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论著

酮替芬对2型糖尿病大鼠胰岛β细胞氧化应激的影响

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摘要 目的 探讨酮替芬对2型糖尿病大鼠胰岛β细胞氧化应激的影响及其作用机制。方法 以高糖高脂饲料对SD大鼠饮食诱导6周，随后一次性ip给予链脲佐菌素制备糖尿病大鼠模型，每天ig给予酮替芬0.09 mg·kg^{-1}，持续8周。检测空腹血糖(FBG)、游离脂肪酸(FFA)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、白介素6(IL-6)、肿瘤坏死因子α(TNF-α)；检测胰腺丙二醛(MDA)含量和超氧化物歧化酶(SOD)活性，检测胰腺细胞线粒体细胞色素C氧化酶(CCO)、琥珀酸脱氢酶(SDH)活性，电镜观察组织形态。结果 与正常对照组比较，模型组大鼠FBG水平显著升高(P<0.01)，FFA，TG和LDL-C水平升高(P<0.05)，IL-6，TNF-α水平升高(P<0.05)，MDA含量增加(P<0.05)，SOD，CCO和SDH活性下降(P<0.05)，与模型组比较，给予酮替芬同步干预后，FBG水平下降((24.5±2.7) *vs* (15.9±1.9) mmol·L^{-1})，FFA，TG和LDL-C水平由1.03±0.23，2.89±0.56和(2.05±0.33) mmol·L^{-1}分别降低至0.71±0.15，2.36±0.40和(1.56±0.30) mmol·L^{-1}，IL-6，TNF-α水平由(58.33±4.94) ng·L^{-1}和(1.98±0.45) μg·L^{-1}分别下降至(33.84±3.82) ng·L^{-1}和(1.12±0.27) μg·L^{-1}，MDA含量减少((1.12±0.20) *vs* (0.87±0.20) μmol·g^{-1}，SOD，CCO和SDH活性由(28.55±4.06) kU·g^{-1}，(13.00±1.14) mmol·g^{-1}和(3.75±0.44) kU·g^{-1}分别增加到(31.34±2.59) kU·g^{-1}，(15.87±1.64) mmol·g^{-1}和(4.92±0.50) kU·g^{-1}，电镜结果显示，酮替芬的干预使胰岛β细胞形态结构得到改善。结论 酮替芬能够降低糖尿病大鼠炎症介质和游离脂肪酸水平，减轻氧化应激损伤，使胰岛细胞线粒体功能改善，实现对胰岛β细胞的保护作用。

关键词 酮替芬 糖尿病 2型 胰岛β细胞 氧化应激
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Effect of ketotifen on oxidative stress of pancreatic beta cells of type 2 diabetic rats

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Abstract

OBJECTIVE To investigate the effect and mechanism of ketotifen on oxidative stress of pancreatic beta cells in streptozotocin-induced type 2 diabetic rats. **METHODS** Male SD rats were fed with high-carbon hydrate-fat diet 6 weeks and ip given STZ to induce a type 2 diabetes model. Rats of ketotifen group were given ketotifen 0.09 mg·kg^{-1} for 8 weeks. The fasting blood glucose (FBG), free fatty acid (FFA), triglyceride(TG) and low density lipoprotein cholesterin (LDL-C), interleukin-6(IL-6) and tumor necrosis factor-alpha (TNF-α) were analyzed,the content of malondialdehyde(MDA) and the activity of superoxide dismutase (SOD) in pancreatic tissue were measured,the activities of cytochrome C oxidase (CCO) and succinate dehydrogenase (SDH) in pancreatic cells mitochondria were tested,Histomorphology were observed by transmission electron microscope. **RESULTS** Compared with normal control group,FBG levels in diabetic rats significantly increased (P< 0.01), FFA, TG and LDL-C levels in diabetic rats increased(P<0.05), IL-6 and TNF-α levels in diabetic rats increased (P<0.05), the content of MDA increased while the activites of SOD, CCO and SDH decreased(P<0.05). Compared with model group, ketotifen 0.09 mg·kg^{-1} suppressed serum glucose in diabetic rats to (15.9

±1.9)mmol • L^{-1}, and reduced FFA, TG and LDL-C levels to 0.71±0.15, 2.36±0.40 and (.56±0.30) mmol • L^{-1}. Ketotifen 0.09 mg • kg^{-1} could significantly decrease IL-6 and TNF-α levels to (33.84± 3.82)ng • L^{-1} and (1.12±0.27)μg • L^{-1}, reduced MDA content to (0.87±0.20)μmol • g^{-1}, and increased the activites of SOD, CCO and SDH to (31.34±2.59)kU • g^{-1}, (15.87±1.64)mmol • g^{-1} and (4.92± 0.50)kU • g^{-1}. Transmission electron microscope observation showed that beta cells morphological