

基础研究

不同胆汁引流方式对梗阻性黄疸大鼠肠黏膜屏障功能的影响及机制

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摘要:

目的: 探讨不同胆汁引流方式对梗阻性黄疸(OJ)大鼠肠黏膜功能的影响及其机制。方法: 将60只SD大鼠采用胆总管结扎法制作OJ模型, 1周后随机均分为无引流组(不行胆汁引流术), 内引流组(行胆汁内引流术)和外引流组(行胆汁外引流术), 引流时间1周。以20只假手术大鼠为对照组, 实验共2周, 结束时分别用ELISA法和Western blot法检测各组血清内毒素水平和小肠黏膜组织闭锁蛋白(occludin)及闭锁小带蛋白1(ZO-1)的表达, 并观察小肠黏膜组织形态学改变。结果: 大鼠造模后出现明显的OJ表现, 二次手术后, 内引流组大鼠一般情况明显好于无引流组和外引流组。无引流组和外引流组OJ大鼠血清内毒素水平明显升高, 与对照组比较, 差异均有统计学意义(均 $P<0.01$), 而无引流组与外引流组间内毒素水平差异无统计学意义($P>0.05$); 内引流组OJ大鼠血清内毒素水平较无引流组和外引流组明显下降(均 $P<0.01$), 与对照组水平无统计学差异($P>0.05$)。与对照组比较, 无引流组和外引流组OJ大鼠小肠黏膜组织occludin及ZO-1蛋白表达均明显降低(均 $P<0.01$), 且外引流组两者表达水平降低较无引流组更为明显(均 $P<0.01$); 内引流组OJ大鼠的occludin及ZO-1的表达水平明显高于无引流组和外引流组(均 $P<0.01$), 且基本接近对照组(均 $P>0.05$)。病理学观察显示, 无引流组和外引流组OJ大鼠肠黏膜结构破坏, 大量或中量炎性细胞浸润, 而内引流组OJ大鼠肠黏膜结构完整, 仅见少量炎性细胞浸润。结论: 胆汁内引流对OJ大鼠肠黏膜屏障具有保护作用, 其机制可能与胆汁维持肠黏膜上皮细胞间紧密连接相关蛋白的表达有关。

关键词: 黄疸 阻塞性; 引流术; 紧密连接部; 闭锁蛋白; 闭锁小带蛋白1; 大鼠

Effects of different biliary drainage methods on intestinal mucosal barrier function in rats with obstructive jaundice

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Abstract:

Objective: To investigate the effects of different biliary drainage methods on the intestinal mucosal barrier function in rats with obstructive jaundice (OJ) and the mechanisms. Methods: Sixty SD rats were used to establish OJ models by common bile duct ligation. One week after operation, the rats were equally randomized into non-drainage group (underwent no biliary drainage), internal drainage group (underwent internal biliary drainage) and external drainage group (underwent external biliary drainage), and the drainage time was one week. Twenty SD undergoing sham operation served as control group and the total experiment time was two weeks. At the end of the experiment, the serum endotoxin level and protein expression of occludin and zona occludens 1 (ZO-1) in the tissues of small intestinal mucosa of each group were determined by ELISA assay and Western blot analysis respectively, and the histomorphological changes in small intestinal mucosa were also observed. Results: Rats presented overt symptoms after OJ model creation, while the general conditions of rats of internal drainage group were better than those of non-drainage group and external group after the second operation. The serum endotoxin levels in OJ rats of non-drainage group and external drainage group were increased markedly, and their differences versus control group reached statistical significance (both $P<0.01$), but no significant difference was observed between the two drainage groups ($P>0.05$); the serum endotoxin level in OJ rats of internal drainage group was significantly lower than that in OJ rats of non-drainage group or external drainage group (both $P<0.01$), and showed no significant difference versus control group ($P>0.05$). Compared with control group, the protein expressions of occludin and ZO-1 in small intestinal mucosa in rats of non-drainage group and external drainage group were significantly decreased (all $P<0.01$), and the degree of decrease in external group was more evident than that in non-drainage group (both $P<0.01$); the expression levels of the two proteins in internal drainage group were significantly higher than those in non-drainage group or external drainage group (all $P<0.01$), and were similar to those in control group (both $P>0.05$). As seen at the pathological examination, the intestinal mucosal integrity was damaged in OJ rats of both non-drainage group and external group with large or moderate amounts of inflammatory cell infiltration, while the intestinal mucosal integrity was

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maintained intact with less inflammation in OJ rats compared with internal drainage group. Conclusion: Internal biliary drainage has protective effect on the intestinal mucosal barrier in OJ rats, and the mechanism is probably due to the maintaining effect of bile on tight junction-related protein expression in intestinal epithelial cells.

Keywords: Jaundice, Obstructive Drainage Tight Junctions Occludin Zona Occludens 1 Rats

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