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别嘌呤醇对慢性心衰大鼠心功能的改善作用(PDF)分享

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Title: Allopurinol improves cardiac function of chronic heart failure rats

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关键词: 别嘌呤醇; 活性氧; 慢性心力衰竭; 心肌能量代谢

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摘要: 目的 探讨别嘌呤醇(allopurinol, ALLO)对慢性心衰大鼠心功能的保护作用及其抗氧化作用机制在其中的作用。 方法 6周龄的雄性SD大鼠35只，体质量（200±20）g，将35只大鼠随机分为ALLO处理组（AMI+ALLO，n=12）、对照组（AMI+NS，n=13）和假手术组（sham-operated +NS，n=10），ALLO处理组和对照组大鼠结扎冠状动脉前降支建立急性心肌梗死（acute myocardium infarction，AMI）模型，假手术组大鼠只穿线不结扎。术后第2天，ALLO处理组给予ALLO [50 mg/(kg·d)]灌胃，对照组和假手术组大鼠给予生理盐水（normal saline，NS）灌胃。8周后，检测并比较分析各组大鼠的心功能、血清脑钠尿肽（brain natriuretic peptide，BNP）含量、黄嘌呤氧化酶（xanthine Oxidase，XO）蛋白表达、丙二醛（malondialdehyde，MDA）含量、线粒体呼吸链酶Ⅰ~Ⅳ的活性、心肌组织形态以及心肌诱导型氧化亚氮合酶（induce-nitri-coxide synthase，iNOS）的表达量。 结果 对照组与假手术组大鼠相比，大鼠心功能、线粒体呼吸链酶Ⅰ、Ⅲ、Ⅳ活性明显降低（P<0.05），血清BNP含量、XO蛋白表达、MDA水平明显升高（P<0.05），HE染色显示心肌组织明显水肿（P<0.05），iNOS表达升高（P<0.05），证明CHF建模成功；ALLO处理组（EF：87.10%）与对照组（EF：68.18%）相比，ALLO处理组大鼠的心功能明显改善（P<0.05），BNP含量、XO蛋白表达、MDA水平均下降（P<0.05），大鼠线粒体呼吸链酶Ⅰ、Ⅲ、Ⅳ活性增加（P<0.05），HE染色显示心肌组织水肿减轻（P<0.05），iNOS表达受抑制（P<0.05）。 结论 CHF建模成功；ALLO可以改善CHF大鼠的心功能，其机制可能与其抗氧化作用有关。

Abstract: Objective To determine the protective effect of allopurinol (ALLO) on cardiac function in rats with chronic heart failure and its antioxidant mechanism in improving cardiac function. Methods Thirty-five of 6-weeks-old male SD rats average weighted (200±20)g, randomly divided into the ALLO treatment group (*n*=12),control group (*n*=13) and sham-operated group (*n*=10).SD rats in ALLO treatment group and the control group were established of acute myocardial infarction (AMI) models by ligation of the left anterior descending coronary artery, and SD rats of sham-operated group underwent the same procedure, including anesthesia and open-chest surgery, but the artery was not ligated. Two days after the surgery, ALLO treatment group underwent gavage administration by ALLO(50 mg/kg·d), while the gavage administration in control group and sham-operated group were only by the saline. Eight weeks later, the cardiac function of SD rats, levels of brain natriuretic peptide (BNP), expression of xanthine oxidase(XO), malondialdehyde (MDA), the activity of mitochondrial complex Ⅰ-Ⅳ, morphological changes in myocardial tissue and the expression of iNOS were detected and analyzed. Results Compared with the rats in sham-operated group,rats in control group showed poor cardiac function (*P*<0.05), significantly increased expression of XO (*P*<0.05), increased BNP content and MDA level(*P*<0.05), significant decrease of the activity of mitochondrial complex Ⅰ, Ⅲ and Ⅳ (*P*<0.05), HE staining revealed obvious myocardial tissue edema and obviously increased iNOS expression (*P*<0.05) in control group, which revealed that the CHF model had been set up successfully. While compared with control group, rats in ALLO treatment group showed better cardiac function (*P*<0.05), decreased XO expression (*P*<0.05) and BNP content and MDA level (*P*<0.05), increased activity of mitochondrial complex Ⅰ, Ⅲ and Ⅳ(*P*<0.05), alleviated tissue loosening and edema (*P*<0.05), markedly inhibited iNOS expression (*P*<0.05). Conclusion CHF model is set up successfully, and ALLO can improve chronic heart failure rats cardiac function. The mechanism maybe associated with its antioxidant role.

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