

论著

肝纤维化状态下小肠药物代谢功能的改变

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摘要 目的 探讨肝纤维化时小肠药物代谢功能的变化, 为合理用药提供依据。方法 在大鼠肝纤维化模型上, 测定小肠粘膜上皮细胞药物代谢酶、抗氧化酶及膜流动性变化, 并与急性肝损伤、慢性肝硬化大鼠小肠相关指标进行比较。结果 与正常对照组相比, 肝纤维化大鼠小肠粘膜上皮细胞药物代谢 I 相酶红霉素N-脱甲基酶 (CYP3A)、7-乙氧异噁唑O-脱乙酰酶 (CYP1A1) 和苯胺羟化酶 (CYP2E1) 活性分别增加2.2、0.6和0.3倍, 而 II 相酶葡萄糖醛酸转移酶 (UDPGT) 和 α - π -谷胱甘肽S-转移酶 (GST) 活性则分别减少15%、43%和57%, 同时膜脂质过氧化产物增加, 抗氧化酶活性减弱, 膜流动性降低。急性肝损伤时, 上述指标无明显变化, 而肝硬化时上述指标与肝纤维化组变化一致, 并进一步增强。结论 肝纤维化可影响小肠粘膜上皮细胞药物代谢功能, 使 I 相氧化功能增强, II 相结合反应减弱。小肠抗氧化功能降低可能与 I 相氧化代谢增强有关。

关键词 [肝纤维化](#) [小肠](#) [药物代谢 I 相和 II 相酶系](#) [抗氧化酶系](#) [膜流动性](#)

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Changes of drug-metabolizing function of small intestinal mucosal epithelial cells in hepatic fibrosis rats

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Abstract

AIM To provide experimental data for rational design of therapeutic scheme. **METHODS** Drug-metabolizing enzymes, antioxidative enzymes and membrane fluidity of small intestinal mucosal epithelial cells were measured in hepatic fibrosis rats and compared with those in acute hepatic injury and hepatic cirrhosis rats. **RESULTS** In hepatic fibrosis, the activities of phase I enzymes-erythromycin N-demethylase (CYP3A), 7-ethoxyresorufindeethylase (CYP1A1) and aniline hydroxylase (CYP2E1) of small intestinal mucosal epithelial cells enhanced 2.2-, 0.6- and 0.3-times respectively, in comparison with control group, however, the activities of phase II enzymes-uridine diphosphateglucuronate transferase, α -, π -glutathione S-transferase decreased 15%, 43% and 57%, respectively. Meanwhile, the content of membrane malondialdehyde increased, and the activities of antioxidative enzymes and membrane fluidity decreased. In acute hepatic injury, the above indexes showed no obvious changes, however in hepatic cirrhosis, the changes were consistent with those in hepatic fibrosis but increased more. **CONCLUSION** Hepatic fibrosis could influence drug metabolism of small intestinal mucosal epithelial cells. Phase I oxidations increased but phase II conjugations decreased. The changes of antioxidative function may be associated with the increase of phase I oxidations.

Key words [liver fibrosis](#) [small intestine](#) [phase I and phase II enzymes](#) [antioxidative enzymes](#) [membrane fluidity](#)

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