Keap1/Nrf2/HO-1 通路在丹皮酚保护小鼠重症急性胰腺炎中的作用及机制研究

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Abstract: *(Objective) To investigate the effect of paeonol on oxidative damage in mice with acute pancreatitis. (Method) In this study, a mouse model of acute pancreatitis was established by injected intraperitoneally with 20% L-arginine, and the experimental animals were randomly assigned to the blank control group acute pancreatitis model group and the paeonol low-medium-high dose group (25, 50, 100 mg/kg·bw). Except blank control group, the other 4 groups were injected intraperitoneally with 20% L-arginine after 5 days of normal gavage of paeonol, and serum of mice were taken to measure the oxidation index (MDA SOD) 6 hours later, and pancreatic tissues of mice were taken to observe the pathological changes; At the same time, immunohistochemical sections of pancreatic tissue MPO were made to observe the histopathological changes, the distribution and activity of MPO. The mRNA expression levels of HO-1、Keap1 and Nrf2 in pancreatic tissues of each group were detected by fluorescence quantitative PCR, and the protein expression levels of HO-1、Keap1 and Nrf2 were detected by Western blot. Conclusion: Paeonol may alleviate oxidative damage induced by L-arginine in mice with acute pancreatitis by activating Keap1/Nrf2/HO-1 signaling pathway. This study provides theoretical reference for the pathogenesis of acute pancreatitis and the development of related drugs.*

Keywords: *paeonol; oxidative injury; pancreatitis; L–arginine; mechanism.*

1.前 言

为了探究丹皮酚对重度急性胰腺炎（SAP）小鼠的保护作用，本试验通过建立小鼠重度急性胰腺炎模型，分别考察不同剂量丹皮酚对、氧化指标、胰腺病理变化、相关基因和蛋白表达情况的影响。以期为临床治疗胰腺炎提供新药。

2.材料与方法

本试验选取昆明雄性小鼠 50 只，随机分成 5 组，即空白对照组、SAP 模型组和丹皮酚高、中、低剂量组。丹皮酚组小鼠分别灌胃 100、50 和 25 $mg \cdot kg^{-1}$ 丹皮酚，同时空白对照组和 SAP 模型组小鼠给予等体积生理盐水。连续灌胃 5 d 后，采用 20%L-精氨酸腹腔注射 SAP 模型组和不同剂量丹皮酚组小鼠，6 h 后取各组小鼠血清测定相关指标（AMS、Ca^{2+}、MDA、SOD），取小鼠胰组织肉眼观察病理学变化，并制作胰腺组织的 MPO 荧光免疫，观察其病理学变化和 MPO 的表达情况。采用荧光定量 PCR 和 Western blot 检测各组胰腺组织中 HO-1、keap1 以及 Nrf2 mRNA 及蛋白表达量。

3.结 果

试验结果发现，与 AP 模型组相比，不同剂量的丹皮酚显著降低小鼠血清 AMS 和 MDA 含量，显著升高 Ca^{2+}和 SOD 含量；不同剂量组丹皮酚显著升高 IκB、HO-1、Nrf2 mRNA 及蛋白表达，同时显著降低 keap1 mRNA 和蛋白表达。

4.结 论

本研究根据课题组前期研究成果，进一步将丹皮酚应用于急性胰腺炎小鼠，探讨基于 Keap1/Nrf2/HO-1 信号通路下丹皮酚对 20%L-精氨酸诱导的小鼠重度急性胰腺炎的保护作用。研究发现，丹皮酚通过调控 Keap1/Nrf2/HO-1 信号通路可以有效阻止炎症爆发所引起的氧化损伤。本试验结果为临床急性胰腺炎的治疗提供有效替代药物，同时也为急性胰腺炎发病机制的研究提供新思路。