

A QUALITATIVE AND QUANTITATIVE ANALYSIS OF REMIFENTANIL-PROPOFOL PHARMACODYNAMIC INTERACTION WITH RESPONSE SURFACE MODEL

Lu Yang, MD, Bin Wei, MD, LiPing Zhang, MD, Min Li, MD, XiangYang Guo, MD, Peking University Third Hospital, Beijing, CHINA

Background: Response surface model (RSM) is a new method to study the pharmacodynamic interactions among anesthetics. The objective of the study was to apply RSM to characterize the interactions between remifentanyl and propofol.

Methods: The study was an open-label, randomized, prospective study using parallel slices design. 70 patients with ASA I or II, aged 18-65 yr, received target-controlled infusion of remifentanyl (0-10ng/ml) and propofol (0-9 μ g/ml) at various target concentration pairs. After reaching pseudo-steady state drug levels, the response to laryngoscopy and cardiovascular side effects were observed for each target concentration pair. The pharmacodynamic interactions were analyzed by RSM. The response surfaces of laryngoscopy and cardiovascular side effects were combined to identify target concentration range of remifentanyl and propofol that provided a high probability of nonresponsiveness to laryngoscopy and a low probability of cardiovascular side effects.

Results: Figure A and Figure B showed the relations between remifentanyl-propofol concentration and the interaction index (I(Q)) for response to laryngoscopy and cardiovascular side effects, respectively. I(Q) described the pharmacodynamic interactions qualitatively and quantitatively, which indicated strongly synergy between remifentanyl and propofol ($P < 0.001$). The dark area in Figure C showed the optimal combinations that blunt laryngoscopy without cardiovascular side effects.

Conclusion: RSM can analyze the pharmacodynamic interactions qualitatively and quantitatively. RSM reveals the tremendous synergy between remifentanyl (0-10ng/ml) and propofol(0-9 μ g/ml) in blunting responses to laryngoscopy and cardiovascular side effects.

