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Effect of cholecystectomy on bile acids as well as relevant enzymes and transporters in mice: Implication for pharmacokinetic changes of rifampicin

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Abstract

Background and Purpose: Long-term medical consequences of cholecystectomy are believed to be uncommon. It has been reported that bile acids (BAs) changed after cholecystectomy. As important signaling molecules, the alternations of BAs might favour the regulatory effect on enzymes and transporters involved in BAs physiological homeostasis at the transcriptional level, which could lead to pharmacokinetic changes of drugs. Here, we determined the effect of cholecystectomy on BAs, relevant enzymes and transporters and pharmacokinetic parameters of rifampicin, and explored the potential mechanisms at the transcriptional regulatory level via nuclear receptors.

Methods: Parameters of BAs in different specimens, mRNA and protein expression of enzymes, transporters and nuclear receptors that relate to BAs homeostasis in liver and ileum, and the pharmacokinetic character of rifampicin were measured in sham-operated and cholecystectomized mice.

Key Results: Cholecystectomy associated with considerable decreased BAs pool size that could attribute to increased fecal excretion. Most notably, as the Fxr and Pxr ligands, the alternations of hepatic and ileal individual BAs affected expression of enzymes Cyp3a11 and transporters Ntcp and Bsep in liver and Asbt in ileum significantly following cholecystectomy. Eventually, the rifampicin bioavailability was improved with depressed clearance in mice without gallbladders.

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