Effect of propofol on functional activities of hepatic and extrahepatic conjugation enzyme systems.

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摘要

Abstract

The effect of propofol on the hepatic and extrahepatic conjugation enzyme systems was assessed in vitro using microsomal and cytosolic preparations of human liver, hamster kidney, lung and gut. The functional activities of phase-II enzymes, including uridine diphosphate-glucuronosyltransferase (UDPGT), glutathione S-transferase (GST) and N-acetyltransferase (NAT) were evaluated in the presence of various concentrations of propofol (0.05-1.0 mmol litre-1), using 1-naphthol, 1-chloro-2,4-dinitrobenzene and p-aminobenzoic acid as substrates respectively. Propofol produced concentration-dependent inhibition of UDPGT activity in human liver microsomes. Propofol did not produce significant inhibition of human hepatic GST activity at concentrations below 1.0 mmol litre-1. In contrast, NAT activity was unaffected by propofol 0.05-1.0 mmol litre-1 in human liver cytosolic preparations. In extrahepatic tissues, hamster renal and intestinal UDPGT activities were significantly inhibited by propofol at 0.25-1.0 mmol litre-1. In these tissues, GST and NAT were unaffected by propofol at 1.0 mmol litre-1. Propofol produced differential inhibition of human liver and hamster extrahepatic conjugation enzymes as a result of different substrate and tissue specificities. The potential interference of the metabolic profile of phase-II enzymes as a result of inhibition by propofol (especially of UDPGT and GST) should be considered when using propofol with other drugs for anaesthesia.