

论著

非酒精性脂肪性肝病FOXO1的表达及意义 FREE

熊清芳, 谢玉桃, 谭德明, 候环荣

中南大学湘雅医院, 湖南 长沙 410008

摘要:

目的 研究非酒精性脂肪性肝病 (nonalcoholic fatty liver disease, NAFLD) 患者分叉头框家族转录因子1 (forkhead box containing protein O subfamily 1, FOXO1) 表达的变化, 以及转录因子和磷酸烯醇式丙酮酸羧激酶(phosphoenolpyruvate carboxykinase,PEPCK)、葡萄糖 6 磷酸酶催化亚基(G6PC)之间的关系。同时探讨FOXO1在NAFLD发病机制中的作用。方法 对临床与病理确诊的NAFLD患者, 用免疫组化法、逆转录聚合酶链反应 (RT PCR) 技术检测肝组织FOXO1的表达以及FOXO1、PEPCK和G6PC的mRNA水平。结果 非酒精性脂肪性肝炎 (nonalcoholic steatohepatitis, NASH) 组、非酒精性单纯性脂肪肝 (simple steatosis, SS) 组的胰岛素抵抗指数 (insulin resistance index, IR) 显著高于健康对照组 ( P <0.001); NASH组的血清丙氨酸转氨酶 (ALT) 显著高于SS组、对照组 ( P <0.001或 P <0.05), 而SS组与对照组之差异无显著性( P > 0.05); 3组的FOXO1阳性细胞数、FOXO1 mRNA、PEPCK mRNA、G6PC mRNA随病情的加重逐渐增加, 组间差异有显著性 ( P <0.001)。FOXO1 mRNA水平与IR、炎症评分和脂肪变性评分、PEPCK mRNA和G6PC mRNA表达正相关。结论 不能根据ALT正常与否决定是否肝穿刺活检。NASH患者的FOXO1表达和活性增强, FOXO1转录因子调节PEPCK和G6PC的表达, 并与胰岛素抵抗有关。推测脂肪变性和炎性反应参与了FOXO1的调节。

关键词: 脂肪肝; 非酒精性脂肪性肝病; 分叉头框家族转录因子1; 胰岛素抵抗

Expression and role of forkhead box containing protein O subfamily 1 in patients with nonalcoholic fatty liver disease FREE

XIONG Qing fang, XIE Yu tao,TAN De ming, HOU Huan rong

Xiangya Hospital, Central South University,Changsha 410008, China

Abstract:

Objective To study the expression of forkhead box containing protein O subfamily 1 (FOXO1) in patients with nonalcoholic fatty liver disease (NAFLD) and relationship with expression of phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6 phosphatase catalytic subunit (G6PC) , and to evaluate the effect of FOXO1 on the pathogenesis of NAFLD. Methods NAFLD patients were confirmed by clinical and pathological methods. Localization of FOXO1 was observed by immunocytochemistry; FOXO1, PEPCK and G6PC mRNA levels were observed by RT PCR. Results The homeostasis model assessment of insulin resistance (HOMA IR) were higher in nonalcoholic steatohepatitis (NASH ) and simple steatosis (SS) group compared with control group ( P < 0.001); alanine transaminase (ALT) was higher in NASH group compared with SS and control group ( both P <0.001,or P <0.05 ), but there was no significant difference between SS and control group ( P >0.05); With the progress of disease, there were a gradual increase of percentage of hepatocytes with FOXO1 and mRNA levels of FOXO1, PEPCK and G6PC in three groups, there was significant difference between each group ( P <0.001). FOXO1 mRNA levels were positive correlated with HOMA IR, the degree of steatosis and necroinflammatory activity, the expression of both PEPCK mRNA and G6PC mRNA. Conclusion NAFLD patients with normal ALT should also undergo liver biopsy. Expression and activity of FOXO1 are increased in hepatocytes in NASH. FOXO1 mediates the effect of insulin on the gluconeogenic genes PEPCK and G6PC. Steatosis and inflammation are involved in FOXO1 regulation .

[Key words] fatty liver; nonalcoholic fatty liver disease; forkhead box containing protein O subfamily 1; insulin resistance

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通讯作者: 谢玉桃

作者简介: 熊清芳(1973-), 女(汉族), 湖北省通山县人, 医师, 主要从事肝病临床研究。

作者Email: E-mail: drXieyutao@tom.com

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