ALTERATION OF TRANSPORTER EXPRESSION AND FUNCTION IN THE SMALL INTESTINE OF BILE DUCT-LIGATED RATS

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Cholestasis occurs from various causes and the bile flow is diminished or stopped, resulting in decrease of bile in the intestine and increase in the concentration of bile components in the blood. Recently, it has been reported that the expression and the function of transporters in the liver and the kidney is affected by cholestasis. Therefore, the aim of this study was to elucidate the expression levels and function of transporters in the intestine of cholestasis model rats. Male Sprague-Dawley rats (7 weeks old at the beginning) were used. Bile duct was surgically ligated and the rats were sacrificed 3 days, 1 week and 4 weeks thereafter. Expression levels of mRNA of several drug transporters were quantified by RT-PCR method. The expression level of MRP2 was significantly decreased in the intestine from 4-week bile duct-ligated (BDL) rats and MRP3 showed the similar milder tendency, while that of ASBT increased in the intestine from 3-day BDL rats. The transport activity was determined by Ussing chamber method using p-aminohippuric acid (PAH), which is a representative substrate for MRP2, across the isolated intestinal tissue form 4-week BDL rats. The secretory-directed transport paralleled the decreased levels in mRNA expression of MRP2 in rat intestine after bile duct ligation, suggesting that alteration of MRP2 expression would accompany its transport function in the intestine after bile duct ligation. However, the taurocholate absorption from the small intestine of 3-day BDL rats, determined by closed loop method, was not significantly different from that of sham-operated rats. The factors that may affect the expression levels of transporters are under investigation.