

益肾通络方改善高糖诱导的肾小管上皮细胞损伤及其对 SIRT3-AMPK/PGC-1 α /CPT1A 通路的影响^Δ

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摘要 **目的** 探讨益肾通络方对高糖诱导的肾小管上皮细胞损伤的改善作用及其对沉默信息调节因子3(SIRT3)-腺苷一磷酸活化蛋白激酶(AMPK)/过氧化物酶体增殖物激活受体 γ 共激活因子1 α (PGC-1 α)/肉碱棕榈酰基转移酶1A(CPT1A)信号通路的影响。**方法** 以人肾小管上皮细胞HK-2为对象,将其分为正常糖组(NC组)、高糖组(HG组)、高糖+益肾通络方低剂量组[HG+L组, 0.5 mg/mL(以总生药量计)]、高糖+益肾通络方高剂量组[HG+H组, 1.0 mg/mL(以总生药量计)]。除NC组外,其余各组细胞均在高糖(30 mmol/L)条件下培养, HG+L、HG+H组细胞同时接受相应质量浓度药液干预。检测各组细胞培养0、24、48 h时的细胞活力,以及培养48 h后的活性氧(ROS)水平、腺苷三磷酸(ATP)含量和SIRT3-AMPK/PGC-1 α /CPT1A信号通路相关分子的表达情况。**结果** 与NC组比较, HG组细胞活力(培养24、48 h)及ATP含量均显著降低, ROS水平显著升高($P<0.05$); SIRT3、PGC-1 α 、CPT1A蛋白表达, PGC-1 α 、CPT1A mRNA表达, 以及AMPK蛋白磷酸化水平均显著下调或降低($P<0.05$)。与HG组比较, HG+L、HG+H组细胞上述指标均显著改善, 且HG+H组的改善更为明显($P<0.05$)。**结论** 益肾通络方可改善高糖诱导的肾小管上皮细胞损伤, 其作用可能与激活SIRT3-AMPK/PGC-1 α /CPT1A信号通路、改善线粒体能量代谢、减轻氧化应激有关。

关键词 益肾通络方; 肾小管上皮细胞; 高糖; 能量代谢; 氧化应激; SIRT3-AMPK/PGC-1 α /CPT1A信号通路

Effects of Yishen tongluo formula on high glucose-induced injury in renal tubular epithelial cells and its impact on the SIRT3-AMPK/PGC-1 α /CPT1A pathway

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ABSTRACT **OBJECTIVE** To investigate the protective effect of Yishen tongluo formula on high glucose-induced injury in renal tubular epithelial cells and its impact on the silence information regulator 3 (SIRT3)-adenosine monophosphate-activated protein kinase (AMPK)/peroxisome proliferator-activated receptor γ coactivator-1 α (PGC-1 α)/carnitine palmitoyltransferase 1A (CPT1A) signaling pathway. **METHODS** Human renal tubular epithelial cells HK-2 were used as the subject. The cells were divided into a normal glucose group (NC group), a high glucose group (HG group), a high glucose+low-dose Yishen tongluo formula group [HG+L group, 0.5 mg/mL (calculated by crude drugs)], and a high glucose+high-dose Yishen tongluo formula group [HG+H group, 1.0 mg/mL (calculated by crude drugs)]. Except for the NC group, cells in all other groups were cultured under high glucose conditions (30 mmol/L), and cells in the HG+L and HG+H groups were simultaneously treated with the corresponding mass concentrations of medicinal liquid. Cell viability was assessed at 0, 24, and 48 h post-incubation, and reactive oxygen species (ROS) level, adenosine triphosphate (ATP) content, and the expression of molecules related to the SIRT3-AMPK/PGC-1 α /CPT1A signaling pathway were measured after 48 h of incubation. **RESULTS** Compared with the NC group, the HG group showed significantly reduced cell viabilities (at 24 and 48 h) and ATP content, along with significantly elevated ROS levels ($P<0.05$). Additionally, the protein expressions of SIRT3, PGC-1 α and CPT1A, as well as the mRNA expressions of PGC-1 α and CPT1A, and the phosphorylation level of AMPK protein were all significantly downregulated or decreased ($P<0.05$). Compared with the HG group, the aforementioned indicators were significantly improved in both HG+L and HG+H groups, with the improvement being more pronounced in the HG+H group ($P<0.05$). **CONCLUSIONS** The Yishen tongluo formula can

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