

Inter-individual variability in propofol pharmacokinetic/pharmacodynamic (PK/PD) model – a sensitivity analysis

ABSTRACT

Inter-individual variability is a major challenge to guarantee adequate anaesthesia in patients across the population. This variability can occur as a result of patient physiology (e.g. age and weight), variations in the pharmacokinetic (PK) process and differences in the pharmacodynamic (PD) function. For a safe and effective drug administration, it is important to recognise which and when these factors of variability cause a higher uncertainty on depth of anaesthesia. This study aimed to quantify the influence of these input factors on the uncertainty in Bispectral Index (BIS). In this study, Sobol' variance-based sensitivity analysis was performed on Schnider PK/PD model. Nine factors were evaluated: age, body weight, height, V1, V3, Cl1, Cl3, Ce50, and γ . The importance of these factors were ranked according to their total sensitivity indices. It was found that Ce50 has the most determining role on BIS prediction. γ is a significant factor during the induction phase. The PD model alone was found to responsible for 70% to 90% of BIS uncertainty during the maintenance phase. The variability of height has negligible influence on BIS prediction and can be omitted from the PK/PD model.

Keyword: Depth of anaesthesia; Pharmacokinetic-pharmacodynamic model; Inter-patient variability; Variance based sensitivity analysis