Title: PROPOFOL PHARMACOKINETICS IN MORBIDLY OBESE PATIENTS

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Introduction. Propofol is a new intravenous agent whose main interest is a rapid and uneventful recovery in most patients. It is a highly lipophilic drug with a high total body clearance and important distribution volumes.[1-2] This study was designed to investigate the pharmacokinetics of propofol administered as a continuous infusion for induction and maintenance of anesthesia in morbidly obese patients.

Methods. Eight patients whose weight was over 50 per cent above maximum of desirable range (ASA 2, 3) and 10 control patients (ASA 1, 2) requiring general anesthesia for a minimum period of 2 hrs were included in the study. Propofol was administered as a continuous infusion to induce and maintain anesthesia according to the following scheme: 21 $mg.kg^{-1}.h^{-1}$ during the first 5 min, 12 $mg.kg^{-1}.h^{-1}$ during the next 10 min and 6 $mg.kg^{-1}.h^{-1}$ during the rest of the procedure. The body weight considered to calculate infusion rates was the real one in control patients and ideal weight +0.4 excess weight in obese patients. Muscle relaxants, N_2O and small doses of fentanyl were administered as required on clinical grounds. Arterial blood samples were collected at regular intervals of time during the infusion (about 25 samples) and during 24 hrs following the infusion discontinuation (24 samples). Blood propofol concentration was also measured when patients opened their eyes on verbal command. Blood propofol concentrations were determined with a HPLC method. The following pharmacokinetic parameters were derived: total clearance (CLE), mean resident time (mrt), elimination half life (T 1/2 E) and distribution volume at steady state (Vdss). Statistical analysis included student t test for comparison of measured parameters and Wilcoxon rank sum test for comparison of derived parameters.

Results. Anthropometric and pharmacokinetic parameters are summarized in the table. Mean resident time and elimination half life were not different in control and obese patients. Total body clearance appeared correlated to Vdss. Mean blood propofol concentration when patients opened their eyes was similar in both groups, about 1 $mg.l^{-1}$ (figure).

Discussion. Our study shows that Vdss and ClE were greater in obese patients than in the control ones. Consequently, T 1/2 E was not different between the two groups. The correlation between ClE and Vdss was unexpected, since Vdss is independant from the metabolic processes of elimination.[3] This finding might be explained by the fact that some storage of propofol in deep compartments was combined with metabolic elimination in the assessment of ClE. This fact was already hinted at in other studies[2] when the rate constant K_{3-1} was found to be much slower than K_{1-3}, meaning that propofol was distributed faster than it returned from the deep compartments.

Table

	Normal patients n = 10	Obese patients n = 8	
age(yrs)	42 ± 12	47 ± 16	NS
weight(kg)	66 ± 15	116 ± 21	≤0,001
infusion time(min)	195 ± 58	152 ± 55	NS
albumin (g/l)	38,0±4,3	40,0±3,7	NS
creat(umol/l)	74 ± 18	88 ± 19	NS
propofol conc. when opening eyes(ng/ml)	1166 ± 388	943 ± 262	NS
Cl E(l/min)	1,761 ± 0,343	2,831 ± 1,130	≤0,01
m.r.t.(min)	182 ± 44	167 ± 43	NS
T 1/2 E (min)	216 ± 49	315 ± 43	NS
Vdss (l.)	153 ± 53	399 ± 206	≤0,01

mean ± SD

References

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