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论著

18 α-甘草酸二铵与格列本脲联用对实验性糖尿病大鼠糖代谢的影响及其机制

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摘要 目的 探讨18 α-甘草酸二铵(DG)是否影响格列本脲(Gli)的代谢及降糖效应，联用的效应及其机制。方法 观察DG (25 mg·kg^{-1}·d^{-1}，ip，×5 d)及与Gli(1 mg·kg^{-1}·d^{-1}，ig，×5 d)联用对实验性糖尿病大鼠空腹血糖、血浆胰岛素、胰岛素敏感性指数、肝糖原及CYP3A活性的影响。免疫组化方法观察胰岛及B细胞形态结构变化，定量分析胰岛素表达水平。结果 与模型组相比，DG与Gli联用比单用Gli进一步降低空腹血糖，上调胰岛素及肝糖原水平。DG单用或联用Gli均抑制CYP3A活性并下调肝损伤指标。DG联用Gli时，随CYP3A活性下降，胰岛素及空腹血糖下降率均提高。免疫组化显示，DG可进一步改善Gli对胰岛及B细胞形态结构的影响，并使胰岛素分泌增加。结论 DG可增强Gli降糖效应，其机制可能与其抑制CYP3A活性，使Gli代谢延缓，致使降糖效应增强并与其促进胰岛B细胞修复和再生有关，提示DG有作为口服降糖药辅助用药的可能性。

关键词 糖尿病, 实验性 18 α-甘草酸二铵 格列本脲 药物协同作用 血糖 胰岛素 细胞色素P450 CYP3A 肝功能试验

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Mechanism of combined action of 18 α-diammonii glycyrrhizinatis and glibenclamide on glucose metabolism in experimental diabetic rats

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Abstract

AIM To investigate whether 18 α-diammonii glycyrrhizinatis(DG) influences the metabolism and hypoglycemic effect of glibenclamide(Gli), their combined action and mechanism. **METHODS** DG(25 mg·kg^{-1}·d^{-1}, ip) and/or Gli(1 mg·kg^{-1}·d^{-1}, ig) were given to the alloxan(150 mg·kg^{-1}, ip)induced diabetic rats for 5 consecutive days. The fasting plasma glucose(FPG), plasma insulin, insulin sensitivity index (ISI), hepatin and the activities of CYP3A were measured. Pathological morphology of pancreatic islets and B cell and the expression of insulin were investigated by immunohistochemical method and image analysis. The markers of liver injury were also observed. **RESULTS** Treated with Gli, FPG reduced by 28%, insulin and hepatin increased by 65% and 64%, respectively, as compared with model group. Treated with DG+Gli, FPG reduced by 69%, insulin and hepatin increased by 172% and 179% as compared with model group, which were significantly different from Gli-treated group. The activities of CYP3A and the markers of liver injury significantly decreased in rats treated with DG and DG+Gli. The activities of CYP3A were negatively correlated with insulin and the reduction rate of FPG in rats treated with DG+Gli. The results of immunohistochemistry showed that DG could potentiate the effect of Gli on the pathological morphology of pancreatic islets and B cell and the intensities of positive immunostaining for insulin. **CONCLUSION** DG potentiates the hypoglycemic effect of Gli, which may be associated with the inhibition of the activities of CYP3A and promoting the repair and regeneration of the damaged islet B cell. The results suggest that DG has the possibility to be used as an adjuvant drug of oral hypoglycemic agents.

Key words diabetes mellitus experimental 18 α-diammonii glycyrrhizinatis glibenclamide drug synergism blood glucose insulin cytochrome P-450 CYP3A liver function tests

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