The Value of Real Time Pharmacokinetic and Pharmacodynamic Modeling in Clinical Care

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A real-time pharmacologic display showing the drug administration history, predicted drug levels, drug interactions, and drug effects could enhance the safety of anesthesia. In the intensive care unit, sedatives and analgesics could be managed more effectively to control agitation and pain.

We have developed a drug display which helps the clinician visualize the pharmacology of the drugs given to the patient. Pharmacokinetic models predict past, present, and future drug concentrations and pharmacodynamic models estimate drug effects on the patient's state of sedation, analgesia, and neuromuscular blockade. The models translated drug doses into drug concentrations and drug effects.

We studied 24 patients who received propofol, remifentanil, and fentanyl during abdominal laparoscopic surgery. We recorded times for loss of responsiveness, tracheal intubation, skin incision, and return of consciousness. We used the pharmacokinetic models to calculate the opioid and propofol effect site concentrations at the time each event occurred. At the end of the case, our sedation response surface model quite accurately predicted return of responsiveness. The tetanic and algometry models also adequately predict the responses observed in the operating room.

A second study was conducted in a high-fidelity anesthesia simulator with 24 anesthesiologists. One-half of the subjects used the drug display. Subjects induced anesthesia, intubated the patient's trachea, cared for the simulated patient throughout a simulated shoulder surgery, and then awoke and extubated the patient following skin closure. Subjects who used the display managed drug delivery more effectively by keeping heart rate and blood pressure closer to normal, reducing the rise in heart rate and blood pressure associated with painful surgical manipulations and the fall in heart rate and blood pressure associated with drug overdose. The simulated patients woke-up faster (4.5±3.3 versus 7.5±2.1 minutes) without hemodynamic complications. Participants who used the display reported a decrease in mental demand, effort, and frustration, and an increase in perceived performance.

Pharmacologic modeling has been successfully incorporated into a display that supports drug management in the operating room. Preliminary clinical studies indicate that the models adequately predict the clinical effects of intravenous anesthetics. A real time presentation of drug pharmacology can result in better patient outcome.