Response to Noxious Stimuli during Closed-loop Controlled Propofol Anesthesia at Different Remifentanil Effect Site Concentrations

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Introduction: Closed-loop controlled anesthesia continually adjusts drug infusion rates using depth of hypnosis feedback. This method has been shown to effectively control anesthetic drug administration during induction and maintenance of anesthesia [1]. We previously speculated [2] that a higher remifentanil effect site concentration [3] (Ce_{Remi}) at the time of intubation could mitigate the heart rate response to intubation better and reduce the consequent controller overshoot in depth of hypnosis (measured by the NeuroSENSE WAV_{CNS}). The purpose of this study is to evaluate the performance of our closed-loop propofol infusion system in providing adequate anesthesia to block responses to endotracheal intubation and skin incision stimuli, given different target controlled infusion effect site concentrations of remifentanil.

Methods: With research ethics board and Health Canada approval and written informed consent, fifty-five patients (22 female) participated in the study. Anesthesia was induced using closed-loop propofol (target WAV_{CNS} of 50) and target-controlled open-loop remifentanil infusion (Ce_{Remi} of 2-6 ng/ml at the anesthesiologists discretion). The patient's airway was instrumented at a time deemed clinically appropriate. Laryngoscopy was performed at a median (range) of 5.1 (2.8-11.5) min after commencement of induction. Rocuronium was used to facilitate intubation in 31 patients. Heart rate (HR), non-invasive systolic blood pressure (SYS), WAV_{CNS}, and times of intubation and skin incision were recorded. Data were split depending on Ce_{Remi} being more or less than 3.1 ng/ml at the time of each intervention. The Ce_{Remi} cutoff was based on a Ce_{Remi} of 3 ng/ml having a high probability for successful intubation [4] when given at a propofol effect site concentration (Ce_{Prop}) of 3 µg/ml, while allowing a little Ce_{Remi} target overshoot.

Results: The patients' median age (range) was 63 (32-82) years with a body mass index of 28 (18-43) kg/m^2. Median (range) of estimated Ce_{Prop} [5] and Ce_{Remi} [3] were 5.27 (2.62-8.31) µg/ml and 3.02 (2.00-6.09) ng/ml respectively at intubation and 2.51 (1.45-8.23) µg/ml and 3.93 (2.00-6.82) ng/ml respectively at the start of procedure. Figure 1 shows WAV_{CNS}, HR and SYS values measured one minute before the stimulus, at the time the stimulus was marked, and 5 minutes after the stimulus for all patients, split by Ce_{Remi}.

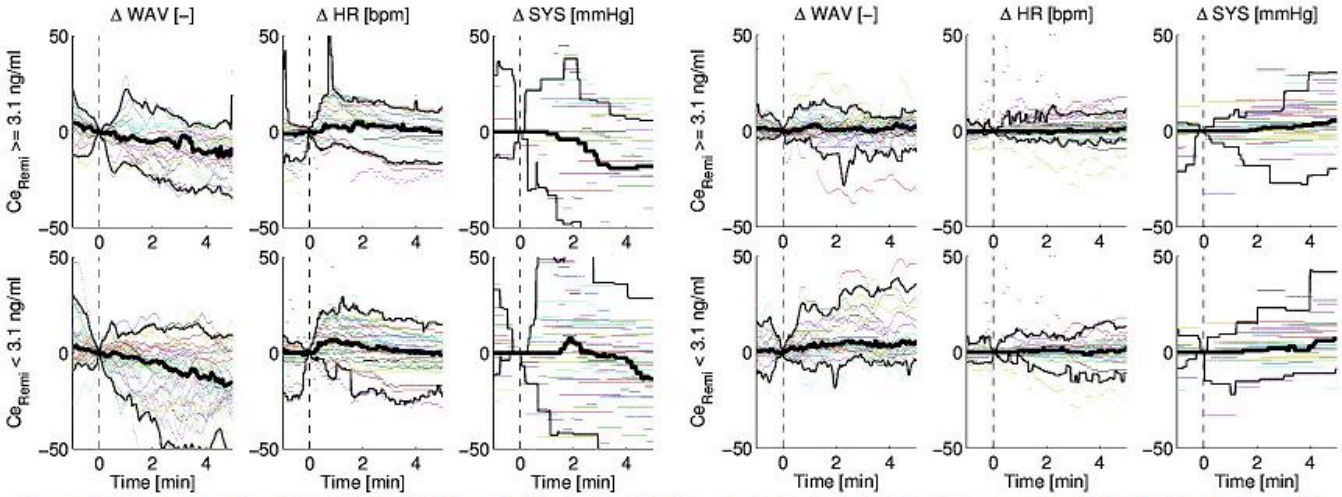

Figure 1: Response to intubation (left subplot) and skin incision (right subplot), split by CeRemi greater than 3.1 ng/ml (top row; n=19 for intubation, n=28 for skin incision) and lower than 3.1 ng/ml (bottom row; n=34 for intubation, n=23 for skin incision). Data are scaled to zero at the time of the stimulus in order to show absolute changes, with population percentile values (5%, 50%, and 95%) overlaid as black lines.

Discussion: As expected, an increased Ce_{Remi} reduces the HR and SYS response to intubation from a median increase of 7 bpm to 4 bpm, and 8 mmHg to -4 mmHg, respectively, and tightens the HR and WAV variability in response to skin incision. A higher Ce_{Remi} reduced the median controller WAV_{CNS} overshoot from 16 to 10 within the 5 min after intubation. While these results do not take the timing of intubation, and WAV_{CNS} at intubation into account, they suggest that a Ce_{Remi} >3.1 ng/ml is more successful in blunting the hemodynamic response to intubation, as we assume that depth of hypnosis is adequately controlled by closed loop propofol administration. Automated control of analgesia may perform better than target controlled infusion; this requires exploration in the near future.

References: [1] Anesth Analg. 2013;117(5):1130-38, [2] Proc 2013 ISAP Ann Mtg;2013; A22, [3] Anesthesiology. 1997;86(1):10-23, [4] Anesthesiology. 2004;100(6):1373-81, [5] Anesthesiology. 1998;88(5):1170-82