REMIFENTANIL-PROPOFOL EFFECT-SITE CONCENTRATIONS THAT LEAD TO AIRWAY OBSTRUCTION AND/OR INTOLERABLE VENTILATORY DEPRESSION: BUILDING A RESPONSE SURFACE MODEL FOR RESPIRATORY COMPROMISE

Cris LaPierre, BS; Ken Johnson, MD; Benjamin Randall, MD; Talmage Egan, MD
University of Utah, Salt Lake City, Utah

Summary: The study aim was to build a response surface model that accounted for both airway obstruction and/or intolerable ventilatory depression. Accounting for both of these effects expanded the propofol-remifentanil effect-site concentration pairs associated with unwanted airway and/or respiratory effects.

Introduction: Prior work has characterized a response surface model of propofol and remifentanil on intolerable ventilatory depression in volunteers with moderate to deep sedation. During this same study, we observed that volunteers would either stop breathing and/or develop airway obstruction. Intolerable ventilatory depression was associated with higher remifentanil effect-site concentrations while airway obstruction was associated with higher propofol effect-site concentrations.

The aim of this study was to build a propofol-remifentanil response surface that accounted for both airway obstruction and/or intolerable ventilatory depression. We have termed this combined effect "respiratory compromise". It was hypothesized that accounting for airway obstruction in addition to intolerable ventilatory depression would expand the propofol-remifentanil effect-site concentrations associated with unwanted airway or respiratory effects.

Methods: After IRB approval, twenty-four volunteers were given target controlled infusions of propofol and remifentanil with increasing effect site concentrations administered in a stepwise fashion. At each target concentration, an assessment of intolerable ventilatory depression and airway obstruction was made. Intolerable ventilatory depression was defined as respiratory rate ≤ 4 breaths in a 1-minute time window. Airway obstruction was defined as average inspired tidal volume < 3 ml/kg AND respiratory rate > 4 breaths in a 25 second window OR absence of airway flow in the presence of a respiratory effort.

Results: Observations of respiratory compromise are presented in figure 1. Open circles indicate the number of assessments made at each concentration pair. Filled circles represent the number of volunteers in which respiratory compromise was present. Fill color indicates whether respiratory compromise was due to airway obstruction (black), intolerable ventilatory depression (red) or both (dark red).

Respiratory compromise was observed in 193 of 381 assessments and at 55 of the 61 concentration pairs tested. At 41 of these, at least 50% of the volunteers evaluated experienced respiratory compromise. Of the 193 assessments, 57 subjects experienced airway obstruction only, 130 experienced intolerable ventilatory depression only, and six experienced both.

Respiratory compromise due to airway obstruction was observed principally at propofol effect-site concentrations > 1.5 mcg/ml and remifentanil effect-site concentrations < 2 ng/ml. Respiratory compromise due to intolerable ventilatory depression was observed principally at remifentanil effect-site concentrations ≥ 3 ng/ml.

Discussion: Our analysis confirmed our study hypothesis. Accounting for airway obstruction in addition to intolerable ventilatory depression expanded the propofol-remifentanil effect-site concentration pairs associated with unwanted airway and/or respiratory effects.