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论著

胰岛素样生长因子-1对高胆固醇血症患者内皮的保护作用及机制

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摘要:

目的:探讨血清胰岛素样生长因子-1 (insulin-like growth factor-1, IGF-1) 对高胆固醇血症血管内皮的保护作用及机制。方法:观察高胆固醇血症患者和正常对照(各25 例) 肱动脉血流介导的血管舒张功能(flow-mediatedarterial diastolic function, FMD), 并检测血清中IGF-1、非对称二甲基精氨酸(asymmetric dimethylarginine, ADMA)、一氧化氮合酶(nitric oxide synthase, NOS) 以及一氧化氮(NO) 水平;将培养的人脐静脉内皮细胞分为3 组:正常对照组、氧化型低密度脂蛋白(oxidized low-density lipoprotein, ox-LDL) 损伤组和IGF-1 干预组, 培养24 h 后, 检测各组细胞培养液中ADMA, NOS, NO 水平, 细胞裂解液中二甲基精氨酸二甲胺水解酶(dimethylarginine dimethylamine hydrolase, DDAH) 活性, 并进行β- 半乳糖苷酶染色, 计算细胞衰老率。结果:临床实验中, 高胆固醇血症患者FMD 显著下降;伴随血清IGF-1, NOS 以及NO 水平的下降, ADMA 水平升高。多元线性回归分析显示IGF-1 与FMD 呈正相关, ADMA 与FMD 呈负相关。细胞实验中, ox-LDL 处理24 h 后, 细胞裂解液DDAH 活性下降;伴随上清液中ADMA 水平升高, NOS 和NO 水平下降和细胞衰老率增加, 给予IGF-1 干预能部分逆转上述作用。结论:血液中IGF-1 水平下降可能是高胆固醇血症患者血管内皮舒张功能受损的重要原因之一;IGF-1 具有抗内皮细胞衰老作用, 其机制可能涉及对DDAH/ADMA 途径的调节。

关键词: 高胆固醇血症 胰岛素样生长因子-1 血管内皮功能 非对称二甲基精氨酸 细胞衰老

Protective effect of insulin-like growth factor-1 on vascular endothelial function in hypercholesterolemia and the underlying mechanism

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Abstract:

Objective: To investigate the relationship between insulin-like growth factor-1 (IGF-1) in the serum and the vascular endothelial function in patients with hypercholesterolemia and the underlying mechanism.
Methods: We examined the flow-mediated arterial diastolic function (FMD), the levels of IGF-1, asymmetric dimethylarginine (ADMA), NO, and the activity of nitric oxide synthase (NOS) in the serum from 25 patients with hypercholesterolemia and from healthy controls. An endothelial cell injury model was established by incubation of the human umbical vein endothelial cells (HUVECs) with oxidized low-density lipoprotein (ox-LDL) for 24 hours. Cells were treated with IGF-1 30 min before ox-LDL treatment. The levels of ADMA, NOS, and NO in the cell supernatant, the activity of dimethylarginine dimethylamine hydrolase (DDAH) in the cell lysate were measured. Beta-galactosidase staining was used to assess the degree of endothelial cell senescence by calculating the senescence rate of cells.
Results: Compared with the control group, the FMD, the levels of IGF-1 and NO, and the activity of NOS in the serum from patients with hypercholesterolemia decreased significantly accompanied with a dramatic increase at ADMA level. Multiple linear regression analysis showed that the change in IGF-1 was positively correlated with FMD while the change in ADMA was negatively correlated with FMD. Compared with the control group, ox-LDL treatments significantly decreased the activities of DDAH and NOS, and the level of NO, accompanied with an increase in ADMA. Betagalactosidase staining showed that the

senescence rate of cells increased in the ox-LDL group. The effect of ox-LDL on HUVECs was significantly attenuated at the presence of IGF-1.
Conclusion: The decrease in IGF-1 in the peripheral blood may contribute to vascular endothelial dysfunction in patients with hypercholesterolemia. IGF-1 can protect HUVECs against ox-LDLinduced senescence, which is likely involved in the regulation of DDAH/ADMA pathway.

Keywords: hypercholesterolemia insulin-like growth factor-1 asymmetric dimethylarginine vascular endothelial function cell senescence
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