea. Red, dark pink, and light pink represent no preoxygenation, 1 minute of preoxygenation, and 3 minutes of preoxygenation with an FiO_2 of 1.0. The green vertical lines represent the time points at which neuromuscular blockade is completely reversed with sugammadex.