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白藜芦醇及其伍用吡喹酮对小鼠日本血吸虫肝纤维化的治疗作用

陈艳*，肖政

华中科技大学同济医学院附属普爱医院（西区）消化科，武汉 430033

Therapeutic Effect of Resveratrol as well as Resveratrol Combined with Praziquantel on the Liver Fibrosis due to Schistosoma japonicum Infection in Mice

CHEN Yan*, XIAO Zheng

Section of Digestive Disease, Puai Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430035, China

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摘要 目的 探讨白藜芦醇及其伍用吡喹酮防治小鼠血吸虫肝纤维化的作用及机制。 方法 80只昆明小鼠感染日本血吸虫尾蚴（25条/鼠）6周后，随机均分为4组。A组小鼠灌胃吡喹酮500 mg/（kg·d）×2 d，B组小鼠灌胃白藜芦醇20 mg/（kg·d）×6周，C组小鼠灌胃吡喹酮500 mg/（kg·d）×2 d后以白藜芦醇20 mg/（kg·d）灌胃6周。D组感染小鼠不作任何治疗。另取20只小鼠为健康对照组（E组）。感染后第12周末处死各组小鼠，取肝组织，观察肝组织病理改变，RT-PCR检测肝组织中血管内皮生长因子（VEGF）mRNA相对含量，ELISA测定肝脏丙二醛（MDA）含量和超氧化物歧化酶（SOD）活性，免疫组化检测血管内皮生长因子（VEGF）和Ⅰ、Ⅲ型胶原的表达情况。 结果 A、B和C组小鼠经治疗后肝纤维化程度减轻。小鼠肝组织中VEGF mRNA相对含量和VEGF蛋白表达水平，A组（0.37±0.06、0.69±0.42）、B组（0.23±0.01、0.38±0.42）、C组（0.11±0.00、0.12±0.17）和E组（0.06±0.03、0.04±0.02）均低于D组（0.60±0.03、0.97±0.36）（P<0.01），A组和B组均低于C组（P<0.01或P<0.05），A组低于B组（P<0.05）。小鼠肝组织中SOD活性和MDA含量，A组（13.56±2.56、7.62±2.30）与B组（14.28±1.56、6.63±2.31）的差异均无统计学意义（P>0.05）。小鼠肝组织中SOD活性，C组（22.36±1.55）高于A组和B组（P<0.05），A、B和C组均高于D组（P<0.05或P<0.01）。MDA含量，C组（2.31±1.31）低于A组和B组（P<0.05），A、B和C组均低于D组（P<0.05或P<0.01）。 结论 白藜芦醇可抑制血吸虫肝纤维化组织VEGF表达，与吡喹酮伍用可发挥增效作用。

关键词： 日本血吸虫病 肝纤维化 白藜芦醇 血管内皮生长因子 氧化应激

Abstract: Objective To study the therapeutical effect and mechanisms of resveratrol and its combination with praziquantel on the liver fibrosis due to Schistosoma japonicum infection. Methods Eighty mice infected with 25 S. japonicum cercariae for 6 weeks were randomly divided into four groups named as praziquantel group (A), resveratrol group (B), resveratrol+praziquantel group (C) and infection group (D). Mice in groups A and B were treated with praziquantel [500 mg/(kg·d)] for 2 d, and resveratrol [20 mg/(kg·d)] for 6 weeks, respectively. Mice in group C were treated with resveratrol [20 mg/(kg·d)] for 6 weeks after praziquantel treatment [500 mg/(kg·d)×2 d]. Group D served as infection control. Twenty normal mice were taken as normal control group (Group E). At the 12th week post-infection, all mice were sacrificed and the liver tissues were removed. Histopathological changes were observed in the liver of all groups. RT-PCR was used to detect the relative VEGF mRNA level in liver tissue. Maleic dialdehyde (MDA) content and superoxide dismutase (SOD) activity in liver were measured by ELISA. The expressions of VEGF, type Ⅰ and type Ⅲ collagen were examined by immunohistochemistry. Results After treatment, the degrees of liver fibrosis in groups A, B and C decreased. The hepatic expression of VEGF mRNA and VEGF protein levels in groups A (0.37±0.06, 0.69±0.42), B (0.23±0.01, 0.38±0.42), C (0.11±0.00, 0.12±0.17) and E (0.06±0.03, 0.04±0.02) were lower than that of group D (0.60±0.03, 0.97±0.36) (P<0.01), those in groups A and B were significantly lower than that of group C (P<0.01 or P<0.05), and those in group A were lower than in group B (P<0.05). There was no significant difference in liver SOD activity and MDA content between group A (13.56±2.56, 7.62±2.30) and group B (14.28±1.56, 6.63±2.31) (P>0.05). Compared with group C (22.36±1.55, 2.31±1.31), mice in groups A and B exhibited decreased an SOD activity, but increased MDA content (P<0.05). SOD activity of groups A, B, and C was higher than that of group D (P<0.05 or P<0.01), and MDA content in the above three groups was lower than that of group D (P<0.05 or P<0.01). Conclusion Resveratrol has an antifibrogenic effect through inhibiting the expression of VEGF and reducing oxidative stress in mice with Schistosoma japonicum egg-induced liver fibrosis. Resveratrol and praziquantel show a synergistic action in antifibrosis treatment.

Keywords: Schistosoma japonicum Liver fibrosis Resveratrol VEGF Oxidative stress

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