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Pharmacokinetics and pharmacodynamics of propofol in patients undergoing abdominal aortic surgery

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Abstract:
Available propofol pharmacokinetic protocols for target-controlled infusion (TCI) were obtained from healthy individuals. However, the disposition as well as the response to a given drug may be altered in clinical conditions. The aim of the study was to examine population pharmacokinetics (PK) and pharmacodynamics (PD) of propofol during total intravenous anesthesia (propofol/fentanyl) monitored by bispectral index (BIS) in patients scheduled for abdominal aortic surgery. Population nonlinear mixed-effect modeling was done with Nonmem. Data were obtained from ten male patients. The TCI system (Diprifusor) was used to administer propofol. The BIS index served to monitor the depth of anesthesia. The propofol dosing was adjusted to keep BIS level between 40 and 60. A two-compartment model was used to describe propofol PK. The typical values of the central and peripheral volume of distribution, and the metabolic and inter-compartmental clearance were V_C = 24.7 l, V_T = 112 l, Cl = 2.64 l/min and Q = 0.989 l/min. Delay of the anesthetic effect, with respect to plasma concentrations, was described by the effect compartment with the rate constant for the distribution to the effector compartment equal to 0.240 min^{-1}. The BIS index was linked to the effect site concentrations through a sigmoidal E_{max} model with EC_{50} = 2.19 mg/l. The body weight, age, blood pressure and gender were not identified as statistically significant covariates for all PK/PD parameters. The population PK/PD model was successfully developed to describe the time course and variability of propofol concentration and BIS index in patients undergoing surgery.

Key words:
propofol, aortic surgery, pharmacokinetics and pharmacodynamics