



激活瞬时受体电位香草醛亚家族1抑制RhoA/Rho激酶改善高脂介导的血管舒张功能异常

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Activation of Transient Receptor Potential Vanilloid 1 Inhibits RhoA/Rho Kinase and Improves Vasorelaxation Dysfunction Mediated by High fat Diet in Mice

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摘要

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摘要 目的探讨膳食辣椒素通过激活瞬时受体电位香草醛亚家族1 (TRPV1) 对高脂饮食介导的血管功能障碍的作用及机制。方法10周龄雄性C57BL/6J小鼠, 分别给予普通饮食(普通饲料)、普通饮食+辣椒素(普食+0.01%辣椒素)、高脂饮食(高脂饲料)、高脂饮食+辣椒素(高脂饲料+0.01%辣椒素)干预, 20周后观察鼠尾血压、离体主动脉环血管收缩和舒张功能、血管电压依赖型钾通道Kv1.4和RhoA/Rho激酶蛋白表达。结果高脂饮食组内皮依赖和非内皮依赖的舒张反应分别为(26±12)%和(18.9±13.0)%, 均明显低于普通饮食组的100%和100%(*P*均<0.01)。高脂饮食+辣椒素组的内皮依赖和非内皮依赖的舒张反应分别为(69±15)%和(46.5±6.0)%, 均明显高于高脂饮食组(*P*均<0.05), 但仍明显低于普通饮食组(*P*<0.05, *P*<0.01)。高脂饮食组大鼠的血压明显高于普通饮食组[(135±7)mmHg比(116±5)mmHg, *P*<0.01]。Western blot检测结果显示, 普通饮食+辣椒素组大鼠的Kv1.4蛋白表达明显高于普通饮食组(*P*<0.05), 高脂饮食+辣椒素组大鼠的Kv1.4蛋白表达明显高于高脂饮食组(*P*<0.05); 高脂饮食组大鼠RhoA/Rho激酶蛋白的表达明显高于普通饮食组(*P*<0.05), 普通饮食+辣椒素组明显低于普通饮食组(*P*<0.05), 高脂饮食+辣椒素组明显低于高脂饮食组(*P*<0.05)。结论膳食辣椒素能够改善高脂介导的血管舒张功能异常, 可能与其激活TRPV1通道, 从而上调钾通道和抑制RhoA/Rho激酶信号通路相关。

关键词: 瞬时受体电位通道 香草醛类受体1型 RhoA/Rho激酶 血管功能 钾通道

Abstract: Objective To investigate the role of dietary capsaicin in activating transient receptor potential vanilloid 1 (TRPV1) and thus influencing the vascular dysfunction mediated by high-fat diet and the potential mechanisms. Methods A total of 80 male C57BL/6J mice aged 10 weeks were equally divided into four groups, in which the mice were fed with normal diet (ND), normal diet plus capsaicin (NC), high-fat diet (HD), or high-fat diet plus capsaicin (HC) for 20 weeks. Tail-cuff blood pressure (BP), vascular function of mice aortic rings, expressions of voltage-gated potassium-channel Kv1.4, RhoA and Rho kinase in aorta were examined. Results Compared with ND group, both nitroglycerin [(18.9±13)% vs. 100%, *P*<0.01] and acetylcholine [(26±12)% vs. 100%, *P*<0.01] induced vasorelaxation of aortic rings were significantly reduced in HD group. Both endothelium dependent and independent aortic rings vasorelaxation in HC group were significantly improved compared with that in HD group [acetylcholine: (69±15)%; nitroglycerin: (46.5±6)%, *P*<0.05], but still reduced compared with that in ND group (*P*<0.05, *P*<0.01). High fat diet induced the expression of RhoA and Rho kinase. Dietary capsaicin down-regulated the expression of RhoA and Rho kinase but up-regulated the expression of Kv1.4 in aorta in mice fed with normal or high fat diet (all *P*<0.05). Conclusion Dietary capsaicin can ameliorate vasorelaxation dysfunction mediated by high-fat diet. The potential mechanisms may be related with TRPV1 activation, which in turn stimulates potassium channel and inhibits RhoA and Rho kinase in the vasculature.

Keywords: transient receptor potential vanilloid 1 RhoA/Rho kinase vasorelaxation voltage-gated potassium-channel

Received 2011-10-08;

Fund:

中华医学会临床科研基金(07060700078)和国家重点基础研究发展计划项目(973计划)(2011CB503902)

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引用本文:

朱振宇, 张莉莉, 王沛坚, 马丽群, 王利娟, 刘道燕, 祝之明. 激活瞬时受体电位香草醛亚家族1抑制RhoA/Rho激酶改善高脂介导的血管舒张功能异常[J] 中国医学科学院学报, 2011, 33(6): 600-605

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