Pharmacokinetics of Propofol in Severely Obese Surgical Patients

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Background/Introduction: Existing PK models of propofol include sparse data from very obese patients. The aim of this study was to develop a PK model based on standardized surgical patients spanning from normal weight to a high number of very obese patients.

Methods: Adult patients scheduled for laparoscopic cholecystectomy or bariatric surgery were studied. Anaesthesia was induced with propofol 2 mg/kg adjusted body weight over 2 minutes followed by 6 mg/kg/hr adjusted body weight over 30 minutes. For the remainder of the operation anaesthesia was maintained with sevoflurane. Remifentanil was dosed according to clinical need. 8 arterial samples were drawn in a randomized block sampling regimen over a span of 24 hours. Time-concentration data were analysed by population PK modelling using non-linear mixed-effects modelling.

Results: 474 serum propofol concentrations were collected from 69 patients aged 19-60 years with a BMI 18.5-67.3 kg/m2. Twenty-one patients had a BMI above 50 kg/m2. A 3-compartment PK model was produced wherein three different body weight descriptors (Lean Body Weight; Predicted Normal Weight; Total Body Weight) and sex were included as covariates in the final model. The allometric exponent of 0.75 improved the objective function of all clearances and was added to the model. Accuracy and precision were 1.4% and 21.7% respectively in post-hoc performance evaluation,

Conclusions: We have made a new PK model of propofol for adult normal weight to severely obese patients based on a high number of very obese patients. The new model should be tested in this patient population and compared with present models.

Table 1. Patients´ characteristics. Values are mean, SD (range) (n=69)

Age (years)	40.4 SD 10 (19–60)
Sex (Male/female) (n)	30/39
Weight (kg)	131.5 SD 40.6 (55–241)

Height (cm)	173.3 SD 10.1 (152–195)
BMI (kg/m^2)	43.4 SD 11.7 (21.6–67.3)
Bolus dose propofol (mg)	197 SD 46 (106–323)
Total dose propofol (mg)	475 SD 105 (266–774)

Table 2. Parameter estimates for the final pharmacokinetic model

Theta	Parameter	Typical Value	CV%	Bootstrap mean	Bootstrap 95% CI		Jackknife mean values	Likelihood Profiling 95% CI	
1	CL L/min	1.964*(WGT/129) **0.75	16.6	1.961	1.868	2.071	1.964	1.874	2.061
2	V1 L (M)	3.863*(LBW/65.1) **1	49.7	3.970	2.968	5.191	3.882	2.926	5.297
3	Q2 L/min	1.230*(LBW/65.1) **0.75)	28.2	1.222	1.068	1.381	1.228	1.098	1.376
4	V2 L	65.585*(LBW/65.1)	23.1	66.279	58.330	73.976	65.765	59.299	73.802
5	Q3 L/min	0.611*(WGT/129) **0.75	16.4	0.615	0.561	0.672	0.611	0.565	0.659
6	V3 L	305.111*(PNWT/78.5)+THETA(8)	.-	302.891	3.454	526.531	304.150	56.208	531.702
7	V1 L (F)	6.200*(LBW/65.1) **1	49.7	6.682	4.103	10.267	6.244	4.633	9.239
8	+ V3 L	404.821	.-	429.069	247.470	739.005	408.329		
Intraindividual error %									
Sigma	0.0402291	20.1							