

论著

二甲双胍对2型糖尿病合并非酒精性脂肪肝大鼠肝脏 SIRT1和UCP2表达的影响

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摘要: 目的: 观察二甲双胍对2型糖尿病(T2DM)合并非酒精性脂肪肝(NAFLD)大鼠肝脏沉默调节蛋白1(SIRT1)、线粒体脱偶连蛋白2(UCP2)表达的影响, 探讨其对T2DM合并NAFLD的干预治疗效果及可能机制。方法: 雄性SD大鼠36只, 随机分为正常对照组(NC组, 12只)、T2DM合并NAFLD对照组(MC组, 12只)和T2DM合并NAFLD二甲双胍治疗组(A组, 12只)。通过高脂高糖饮食加小剂量链脲佐菌素建立T2DM合并NAFLD大鼠模型。建模成功后, A组给予二甲双胍300 mg/(kg.d)灌胃8周。实验结束时测各组大鼠空腹血糖(FBG)、肝功能、血脂、游离脂肪酸(FFA)、空腹胰岛素(FINs); 观察肝组织的病理变化; 免疫组织化学法及Real-time PCR法测定肝组织中SIRT1和UCP2的表达情况。结果: MC组大鼠FBG, ALT, AST, TC, TG, LDL-C, VLDL, FFAs, FINs, HOMA-IR均较NC组大鼠升高($P<0.05$), HDL-C较NC组减低($P<0.05$); 给予二甲双胍治疗后, 大鼠上述血清学指标均较MC组有所改善($P<0.05$), MC组大鼠肝脏SIRT1表达较NC组明显降低($P<0.05$), 而UCP2表达较NC组明显升高($P<0.05$), 经二甲双胍治疗后, SIRT1表达较MC组升高($P<0.05$), 而UCP2较MC组降低($P<0.05$)。SIRT1与UCP2的表达呈负相关($r=-0.61$, $P<0.01$)。结论: 在T2DM合并NAFLD大鼠肝组织中SIRT1表达明显降低, UCP2表达明显升高, 而二甲双胍可以上调SIRT1的表达及下调UCP2的表达, 并且SIRT1与UCP2的表达存在负向调节关系。

关键词: 2型糖尿病 非酒精性脂肪肝 沉默调节蛋白1 线粒体脱偶连蛋白2 二甲双胍

Effect of metformin on the expression of SIRT1 and UCP2 in rat liver of type 2 diabetes mellitus and nonalcoholic fatty liver

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Abstract: Objective: To observe the effect of metformin on the expression of SIRT1 and UCP2 in rat liver of type 2 diabetes mellitus (T2DM) with nonalcoholic fatty liver disease (NAFLD), and discuss the pathogenesis of T2DM with NAFLD, and the treatment with and possible mechanism of metformin. Methods: Thirty-six male SD rats were randomly divided into a normal control group (group NC, $n=12$), a T2DM with NAFLD group (group MC, $n=12$), and a metformin group (group A, $n=12$). We established the model of T2DM with NAFLD rats by feeding high-fat and high-sugar diet and injecting STZ. After the success establishment of the model, the metformin group was given metformin 300 mg/(kg.d) for 8 weeks. At the end of the experiment, we measured FBG, ALT, AST, TC, TG, HDL-C, LDL-C, VLDL, FFAs, FINs and HOMA-IR respectively in group NC, MC and A. We observed the change of liver tissue pathology by HE, determined the expression of SIRT1 and UCP2 in rat liver by immunohistochemical method and real-time quantitative method.

Results: FBG, ALT, AST, TC, TG, LDL-C, VLDL, FFAs, FINs and HOMA-IR were higher in group MC than in group NC ($P<0.05$), while HDL-C was obviously lower in group MC than in group NC ($P<0.05$). After the metformin treatment, the serum parameters in the rats had improved in group NC compared with in group MC ($P<0.05$). On immunohistochemical staining and mRNA level, the expression of SIRT1 was obviously lower in group MC than in group NC ($P<0.05$), and the expression of UCP2 was obviously higher in group MC than in group NC ($P<0.05$). After the metformin treatment, the expression of SIRT1 was higher than in group MC ($P<0.05$), and the expression of UCP2 was lower than in group MC ($P<0.05$). There was negative correlation between the expression of SIRT1 and UCP2 ($r=-0.61$, $P<0.01$). **Conclusion:** The expression of SIRT1 is low and the expression of UCP2 is high in rat liver of T2DM with NAFLD. Metformin can increase the expression of SIRT1 and reduce the expression of UCP2, with negative correlation between the expression of SIRT1 and UCP2.

Keywords: type 2 diabetes mellitus nonalcoholic fatty liver disease SIRT1 UCP2 metformin

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