中南大学学报(医学版) 2011, 36(10) 949-957 DOI: 10.3969/j.issn.1672-7347.2011.10.004 ISSN: 1672-7347 CN: 43-1427/R

药理学专栏

视黄醇结合蛋白4基因多态性对中国2型糖尿病患者服用罗格列酮疗效的影响

周芳[1,2], 黄琼[1], 戴幸平[1], 尹继业[1], 吴静[3], 周宏灏[1], 龚志成[4], 刘昭前[1]

1. 中南大学临床药理研究所,遗传药理学湖南省重点实验室, 长沙 410078;
2. 岳阳职业技术学院生物医药系, 湖南 岳阳 414000;
3. 湘雅医院内分泌科, 长沙 410008;
4. 湘雅医院药剂科, 长沙 410008

摘要：

目的: 研究视黄醇结合蛋白4(retinol binding protein 4, *RPB4*)基因rs3758539 *G-803A* 和rs10882283 *T-179G* 多态性对中国人群2型糖尿病患者使用罗格列酮疗效的影响。方法: 使用PCR-RFLP方法对472名2型糖尿病患者和198名健康对照者进行 *RPB4基因G-803A* 和 *T-179G* 多态性位点的基因分型。随机选择42名携带不同 *RBP4* 基因型的2型糖尿病患者给予12周每天4 mg的罗格列酮口服治疗。检测用药前后空腹血糖(fasting plasma glucose, FPG)、餐后血糖(postprandial plasma glucose, PPG)、空腹胰岛素(fasting serum insulin, FINS)、餐后胰岛素(postprandial serum insulin, PINS)、糖化血红蛋白(glycated hemoglobin, HbAlc)、甘油三酯(triglyceride, TG)、低密度脂蛋白胆固醇(low-density lipoprotein-cholesterol, LDL-c))和高度脂蛋白胆固醇(high-density lipoprotein-cholesterol, HDL-c)等指标。结果: 携带 *RBP4 G-803A* GG基因型的患者其TG和LCL-c水平显著低于GA+AA基因型患者。携带 *T-179G* TT基因型的患者其腰臀比、FPG和FINS值显著低于TG+GG基因型患者。携带 *RBP4 G-803A* GG基因型的患者服用罗格列酮后FPG和FINS下降值优于 GA+AA基因型患者。携带 *T-179G* TG+GG基因型的患者服用罗格列酮后的HbAlc下降值优于TT基因型患者。结论: *RBP4 G-803A* 和 *T-179G* 基因多态性与2型糖尿病相关且影响罗格列酮的疗效。

关键词： 视黄醇结合蛋白4 基因多态性 2型糖尿病 罗格列酮 疗效

Impact of retinol binding protein 4 polymorphism on rosiglitazone response in Chinese Type 2 diabetic patients

ZHOU Fang[1,2], HUANG Qiong[1], DAI Xingping[1], YIN Jiye[1], WU Jing[3], ZHOU Honghao[1], GONG Zhicheng[4], LIU Zhaoqian[1]

1. Institute of Clinical Pharmacology, Hunan Key Laboratory of Pharmacogenetics, Central South University, Changsha 410078;
2. Department of Biomedical, Yueyang Vocational and Technical College, Yueyang Hunan 414000;
3. Department of Endocrinology, Xiangya Hospital, Central South University, Changsha 410008;
4. Department of Pharmacy, Xiangya Hospital, Central South University, Changsha 410008, China

Abstract:

Objective To explore the association between rs3758539*G-803A* and rs10882283*T-179G* polymorphism of retinol binding protein 4 (RBP4) and rosiglitazone response in Chinese type 2 diabetes mellitus (T2DM) patients. Methods A total of 472 Chinese T2DM patients and 198 healthy subjects were enrolled to identify *G-803A* and *T-179G* genotypes using a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay. Forty-two T2DM patients with different *G-803A* or *T-179G* genotypes were selected to undergo a 12-week rosiglitazone treatment (4 mg/d). Serum fasting plasma glucose (FPG), postprandial plasma glucose (PPG), fasting serum insulin (FINS), glycated hemoglobin (HbAlc), postprandial serum insulin (PINS), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-c), and high-density lipoprotein-cholesterol (HDL-c) were determined before and after the rosiglitazone treatment. Results T2DM patients with *RBP4 G-803A* GG genotype showed lower TG and LDL-c concentrations compared with that in the GA+AA genotype subjects. T2DM patients with RBP4 *T-179G* TT genotype showed lower waist-to-hip ratio (WHR), FPG and FINS values compared with that in the TG+GG genotype individuals. Patients with GG genotype of *RBP4 G-803A* had an enhanced rosiglitazone efficacy on FPG and FINS compared with that in the GA+AA genotype group. Patients with RBP4 *T-179G* TG+GG genotype showed an enhanced rosiglitazone efficacy on HbAlc level compared with that in the TT genotype group. Conclusion *RBP4 G-803A* and *T-179G* polymorphism might be associated with the development of T2DM and affect the therapeutic efficacy of rosignitazone in Chinese T2DM patients.

Keywords: retinol binding protein 4 polymorphism Type 2 diabetes mellitus rosiglitazone therapeutic efficacy

收稿日期 2010-12-15 修回日期 网络版发布日期

DOI: 10.3969/j.issn.1672-7347.2011.10.004

基金项目:

This work was supported by the National High-Tech R&D Program of China ("863" Program) (2009AA22704), the National Natural Science Foundation of China (30873089, 81173129), the Program for Changjiang Scholars and Innovative Research Team in University (IRT0946), the Open Foundation of Innovative Platform in University of Hunan Pro-vince of China (10K078), and the Science and Technology Plan Key Grant of Hunan Province of China (2009TP4068-2), the Fundamental Research Funds for the Central Universities (201023100001).

通讯作者: LIU Zhaoqian, E-mail:liuzhaoqian63@126.com

作者简介: ZHOU Fang, Ph.D., lecturer, mainly engaged in the research of clinical pharmacology.

作者Email: liuzhaoqian63@126.com

参考文献:

[1] Stumvoll M, Goldstein B J, van Haeften T W. T2DM: principles of pathogenesis and therapy [J] . Lancet, 2005,365(9467):1333-1346.

[2] Graham T E, Yang Q, Bluher M, et al. Retinol-binding protein 4 and insulin resistance in lean, obese, and diabetic subjects [J] . N Engl J Med, 2006,354(24):2552-2563.

[3] Kloting N, Graham T E, Berndt J, et al. Serum retinol-binding protein is more highly expressed in visceral than in subcutaneous adipose tissue and is a marker of intra-abdominal fat mass [J] . Cell Metab, 2007,6(1):79-87.

[4] Yang Q, Graham T E, Mody N, et al. Serum retinol binding protein 4 contributes to insulin resistance in obesity and T2DM [J] . Nature, 2005,436(7049):356-362.

[5] Elte J W, Blickle J F. Thiazolidinediones for the treatment of T2DM [J] . Eur J Intern Med, 2007,18 (1):18-25.

[6] Duggirala R, Blangero J, Almasy L, et al. Linkage of T2DM mellitus and of age at onset to a genetic location on chromosome 10q in Mexican Americans [J] . Am J Hum Genet, 1999,64(4):1127-1140.

[7] Meigs J B, Panhuysen C I, Myers R H, et al. A genome-wide scan for loci linked to plasma levels of glucose and HbA(1c) in a community-based sample of Caucasian pedigrees: the framingham offspring study [J] . Diabetes, 2002,51(3):833-840.

[8] Munkhtulga L, Nakayama K, Utsumi N, et al. Identification of a regulatory SNP in the retinol binding protein 4 gene associated with T2DM in Mongolia [J] . Hum Genet, 2007,120(6):879-888.

[9] Craig R L, Chu W S, Elbein S C. Retinol binding protein 4 as a candidate gene for T2DM and prediabetic intermediate traits [J] . Mol Genet Metab, 2007,90(3):338-344.

[10] Kovacs P, Geyer M, Berndt J, et al. Effects of genetic variation in the human retinol binding protein-4 gene (RBP4) on insulin resistance and fat depot-specific mRNA expression [J] . Diabetes, 2007,56 (12):3095-3100.

[11] Hu C, Jia W, Zhang R, et al. Effect of RBP4 gene variants on circulating RBP4 concentration and T2DM in a Chinese population [J] . Diabet Med, 2008,25(1):11-18.

[12] Alberti K G, Zimmet P Z. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation [J] . Diabet Med, 1998,15(7):539-553.

[13] Friedewald W T, Levy R I, Fredrickson D S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge [J] . Clin Chem, 1972,18(6):499-502.

[14] Barrett J C, Fry B, Maller J, Daly M J. Haploview: analysis and visualization of LD and haplotype maps [J] . Bioinformatics, 2005,21(2):263-265.

[15] Stephens M, Donnelly P. A comparison of bayesian methods for haplotype reconstruction from population genotype data [J] . Am J Hum Genet, 2003,73(5):1162-1169.

[16] Gavi S, Stuart L M, Kelly P, et al. Retinol-binding protein 4 is associated with insulin resistance and body fat distribution in nonobese subjects without T2DM [J] . J Clin Endocrinol Metab, 2007,92(5):1886-1890.

[17] Janke J, Engeli S, Boschmann M, et al. Retinol-binding protein 4 in human obesity [J] . Diabetes, 2006,55(10):2805-2810.

[18] Silha J V, Nyomba B L, Leslie W D, et al. Ethnicity, insulin resistance, and inflammatory adipokines in women at high and low risk for vascular disease [J] . Diabetes Care, 2007,30(2):286-291.

[19] Lee DC, Lee J W, Im J A. Association of serum retinol binding protein 4 and insulin resistance in apparently healthy adolescents [J] . Metabolism, 2007,56(3):327-331.

[20] Combs T P, Wagner J A, Berger J, et al. Induction of adipocyte complement-related protein of 30 kilodaltons by PPARgamma agonists: a potential mechanism of insulin sensitization [J] . Endocrinology, 2002,143(3):998-1007.

[21] Kang E S, Park S Y, Kim H J, et al. The influence of adiponectin gene polymorphism on the rosiglitazone response in patients with T2DM［J］. Diabetes Care, 2005,28(5):1139-1144.
[22] Sun H, Gong Z C, Yin J Y, et al. The association of adiponectin allele 45T/G and -11377C/G polymorphisms with T2DM and rosiglitazone response in Chinese patients［J］. Br J Clin Pharmacol, 2008,65(6):917-926.
[23] Liu H L, Lin Y G, Wu J, et al. Impact of genetic polymorphisms of leptin and TNF-alpha on rosiglitazone response in Chinese patients with T2DM［J］. Eur J Clin Pharmacol, 2008,64(7):663-671."

本刊中的类似文章

1．刘双珍； 吴小影； 王平宝； 谭星平； 胡生发；.准分子激光屈光性角膜切削术治疗近视和近视散光3年疗效分析[J]. 中南大学学报(医学版), 2001,26(6): 553-
2．许卫国； 易振佳； 金益强；.2型糖尿病不同中医证型骨密度及骨代谢改变的临床研究[J]. 中南大学学报(医学版), 2002,27(5): 432-
3．周顺科； 张子曙； 朱晖； 谭利华； 沈树斌； 杨树仁； 肖恩华； 伍玉枝； 朱美香；.大直径球囊治疗贲门失驰缓症[J]. 中南大学学报(医学版), 2002,27(6): 559-
4．陈淑华； 谷亚鹏； 曾卫民； 宋惠萍；.胰岛素受体底物-1基因3′非翻译区的突变与中国人2型糖尿病的关系[J]. 中南大学学报(医学版), 2003,28(1): 33-
5．刘征； 邓昊； 唐炜立； 夏家辉； 唐北沙； 戴和平； 周智广； 邓汉湘； 夏昆；.中国迟发型2型糖尿病患者葡萄糖激酶基因突变研究[J]. 中南大学学报(医学版), 2003,28(2): 99-
6．陈滢，邓展生，张薇，李桂元．无导镜指导下治疗髌骨不稳定的初步探讨[J]．中南大学学报(医学版)，2006,31(01)：104-107
7．钟惠菊，王敏，廖岚，陈慧玲，郭丽娟．2型糖尿病的个同阶段胰岛β细胞的早期分泌相变化[J]．中南大学学报(医学版)，2006,31(02)：232-235
8．黄卓，雷闽湘，柳岚，唐启斌．多格列酮对初诊2型糖尿病患者IMT和血清MMP-9水平的影响[J]．中南大学学报(医学版)，2006,31(03)：367-372
9．谢建萍，龚先琼，谭德明，刘菲，周建亮．雌激素受体基因多态性与乙型肝炎肝硬化的相关性研究[J]．中南大学学报(医学版)，2006,31(03)：379-382
10．吴静，雷闽湘，柳岚，黄渊金．多格列酮对2型糖尿病内皮依赖性血管舒张功能的影响[J]．中南大学学报(医学版)，2006,31(04)：570-574
11．黄建军，刘洪波，徐雷，宋惠萍．胰岛素受体底物-1基因5′-调控区的一种变异对基因表达的影响[J]．中南大学学报(医学版)，2006,31(06)：819-824
12．张莲萍， 彭风华， 杨罗艳， 赵晓昆， 杨金瑞， 张选志.体外冲击波碎石治疗不同术式术后残留肾结石的疗效[J]. 中南大学学报(医学版), 2009,34(07): 634-637
13．胡志勇， 徐勇强， 梁捷予， 李康华， 廖前德 .外展支具配合学步车治疗发育性髋关节脱位的疗效评价[J]. 中南大学学报(医学版), 2009,34(07): 667-671
14．周华英， 郑煜煌， 何艳， 龚国忠， 谌资， 刘猛， 尹伟， 刘纯.高效抗逆转录病毒治疗艾滋病毒感染者和艾滋病患者的6年临床疗效及安全性观察[J]. 中南大学学报(医学版), 2009,34(08): 731-737
15．徐诣, 陈先礼, 刘宝恒, 丑克, 刘振东, 邓俭良.2型糖尿病大鼠骨髓腔内PPARγ和Cbf&agr;1 mRNA的表达与骨折愈合障碍的关系[J]. 中南大学学报(医学版), 2009,34(10): 957-964