

Interactive Web Simulation For Propofol and Fospropofol, A New Propofol Pro-drug



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INTRODUCTION

- Using published pharmacokinetic and pharmacodynamic data^{1,2} we have developed interactive on-line simulations to model administration of propofol and fospropofol, a new water-soluble prodrug formulation of propofol.^{3,4}
- We believe such interactive models may provide a realistic and real time method to learn about a new drug and experiment with different administration regimes and targets.

MATERIALS & METHODS

- Based on a review of the literature, propofol is modeled using a three-compartment model with peripheral, central, and slow compartments.^{1,5}
- The conversion of the fospropofol prodrug introduces two additional compartments leading to a five-compartment model.¹
- The on-line simulation displays drug concentration (Y-axis) plotted against time (X-axis).
- The drug concentration range is further demarcated by user-adjustable levels of return of consciousness (ROC) and loss of consciousness (LOC), default settings from the literature of 1.3 and 2.1 mcg/ml respectively.⁶

RESULTS

- Our computer simulations were validated by comparing plots of propofol concentration in the central compartment following infusion of 290, 580, and 1160 mg of fospropofol over ten minutes to graphs generated from administration of the same doses in the same fashion to test subjects (Figure 1).¹
- The simulation models allow users to adjust the following variables: patient weight, infusion rate, infusion duration, initial and second bolus dose, timing of second bolus, and to choose between two models (Fechner or Gepts).
- Drug concentrations in any of the five compartments can be visualized (Figure 2).

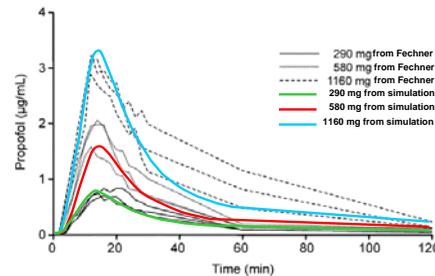


Figure 1: Comparison of the simulation-generated and actual measured propofol concentrations after administration of 290, 580, and 1160 mg fospropofol. Figure adapted from Fechner, et al. Pharmacokinetics and clinical pharmacodynamics of the new propofol prodrug GPI 15715 in volunteers. *Anesthesiology*. 2003 99(2):303-13.

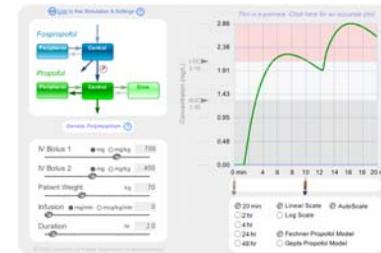


Figure 2: Sample screen shot for simulation of fospropofol administration.

DISCUSSION

- We believe such interactive models may provide a realistic and real time method to learn about a new drug and experiment with different administration regimes and targets.
- The on-line presence of the simulations allow incorporation into wikis, providing a venue to describe and discuss clinical and modeling issues.⁷
- The simulations for propofol and fospropofol are available at <http://vam.anest.ufl.edu/simulations/simulationportfolio.php>.^{3,4}

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