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硝苯地平对ApoE$^{-/-}$小鼠RAW264.7巨噬细胞源性胆固醇逆向转运的影响(PDF)

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Title: Effect of nifedipine on macrophage reverse cholesterol transport in ApoE$^{-/-}$ mice

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关键词: 胆固醇逆向转运; 巨噬细胞; 硝苯地平; ApoE$^{-/-}$小鼠

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摘要: 目的 探讨硝苯地平对ApoE$^{-/-}$小鼠RAW264.7巨噬细胞源性胆固醇逆向转运的影响。 方法 8周龄左右ApoE$^{-/-}$小鼠16只，用高脂饲料喂养作为模型，按完全随机分组法分为对照组（n=8）和硝苯地平组（n=8）。将[^{3}H]-胆固醇标记的荷脂RAW264.7小鼠巨噬细胞注入小鼠腹腔，24、48 h时取血液标本，酶法检测血浆总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-c)和高密度脂蛋白胆固醇(HDL-c)的浓度。处死后取小鼠肝脏和小肠，实时定量PCR检测肝脏及小肠ABCA1、ABCG1、SR-BⅠ、LXRα基因的mRNA表达，Western blot检测其蛋白表达。同时，收集48 h小鼠粪便，进行闪烁液计数，分别比较2组[^{3}H]的含量。 结果 与对照组相比，经硝苯地平处理组血浆血脂蛋白水平均无明显变化（P>0.05）；血浆24、48 h闪烁值较对照组分别增加37.02%、22.72%（P<0.05），粪便[^{3}H]闪烁值较对照组增加43.18%（P<0.05）；硝苯地平组ABCA1、ABCG1、SR-BⅠ、LXRα基因的mRNA和蛋白的表达均有明显升高。 结论 硝苯地平通过增加LXRα及其下游基因ABCA1、ABCG1、SR-BⅠ的表达，从而增强ApoE$^{-/-}$小鼠巨噬细胞源性胆固醇逆向转运的效果。

Abstract: Objective To investigate whether nifedipine increases macrophage reverse cholesterol transport in ApoE$^{-/-}$ mice and its effect on the expression of related genes. Methods Sixteen eight-week-old male ApoE$^{-/-}$ mice (fed with high

fat and cholesterol) were randomly divided into 2 groups, control group and nifedipine group. RAW264.7 macrophages were loaded with cholesterol by incubation with acetylated-LDL, labeled with [^{3}H]-cholesterol, and then intraperitoneally injected into the mice. The blood samples were collected in 24 and 48 h after injection, the tissues and feces were collected in 48 h, and plasma concentrations of lipids, including TC, TG, LDL and HDL, were measured by biochemistry analyzer. Blood and feces were analyzed for tracer counts using a liquid scintillation counter. Related mRNA and protein levels of several well-characterized proteins involved in reverse cholesterol transportation, including ABCA1, ABCG1, SR-B Ⅰ and LXRα, were detected by quantitative real-time PCR and Western blotting. Results There was no significant difference in plasma lipid concentrations between the 2 groups（*P*>0.05）. The amount of [^{3}H]-tracer were 37.02% and 22.72% higher respective in the 24 and 48 h plasma than in control group, and was 43.18% higher in 48 h feces than in control group (*P*<0.5). The expression of related genes and proteins was all significantly enhanced in the nifedipine group than in the control group. Conclusion Nifedipine promotes the macrophage reverse cholesterol transportation through the stimulation of LXRα-dependent expression of ABCA1, ABCG1 and SR-B Ⅰ.

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