中国病理生理杂志 2008 24 (12): 2339-2343 ISSN: 1000-4718 CN: 44-1187/R

论著

二甲双胍对兔动脉粥样硬化NF-κB表达及血清高敏C反应蛋白水平的影响

李松南[1],王祥[1△],曾秋棠[1],冯义柏[1],郭和平[1],王天红[1],邓荷萍[2]

华中科技大学同济医学院心血管病研究所，协和医院 1心内科,2超声科,湖北 武汉 430022

收稿日期 2007-10-14 修回日期 2008-2-28 网络版发布日期 2009-2-22 接受日期 2008-2-28

摘要 目的： 研究二甲双胍对动脉粥样硬化家兔主动脉血管壁中NF-κB、IκBα表达和血清中高敏C反应蛋白（hs－CRP）浓度的影响，探讨其可能的抗动脉粥样硬化机制。方法:24只新西兰大耳白兔随机分为3组：空白对照组（control组）、粥样硬化组（AS组）和二甲双胍治疗组（Met组）。采用免疫内皮损伤加高胆固醇饮食的方法复制家兔动脉粥样硬化模型并经升主动脉高频超声证实，然后Met组给予二甲双胍150 mg·kg-1·d-1喂养8周,至第16周实验结束时抽血检测血脂、血清高敏C反应蛋白（hs-CRP）,分别采用免疫组织化学和Western blotting方法检测家兔主动脉中NF-κB p65亚基及其抑制蛋白IκBα的表达。 结果:与control组相比，AS组血清〖JP2〗hs-CRP显著增高（1.27±0.43 vs 3.96±0.63,P<0.01），主动脉血管壁中胞核NF-κB p65亚基表达增强（P<0.01）、〖JP〗胞浆IκBα表达明显减弱（P<0.01）；与AS组比较，Met组血清hs-CRP明显降低（2.79±0.40 vs 3.96±0.63,P<0.05），胞核NF-κB p65亚基表达减弱（P<0.05）、胞浆IκBα表达增强（P<0.05）。结论：二甲双胍能够抑制动脉粥样硬化家兔血管壁中IκB的降解和NF-κB的活化，并降低血清中hs-CRP，提示二甲双胍具有抗炎症作用，可能是其抗动脉粥样硬化的机制之一。

关键词 二甲双胍 动脉硬化 NF-κB C反应蛋白质 炎症

分类号 R363

Effects of metformin on nuclear factor-κB expression and serum high sensitivity C-reactive protein level in atherosclerosis model of rabbit

LI Song-nan[1],WANG Xiang[1],ZENG Qiu-tang[1],FENG Yi-bo[1],GUO He-ping[1],WANG Tian-hong[1],DENG He-ping[2]

1Department of Cardiology,2Department of Echocardiography,Union Hospital,Tongji Medical College,Huazhong University of Science and Technology,Wuhan 430022,China.E-mail: wxiang128@163.com

Abstract

<FONT face=Verdana>AIM: To investigate the effects of metformin on nuclear factor-κB (NF-κB),its inhibitor IκB,and the level of serum high sensitivity C-reactive protein (hs-CRP) in rabbits.
METHODS: 24 New Zealand male rabbits were randomly divided into control group,atherosclerosis (AS) group and metformin (Met) group.AS group and Met group were made as models by cholesterolenriched diets feeding and vascular intimal immunologic injury.The AS model was confirmed by high frequency ultrasound.Met group were given metformin 150 mg·kg-1·d-1 for 8 weeks.At the end of experiment,serum hs-CRP and serum lipids in all three groups were detected.Immunohistochemistry and Western blotting technique were applied to detect the expression of nucleus NF-κB p65 and cytoplasma IκBα in aorta in all three groups.
RESULTS: Compared to normal control group,the level of serum hs-CRP was elevated (1.27±0.43 vs 3.96±0.63,P<0.01),the expression of nucleus NF-κB p65 increased significantly (P<0.01) while the expression of IκBα reduced significantly (P<0.01).Compared to AS group,metformin significantly reduced the level of serum hs-CRP (2.79±0.40 vs 3.96±0.63,P<0.05) and the expression of nucleus NF-κB p65 (P<0.01),and increased the expression of IκBα (P<0.05).
CONCLUSION: Metformin inhibits the activation of NF-κB p65 and the degradation of IκBα,and decreases the levels of serum hs-CRP in AS rabbits.These results suggest that metformin exerts direct vascular anti-inflammatory effects.It may be one important mechanism of metformins antiatherogenic properties.</FONT>

Key words Metformin Arteriosclerosis NF-kappa B C-reactive protein Inflammation

DOI: 1000-4718

通讯作者 王祥 wxiang128@163.com