Crowdsourcing Pharmacokinetics

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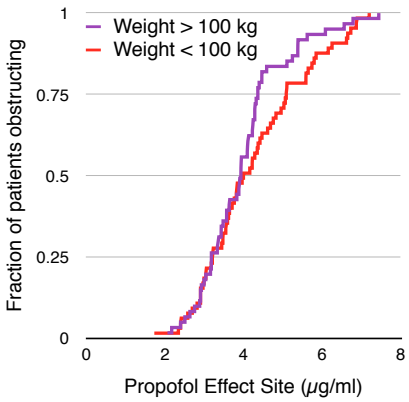
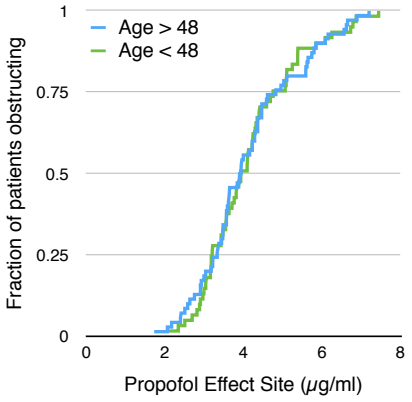
We have demonstrated that by incorporating the observation of a transition to a clinical endpoint into a control loop, the error in maintaining this clinical endpoint is reduced in comparison to targeting an effect site estimate associated with the 50% probability of achieving the endpoint.[1] A limitation of this method is the propriety of the PKPD models, which are derived from small number of volunteers in a research setting using infusion sequences and clinical endpoints different from those in clinical care. We describe an approach to generating and using data from large groups of patients undergoing clinical care to refine PKPD models.



Data from 120 patients undergoing drug induced sleep endoscopy was utilized in this effort.[2] Propofol was administered using infusion sequences designed to produce a monotonic increase that would be similar for patients across a range of ages and weights. Effect site concentrations at the time of airway collapse were estimated,[3] and the cumulative probability of airway collapse was determined for patients above and below the median age (48) and above and below the median weight (100 kg), as depicted in the figures. Parameters of the PK model were adjusted by numerical methods to minimize the difference between each subgroup probability distribution and the distribution for the entire cohort. Given significantly larger cohorts, models tuned to finer gradations of age and weight could be obtained. A web-based system will be demonstrated that provides a dosing schedule for DISE for a given age and weight and record the time of airway collapse. The system can be used by any clinician with a syringe pump and an internet connection.



References

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