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论著

甘草酸二铵对肝纤维化大鼠肝脏脂质过氧化与间质性胶原酶活性的影响

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摘要 目的：探讨甘草酸二铵影响纤维化肝脏脂质过氧化与间质性胶原酶活性的抗肝纤维化作用机制。 方法：以四氯化碳(CCl4)皮下注射与高脂肪低蛋白饮食复合因素诱导大鼠肝纤维化模型，而后予以甘草酸二铵口服治疗，正常大鼠与模型对照组给予等量生理盐水。HE染色与胶原染色观察大鼠肝组织炎性坏死与胶原沉积病理改变，按试剂盒方法检测血清肝功能（ALT、AST、Alb与总胆红素等）变化，检测肝组织主要过氧化损伤指标：超氧化物歧化酶（SOD）活性, 丙二醛（MDA）含量，谷胱甘肽（GSH）含量与谷胱甘肽过氧化物酶（GSH-Px）活性，水解法测定肝组织羟脯氨酸含量，酶底物反应法分析肝组织间质性胶原酶活性变化，RT-PCR法分析肝组织Ⅰ型前胶原基因表达。 结果： 与正常大鼠相比，模型大鼠肝脏有明显胶原沉积与肝纤维化，伴有不同程度的肝细胞炎性损伤坏死；甘草酸二铵药物组明显减轻模型大鼠肝组织损伤坏死与胶原沉积等病理变化。模型大鼠肝功能指标,包括血清总胆红素含量、ALT与AST活性、白蛋白含量均明显减少（P<0.01）。药物组大鼠血清总胆红素含量、AST与ALT活性显著低于模型组（P<0.05），而白蛋白含量高于模型组（P<0.05）。此外，药物组大鼠肝组织羟脯氨酸含量(151.3±37.3 μg/g)明显少于模型组(170.9±15.3 μg/g，P<0.05)，Ⅰ型前胶原基因表达弱于模型组（P<0.05）；肝组织MDA含量(1.96±0.23 μmol/g)低于模型组(2.44±0.32 μmol/L，P<0.05)，SOD水平(19.60±0.97 NU/g)高于模型组(20.60±0.33 NU/g，P<0.05)，GSH含量(47.0±9.1 g/g)与GSH-Px活性(53.1±4.1 U/g)高于模型组(41.2±3.5 g/g；46.7±6.1 U/g，P<0.05)；肝组织间质性胶原酶活性(43.89±7.74 U)高于模型组(32.01±2.75 U，P<0.05)。 结论： 甘草酸二铵有明显抗肝纤维化大鼠肝脏脂质过氧化损伤与提高肝组织间质性胶原酶活性的作用，该作用是药物抗肝纤维化的重要机制。

关键词 甘草酸； 肝硬化； 过氧化脂质类； 胶原酶类

分类号 R363

Effects of diammonium glycyrrhizinate on the lipid peroxidation and interstitial collagenase activity in fibrotic liver in rats

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Abstract

<FONT face=Verdana>AIM: To investigate the effect of diammonium gycyrrhizinate (Ganlixin) against liver fibrosis through preventing lipid peroxidation and regulating interstitial collagenase activity. METHODS: The liver fibrotic model was induced through subcutaneous injection of CCl4 and the feeding with high fat and low protein in rats. Diammonium gycyrrhizinate was administered (70 mg/kg rat BW). Hepatic inflammation and collagen were observed with H-E and Sirius red staining. The liver function including serum ALT, AST activity, Alb and total bilirubin levels were determined. The hepatic lipid peroxidation including SOD and GSH-Px activities, MDA and GSH content were also measured. Hepatic hydroxyproline (Hyp) content was detected with Jamall's method. The activity of interstitial collagenase in liver was assayed by the reaction with ［3H］ labeled type I collagen, and the gene expression of α1(Ⅰ) pro-collagen was analyzed by RT-PCR. RESULTS: The model rats had remarkable inflammatory necrosis, collagen accumulation and fibrosis at liver, while the diammonium gycyrrhizinate treated group showed slighter hepatic injury and collagen deposition, and the much better liver function than the model. The diammonium gycyrrhizinate-treated group had lower levels of hepatic MDA, Hyp and α1 (Ⅰ) pro-collagen mRNA expression than those in the model group, but had higher levels of interstitial collagenase activity, GSH content, SOD and GSH-Px activity than those in the model group. CONCLUSION:

Diammonium gycyrrhizinate has a good effect against liver fibrosis, which may be related to the prevention from lipid peroxidation and improvement of interstitial collagenase activity in fibrotic livers. </FONT>

Key words Glycyrrhizic acid Liver cirrhosis Lipid peroxides Collagenases

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