Propofol inhibis renal cytochrome P450 activity and enflurane defluorination in vitro in hamsters

陳廷貴;戴裕庭;陳大樑

Chen TL;Chen TG;Tai YT;Chang HC;Chen RM;Lin CJ and Ueng TH.

摘要

Abstract

Purpose:To determine the effect of propofol on renal cytochrome P450 activity and deflurination of enflurane. Methods: Renal microsomes were prepared by homogenization and differential centrifugation from pooled hamster kidneys. Defluorination of enflurane was assessed by measuring free fluoride metabolites after reacting enflurane with renal microsomes incubated with various concentrations, 0.05-1.0 mmol/L propofol in the NADPH-generating system. Drug metabolizing activities of renal cytochrome P450 mono- oxygenase enzymes were evaluated within microsomes preincubated with propofol and reacted with the specific marker substrates, aniline, benzo(a)pyrene, erythromycin and pentoxyresorufin, for cytochrome P450 2E1 , 1A1, 3A4 and 2B1 , respectively. Results: Renal defluorination of enflurane was inhibited by clinical concentrations, 0.05 mmol/L of ppropofol (P<0.05). Dose-dependent inhibition of defluorination, aniline and benzo(a)pyrene hydroxylase within kidney microsomes was related to propofol concentration. Propofol demonstrated a profound inhibition of renal pentoxyresorufin dealkylase activity even at low concentrations, 0. 05 mmol/L (P<0.01). Propofol did not exhibit inhibition of erythromycin N- demethylation of kidney microsomes except at high concentration, 1.0 mmol/ L. Spectral analyses of key coenzymes of renal cytochrome P450 monooxygenase, cytochrome b5 and cytochrome c reductase, demonstrated an inhibition when incubated with high concentraions of propofol (P<0.05). Conclusion: In an in vitro study in an NADPH-generating system of hamster kidney microsomes, propofol, in clinical concentrations, exhibited a broad -spectrum of inhibition to renal monooxygenase activities and enflurane defluorination.