INFLUENCE OF MIDAZOLAM ON PHARMACOKINETICS OF VERAPAMIL IN RABBITS

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Calcium channel blockers can get involved in pharmacological interactions when used concomitantly with other drugs. Previous reports indicate a differential influence of various general anesthetics on verapamil pharmacokinetics. A tendency of a faster transfer of verapamil from the central compartment to the tissue compartment was found to be associated with a slower drug return from the tissue at the given verapamil doses during thiopental or propofol anesthesia. Thus, an increased storage of verapamil in tissue compartment and prolongation of the drug action may occur due to those interactions.

The aim of the study was to investigate the influence of midazolam on the plasma concentrations and pharmacokinetic parameters of verapamil after intravenous bolus administration in rabbits during 2 h of observation.

Verapamil and midazolam were administered intravenously at a dose of 0.2 mg/kg. Verapamil levels in plasma were determined by radioanalysis using \(^{3}H\)verapamil. Levels of verapamil were determined in plasma at 5, 10, 15, 30, 45, 90 and 120 min after the administration, and plasma disappearance was analyzed according to the non-compartmental and 2-compartmental model. After administration of midazolam together with verapamil, a decrease in verapamil concentration in plasma was seen, with an increased verapamil transfer to the tissue compartment, increased steady state distribution volume and shortened residency time of the drug in the plasma.

\textbf{Key words:} verapamil, midazolam, pharmacokinetic parameters, rabbits