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基础研究

锌预处理对小鼠肾缺血再灌注损伤的预防作用

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摘要：

目的：探讨锌预处理对小鼠肾缺血再灌注损伤(RIRI)的预防作用，为RIRI的防治提供实验依据。方法：50只雄性小鼠随机分为假手术组、模型组、硫酸锌预处理高剂量组（高锌组，60 mg•kg^{-1} ）、硫酸锌预处理中剂量组（中锌组，30 mg•kg^{-1} ）和硫酸锌预处理低剂量组（低锌组，15 mg•kg^{-1} ），每组10只。各剂量锌处理组小鼠每日灌胃给予硫酸锌1次，连续2周。模型组和假手术组给予等体积生理盐水。2周后制备RIRI模型。缺血30 min再灌注24 h后取出肾脏组织，固定、包埋，HE染色观察病理组织学表现，TUNEL法检测细胞凋亡，免疫组化法检测c-Fos表达。结果：病理组织学表现，模型组小鼠肾脏组织中肾皮质可见肾小管管腔扩张，内可见管型，肾小管上皮细胞空泡变性和坏死，皮髓交界处髓质损伤较重，可见充血及成片坏死区。高锌组病理改变无改善，中锌和低锌组病理组织改变较轻，小鼠肾切片可见肾小管上皮细胞部分肿胀，皮髓交界处肾小管充血、细胞坏死较少，低锌组好于中锌组。TUNEL法结果，模型组凋亡细胞较多，显著高于低锌和中锌组（P<0.05），低锌组凋亡细胞显著低于中锌组（P<0.05）。免疫组化结果，与假手术组相比较，模型组和锌预处理组c- Fos阳性细胞率显著增加 (P<0.05)；与模型组比较，中锌和低锌组c- Fos阳性细胞率显著减少(P<0.05)；低锌组c-Fos阳性细胞率显著低于中锌组（P<0.05）。结论：在一定剂量范围内，硫酸锌对RIRI所导致的肾功能损害具有保护作用，其机制可能与凋亡细胞减少、c-Fos表达降低有关。

关键词：

Protective effect of zinc preconditioning on renal ischemia-reperfusion injury in mice

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Abstract:

Abstract:Objective To discuss the preventive effect of zinc preconditioning on renal ischemia-reperfusion injury (RIRI) in mice and provide experimental basis for prevention and treatment of RIRI in clinic. Methods 50 male mice were randomly divided into 5 groups: sham operation group,RIRI model group,high dose zinc treatment group (60 mg•kg^{-1}),middle dose zinc treatment group (30 mg•kg^{-1}) and low dose zinc treatment group (15 mg•kg^{-1}) ,10 mice in each group. The mice in zinc treatment groups were administrated with ZnSO4 solution daily by gastric gavage for two weeks,while the equal volume normal saline was given to the mice in model group and sham operation group. Then the RIRI model was prepared. After 30 min ischemia and 24 h reperfusion,the pathologic changes in kidney tissue of mice were observed by the method of HE staining;the apoptotic cells and the expression of c-fos were detected by TUNEL staining and immunohistochemistry,respectively. Results The pathohistological results showed the pathological changes in kidneys of mice in model group,such as tubular dilation with cast formation,vacuolization and necrosis of renal tubular epithelial cells in renal cortex,the more serious changes occurring in the location between cortex and medulla with severe blood congestion and necrosis region. The mice in high dose zinc treatment group appeared the above pathological changes. In middle dose and low dose zinc treatment group,the abov changes were improved,which were swelling of renal tubular epithelial cell,less congestion and cell necrosis in the location between cortex and medulla. The pathological improvement in low dose zinc treatment group was better than that in middle dose zinc treatment. TUNEL staining showed that the number of apoptotic cells in model group was significantly higher than those in middle and low dose zinc treatment group （P<0.05） ,and the number of apoptotic cells in low dose zinc treatment group was significantly lower than that in middle dose zinc treatment group（P<0.05）. The

immunohistochemical results showed that compared with sham operation group,the c-Fos-positive cell rates in model group and zinc treatment groups were significantly increased (P<0.01);compared with model group, the c-Fos-positive cellrate in middle and low dose zinc treatment groups were significantly decreased (P<0.05);the c-Fos-positive cell rate in low dose zinc treatment group was significantly lower than that in middle dose treatment group (P<0.05). Conclusion Zinc sulfate has a protective effect on RIRI in a certain dosage range and the possible mechanism may be associated with the decreasing of apoptotic cells and c-Fos expression induced by zinc.

Keywords: zinc;ischemia-reperfusion injury;apoptosis;c-fos；HE staining

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