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论著

氯沙坦对自发性高血压大鼠细胞外信号调节激酶活性和B型利钠肽表达的影响

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摘要 目的 探讨氯沙坦治疗高血压心肌肥厚的作用机制。方法 选择同周龄Wistar Kyoto（WKY）大鼠作正常对照，将21只14周龄雄性自发性高血压大鼠（SHR）随机分成3组：模型组、肼屈嗪组(10 mg·kg^{-1}·d^{-1})和氯沙坦组(10 mg·kg^{-1}·d^{-1})。用Western印迹方法检测大鼠心肌总细胞外信号调节激酶(t-ERK)、磷酸化ERK（p-ERK）及有丝分裂素激活蛋白激酶磷酸酶-1（MKP-1）水平；用RT-PCR法半定量测定大鼠心肌中B型利钠肽(BNP)mRNA的含量；酶联免疫吸附法检测大鼠血浆BNP水平。结果 喂药10周后，氯沙坦组和肼屈嗪组血压相似，均显著低于模型组（n=7, P<0.01）。氯沙坦组心肌肥厚指数显著低于肼屈嗪组和模型组（n=7, P<0.01），与WKY组无差异（n=7, P>0.05）；肼屈嗪组和模型组心肌肥厚指数无差异（n=7, P>0.05）。4组大鼠t-ERK水平无显著性差异（n=7, P>0.05）；氯沙坦组心肌p-ERK, p-ERK/t-ERK及MKP-1水平均显著低于SHR肼屈嗪组和SHR模型组（n=7, P<0.05），与WKY组无差异（n=7, P>0.05）。肼屈嗪组和模型组心肌p-ERK, p-ERK/t-ERK及MKP-1水平无差异（n=7, P>0.05）。氯沙坦组大鼠心肌BNP mRNA和血浆BNP水平显著低于SHR肼屈嗪组和模型组（n=7, P<0.05），与WKY组无差异（n=7, P>0.05）；肼屈嗪组和SHR模型组大鼠心肌BNP mRNA和血浆BNP水平无差异（n=7, P>0.05）。结论 氯沙坦能通过抑制ERK活性逆转心肌肥厚，伴随BNP水平下降；肼屈嗪却不能，提示BNP的变化可反映降压药物逆转心肌肥厚的疗效。

关键词 氯沙坦 肼屈嗪 MAP激酶信号系统 利钠肽, B型 高血 压 肥大, 左心室

分类号 R972.4

Effect of losartan on extracellular signal-regulated kinases activity and expression of B-type natriuretic peptide in spontaneously hypertensive rats

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Abstract

AIM To investigate the mechanism of therapeutic effect of losartan on myocardial hypertrophy. **METHODS** Wistar Kyoto rats were chosen as normal control group. Twenty one 14 week old spontaneously hypertensive rats(SHR) were randomly divided into 3 groups, 7 rats each: losartan group (10 mg·kg^{-1}·d^{-1}), hydralazine group (10 mg·kg^{-1}·d^{-1}) and model group. Protein expression of total extracellular signal-regulated kinases(t-ERK), phosphorylated-ERK (p-ERK) and mitogen-activated protein kinase phosphatase-1 (MKP-1) in myocardial tissue was detected by Western blot. B-type natriuretic peptide(BNP) mRNA in myocardial tissue was examined by RT-PCR, and protein expression of plasma BNP was detected by ELISA. **RESULTS** Losartan and hydralazine lowered the blood pressure after 10 weeks treatment（n=7, P<0.01）. The ratio of LVW/BW in SHR losartan group was significantly lower than that in SHR hydralazine group and SHR model group（n=7, P<0.01）, and similar to that in WKY group（n=7, P>0.05）. There was no significant difference of LVW/BW between SHR hydralazine group and SHR model group（n=7, P>0.05）. There was no significant difference of t-ERK expression in 4 groups of rats （n=7, P>0.05）. The protein expression of p-ERK, MKP-1 and the ratio of p-ERK/t-ERK in myocardial tissue in SHR losartan group were significantly lower than that in SHR hydralazine group and SHR model group（n=7, P<0.01）, and similar to that in WKY group（n=7, P>0.05）. There was no significant difference of p-ERK, MKP-1 and p-ERK/t-ERK between SHR hydralazine group and SHR model group（n=7, P>0.05）. The level of plasma BNP and BNP mRNA in myocardial tissue in SHR losartan group was significantly lower than that in SHR hydralazine group and SHR model group（n=7, P<0.01）, and similar to that in WKY group（n=7, P>0.05）. There was no significant difference of plasma BNP and BNP mRNA in myocardial tissue between SHR hydralazine group and SHR model group（n=7, P>0.05）. **CONCLUSION** Losartan could inhibit ERK activation to regress myocardial hypertrophy, accompanied by the reduction of BNP level, while hydralazine could not. BNP level might serve as a therapeutic index for myocardial hypertrophic regression of anti-hypertensive drugs.

Key words losartan hydralazine MAP kinase signaling system natriuretic peptide B-type hypertension hypertrophy left ventricular

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