中国药理学与毒理学杂志 2006 20 (5): 381-386 ISSN: 1000-3002 CN: 11-1115/R

论著

阿伐他汀伍用大豆异黄酮预防大鼠脂质代谢紊乱的作用

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收稿日期 2006-3-7 修回日期 网络版发布日期 2008-5-22 接受日期 2006-5-22

摘要 目的 探讨阿伐他汀(AT)伍用大豆异黄酮(SI)调节大鼠脂质代谢紊乱的药效学及相关分子机制以提供联合疗法的科学依据。方法 采用喂养法建立食物性高脂血症大鼠模型，正常对照组和模型组给予蒸馏水，其他供试组给予不同剂量的药物: AT 20 mg·kg^{-1}, AT伍用SI(40 mg·kg^{-1}+120 mg·kg^{-1}, 20 mg·kg^{-1}+60 mg·kg^{-1}, 10 mg·kg^{-1}+30 mg·kg^{-1})，每日给药一次，连续给药12周。酶法测定血清中各项脂蛋白含量；制作冰冻切片进行病理学观察；RT-PCR检测肝脏组织低密度脂蛋白受体(LDLR)和载脂蛋白apoA-1的mRNA表达, Western 印迹检测LDLR蛋白表达变化。结果 AT伍用SI (40 mg·kg^{-1}+120 mg·kg^{-1}, 20 mg·kg^{-1}+60 mg·kg^{-1}) 与单用AT 20 mg·kg^{-1}相比，明显降低血清总胆固醇（TC）、甘油三酯（TG）、低密度脂蛋白（LDL-C）（P<0.05），明显升高高密度脂蛋白（HDL-C）（P<0.05）；AT伍用SI（10 mg·kg^{-1}+30 mg·kg^{-1}）与单用AT 20 mg·kg^{-1}相比，对指标TC, TG及LDL-C的作用具有药效等效性，明显升高HDL-C（P<0.05）；能够减少肝脏对脂蛋白颗粒的蓄积，RT-PCR实验和Western 印迹实验表明能够增强大鼠肝脏LDLR mRNA和蛋白的表达，并上调HDL-C代谢相关蛋白apoA-1 mRNA的表达。结论 AT伍用SI对高脂血症大鼠的血脂和脂蛋白代谢紊乱有预防作用，该脂质代谢紊乱调节作用机制与上调LDLR和apoA-1 mRNA表达及促进LDLR蛋白表达有相关性。

关键词 阿伐他汀 大豆异黄酮 脂蛋白 代谢

分类号 R972.6

Combined effects of atorvastatin and soybean isoflavones on hypercholesterolemia and lipoprotein metabolism

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Abstract

AIM To study the combined effects of atorvastatin and soybean isoflavones on hypercholesterolemia and lipoprotein metabolism to provide scientific basis for the combination therepy. **METHODS** The Sprague-Dawley rats were fed with high fatty diet for 12 consecutive weeks as hyperlipidemia model. The content of lipoprotein in serum, pathological process and mRNA expression of low density lipoprotein receptor and apoA-1 were detected by enzymatic analysis, frozen section, RT-PCR and Western blot respectively. **RESULTS** The combination of atorvastatin and soybean isoflavones decreased the contents of total cholesterol (TC), low density lipoprotein-C (LDL-C) and increased the content of high density lipoprotein-C(HDL-C), superior than using atorvastatin alone（P<0.05）. It inhibited the deposition of lipoprotein in liver. The results of RT-PCR and Western blot test showed the combination atorvastatin and soybean isoflavones (40 mg·kg^{-1}+120 mg·kg^{-1}, 20 mg·kg^{-1}+60 mg·kg^{-1}) were better than atorvastatin 20 mg·kg^{-1} in regulating the expression of LDL receptor(LDLR) and apoA-1 mRNA and LDLR protein expression (P<0.05), combination of atorvastatin and soybean isoflavones (10 mg·kg^{-1}+30 mg·kg^{-1}) upregulated apoA-1 mRNA expression better than atorvastatin 20 mg·kg^{-1} (P<0.05). **CONCLUSION** Combination of atorvastatin and soybean isoflavones can prevent lipid metabolism disorders through upregulation of LDLR and apoA-1 transcription level and LDLR protein level.

Key words atorvastatin soybean isoflavones lipoproteins metabolism

DOI:

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