

目的 通过制备糖尿病肾病微炎性反应动物模型,探讨慢性炎性反应在糖尿病肾病进展中的作用及意义。方法 选取8周龄雄性db/db小鼠及对照组db/m小鼠,分别按随机数字表法分为db/db、db/m、db/m+酪蛋白组及db/db+酪蛋白组,每组均为8只。db/m+酪蛋白组及db/db+酪蛋白组隔日给予背部皮下注射10%酪蛋白溶液0.5 ml以刺激产生慢性、持续性、微炎性反应;db/m组及db/db组隔日给予背部皮下注射蒸馏水0.5 ml。每周称体质量、收集24 h尿液、检测24 h尿蛋白量,8周后处死,收集血清标本、留取肾组织,检测血清淀粉样蛋白A(SAA)、肿瘤坏死因子 $\alpha$ (TNF- $\alpha$ )浓度,病理染色及免疫组化观察肾小球病理改变,免疫组化及Western印迹法观察肾脏炎性因子及足细胞特异性标志蛋白的表达情况,并评估微炎性反应模型的建立在糖尿病肾病研究中的作用及意义。结果 db/m+酪蛋白组及db/db+酪蛋白组血清炎性因子SAA[(13.83 $\pm$ 0.29) mg/L比(1.52 $\pm$ 0.19) mg/L, P<0.05; (13.84 $\pm$ 0.28) mg/L比(1.67 $\pm$ 0.58) mg/L, P<0.05]及TNF- $\alpha$ [(14.23 $\pm$ 1.42) ng/L比(10.70 $\pm$ 1.38) ng/L, P<0.05; (14.54 $\pm$ 1.91) ng/L比(10.88 $\pm$ 1.22) ng/L, P<0.05]水平均显著高于其对照组,且肾组织中单核细胞趋化蛋白1(MCP-1)、TNF- $\alpha$ 蛋白表达亦高于其对照组;db/db+酪蛋白组小鼠尿蛋白量、肾小球病理改变、足突结构改变及数量减少程度与db/db组相比明显加重,但db/m+酪蛋白组与db/m组间无明显差别。结论 本研究通过构建糖尿病肾病微炎性反应动物模型证实,持续存在的慢性炎性反应在加速糖尿病肾病进展中扮演着重要作用。

Objective To investigate the effects of inflammatory stress on the progression of diabetic nephropathy (DN) through making an inflamed animal model of DN. Methods Male db/db mice and db/m mice were randomly divided into four groups: db/m group (control, n=8), casein injected db/m (db/m+casein, n=8), db/db mice (db/db, n=8), and casein injected db/db mice (db/db+casein, n=8). Chronic inflammation was induced by subcutaneously injection of 0.5 ml 10% casein to db/m+casein and db/db+casein groups every another day while db/m and db/db mice as the control were injected with 0.5 ml distilled water. Body weight and 24-hour urinary protein were measured every week. The plasma levels of serum amyloid A (SAA) and tumor necrotic factor- $\alpha$  (TNF- $\alpha$ ) were detected by enzyme-linked immunosorbent assay. Renal pathological changes were detected and evaluated by renal pathological staining and electron microscope. Immunohistochemical staining and Western blotting were used to detect the expression of podocyte specific proteins and inflammatory cytokines. Results The plasma levels of SAA[(13.83 $\pm$ 0.29) mg/L vs (1.52 $\pm$ 0.19) mg/L, P<0.05; (13.84 $\pm$ 0.28) mg/L vs (1.67 $\pm$ 0.58) mg/L, P<0.05] and TNF- $\alpha$ [(14.23 $\pm$ 1.42) ng/L vs (10.70 $\pm$ 1.38) ng/L, P<0.05; (14.54 $\pm$ 1.91) ng/L vs (10.88 $\pm$ 1.22) ng/L, P<0.05] were significantly increased in db/m+casein and db/db+casein group compared to that in db/m and db/db group respectively. Furthermore, the 24-hour urinary protein in casein injected db/db mice was markedly increased compared with db/db group. There were more significant renal pathological injuries and podocyte damage in casein injected db/db mice compared with db/db mice when compared with db/db group. There were no difference in casein injected db/m mice compared with db/m mice. Conclusion Inflammatory stress plays important roles in accelerating the progression of DN.



## 慢性炎性反应对糖尿病肾病的促进作用

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### Inflammatory stress exacerbates the progression of diabetic nephropathy

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摘要

图/表

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