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论著

六味地黄汤活性成分组方LW-AFC对高热量饲料诱导小鼠代谢综合征的改善作用

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摘要 目的 研究中药新药LW-AFC对代谢综合征(MS)的作用及其作用机制。方法 高热量饲料喂养昆明小鼠6周，同时每天ig给予二甲双胍(阳性对照药)0.2 g·kg^{-1}和LW-AFC 0.2,0.8和3.2 g·kg^{-1}。实验结束时测量小鼠体质量和摄食量，检测空腹血清总胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)、C肽、血糖(FBG)和胰岛素(FINS)含量，并计算稳态模型胰岛素抵抗评价指数(HOMA-IR)；测定小鼠内脏脂肪质量(VFM)、计算内脏脂肪系数(VFC)，并检测血清瘦素、抵抗素、肿瘤坏死因子α(TNF-α)、白细胞介素6(IL-6)和下丘脑神经肽Y(NPY)含量。TC和FBG含量用酶比色法检测，LDL-C和HDL-C含量用清除法检测，FINS和NPY含量用放射免疫分析法检测，C肽含量用均相酶联免疫法检测，瘦素、抵抗素、TNF-α和IL-6含量用液相芯片(luminex)法检测，并采用伊红染色法观察肝脏病理改变。结果 与正常对照组比较，模型组小鼠腹型肥胖相关指标VFM和VFC、脂代谢相关指标TC和LDL-C和糖代谢相关指标FBG增高(P<0.01)，肝细胞呈弥漫性小泡性脂变，日均摄食量增高(P<0.01)，促食欲肽NPY、抑食欲激素瘦素和抵抗素增高(P<0.05)。与模型组比较，LW-AFC 0.2,0.8和3.2 g·kg^{-1}可降低TC(P<0.05)和LDL-C(P<0.01)、升高HDL-C(P<0.05, P<0.01)等脂代谢相关指标水平，降低FBG, HOMA-IR和C肽(P<0.05, P<0.01)等糖代谢相关指标的水平，并可减轻肝脏小泡性脂变等病理损害，提示LW-AFC对模型小鼠糖脂代谢紊乱及肝脏病理损伤具有改善作用。LW-AFC 0.2,0.8和3.2 g·kg^{-1}可降低小鼠的日均摄食量和促食欲肽NPY水平(P<0.05)，但可显著增高抑食欲激素瘦素的水平(P<0.01)，提示LW-AFC对模型小鼠的食欲具有抑制作用。不同剂量的LW-AFC还可降低血清脂肪因子抵抗素和炎症细胞因子TNF-α和IL-6的水平(P<0.05, P<0.01)；变量聚类分析结果表明，炎症因子IL-6与脂代谢关系密切，抑食欲激素瘦素与糖代谢关系密切，而抵抗素与炎症及食欲关系密切。结论 LW-AFC可调节血脂、降血糖、改善胰岛素敏感性、减轻肝脏病理损伤，从而改善代谢综合征。通过降低促食欲激素、升高抑食欲激素水平而抑制食欲以及降低炎症细胞因子分泌可能是其改善代谢综合征的部分作用机制。

关键词 代谢综合征 高热量饲料 炎症 抵抗素 食欲 六味地黄汤 LW-AFC

分类号 R285

Improvement effect of LW-AFC, an active component of prescription from Liuwei Dihuang decoction, on metabolic syndrome induced by high energy diet in mice

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Abstract

OBJECTIVE To evaluate the effect and mechanism of LW-AFC, an active component from Liuwei Dihuang decoction, against metabolic syndrome (MS) in a high-energy-diet induced model mice with similar characters of human MS. **METHODS** The models of high-caloric-diet-induced Kunming mice were ig given with metformin 0.2 g·kg^{-1} or LW-AFC 0.2, 0.8 and 3.2 g·kg^{-1} consecutively for 6 weeks. At the end of the expreiment, the food intake and body mass of mice were dynamically weighted, and the fast blood total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), connecting peptide, glucose (FBG), and fasting blood insulins (FINS) were measured. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated after that. The mice were sacrificed, and the coel-fat and orchio-fat were collected and weighted as visceral fat mass (VFM), and the visceral fat coefficient (VFC) was calculated. The levels of serum leptin, resistin, tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) (Luminex method), TC and FBG (oxidase method), LDL-C and HDL-C (clearance method), FINS and NPY (radioimmunoassay) were also detected. Histological micrographs of liver were stained by hematoxylin-eosin. **RESULTS** Compared with normal control group, TC, LDL-C, FBG, HOMA-IR and connecting peptide significantly decreased (P<0.01) in diet induced mouse MS model. LW-AFC improved hepatic steatosis, decreased food intake (P<0.05), NPY (P<0.05), resistin (P<0.05), TNF-α (P<0.05) and IL-6 (P<0.05, P<0.01), and increased leptin levels (P<0.01), though it had no effect on abdominal obesity and serum insulin levels. The variable cluster analysis showed that IL-6 level was close to lipid metabolism, the level of leptin was close to glucose metabolism, and resistin level was close to appetite and

inflammation. **CONCLUSION** LW-AFC might improve MS by reducing hyperglycemia, improving dyslipidemia, increasing insulin sensitivity and reducing the pathologic damage of fatty liver. The possible mechanism might be partly related to its suppressing the appetite and decreasing the levels of inflammatory cytokines.

Key words metabolic syndrome high energy diet inflammation resistin appetite Liuwei Dihuang decoction LW-AFC

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