糖尿病前期受高尿酸血症影响的相关因素分析

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【摘要】　目的　探讨高尿酸血症影响糖尿病前期(PDM)的相关因素及其两者的关系。方法　在2009年2月至2010年2月哈尔滨医科大学附属第二医院未使用噻嗪类药物的20～75岁PDM患者中,随机抽取157例,按尿酸水平分为正常尿酸(NUA)组(81例)和高尿酸(HUA)组(76例),对两组临床资料应用 t 检验以及Pearson相关分析进行统计分析,比较两组间BMI、腰围身高比(WSR)、TC、TG、HDL-C、LDL-C、稳态模型胰岛素抵抗指数(HOMA-IR)、糖化血红蛋白(HbA1c)的差异以及各指标与尿酸的相关性。结果　(1)HUA组BMI为(27.74±2.88)kg/m², WSR为(0.55±0.41)、TC为(6.61±0.73)mmol/L、TG为(3.94±1.97)mmol/L、LDL-C为(3.60±0.45)mmol/L、HOMA-IR为(3.09±1.20),均高于NUA组,差异有统计学意义($P<0.05$);(2)PDM患者的尿酸水平与TG、TC、LDL-C及HOMA-IR呈正相关(分别为 $r=0.29$, $r=0.33$, $r=0.49$, $r=0.51$, $P<0.05$),与HbA1c呈负相关($r=-0.30$, $P<0.05$)。结论　PDM患者血尿酸水平受BMI、TC、TG、LDL-C、HOMA-IR等因素影响。体内HUA状态与胰岛素抵抗密切相关,促使PDM患者进展为糖尿病,并引发血脂代谢紊乱。

【关键词】　糖尿病前期；高尿酸血症；稳态模型胰岛素抵抗指数；相关性分析

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【Abstract】　**Objective**　To investigate the relationship and the influence between pre-diabetes mellitus (PDM) and hyperuricemia (HUA). **Methods**　157 PDM patients, aged 20 to 75 years old were selected from the Second Clinical Medical College of Harbin Medical University, from 2009 February to 2010 February and were divided into HUA group (76 cases) and NUA group (81 cases). All the patients had not been on thiazide drugs. T-test and Pearson correlation analysis were used to calculate the differences and correlation between uric acid and biochemical indicators. **Results**　In the HUA group, BMI was (27.74±2.88)kg/m², waist to height ratio (WSR) was (0.55±0.41), TC was (6.61±0.73)mmol/L, TG was (3.94±1.97)mmol/L, LDL-C was (3.60±0.45)mmol/L and homeostasis model assessment-insulin resistance index (HOMA-IR) was (3.09±1.20). There were significant differences noticed in BMI, TG, TC, LDL-C, HOMA-IR at higher level in the HUA group than those in the NUA group. Pre-diabetes uric acid levels were positively correlated with TG, TC, LDL-C while HOMA-IR (TG: $r=0.29$, TC: $r=0.33$, LDL-C: $r=0.49$, HOMA-IR: $r=0.51$, $P<0.05$) was negatively correlated ($r=-0.30$, $P<0.05$) with the HbA1c. **Conclusion**　The levels of PDM uric acid might both be related with TC, TG, LDL-C and HOMA-IR. The High level of uric acid status in vivo appeared closely related to HOMA-IR, which could further promote the progress of pre-diabetic patients to diabetes and causing dyslipidemia. Our findings suggested that the levels of pre-diabetes uric acid levels should be under concern.

【Key words】　Pre-diabetes mellitus; Hyperuricemia; Homeostasis model assessment-insulin resistance index; Correlation analysis

2型糖尿病(T2DM)在我国以及其他发展中国家呈迅猛增长的流行趋势[1,2]。糖尿病前期(PDM)使其进展为糖尿病的可能显著提高[3],而出现大血管和微血管并发症的危险是普通人群的数倍[4]。PDM是糖尿病自然病程的重要阶段,也是有助于预测糖尿病的临床标志。目前研究发现,高尿酸血症与胰岛素抵抗二者关系密切[5,6],甚至在PDM时该影响作用已显现。为此本研究对哈尔滨医科大学附属第二医院内的157例PDM患者进行临床观察,以

探讨高尿酸血症与PDM的关系。

对象与方法

1. 研究对象:从2009年2月至2010年2月哈尔滨医科大学附属第二医院慢性病患者中依据空腹血糖(FPG)和口服葡萄糖耐量试验(OGTT)筛检结果,确定PDM人群,并随机抽取157例(男85例,女72例),年龄20～75岁。PDM诊断标准:FPG>6.1 mmol/L FPG<7.0 mmol/L 和(或)糖耐量试验2小时血糖(2hPG)>7.8 mmol/L 2hPG<11.1 mmol/L。根据血尿酸(UA)浓度分为高尿酸(HUA)组和正常尿酸(NUA)组。由于目前国内外对高尿酸血症的诊断标准不一,选取一般定义值即UA水平男性>420 μmol/L,女性>360 μmol/L。HUA组76例(男46例,女30例),平均年龄(54.9±5.1)岁;NUA组81例(男39例,女42例),平均年龄(45.6±7.4)岁。所有病例均未使用影响UA代谢的药物。

2. 研究方法:所有研究对象接受统一的问卷调查及体检,测量身高、体重、腹围、计算BMI、腰围身高比(WSR),抽取空腹外周静脉血测定FPG、空腹胰岛素(FINS)、TG、TC、UA、LDL-C、HDL-C、糖化血红蛋白(HbA1c),按稳态模型评估法计算胰岛素敏感指数(ISI),以HOMA胰岛素抵抗指数(HOMA-IR)评价胰岛素抵抗(IR):HOMA-IR=(FPG×FINS)/22.5,ISI=INS/(FPG×FINS)。采用全自动生化仪测定HbA1c和血脂水平,放射免疫法测定血清胰岛素水平。

3. 统计学分析:数据分析采用SPSS 17.0统计软件,计量资料符合正态分布,用$\bar{x}\pm s$表示,组间比较采用两独立样本 t 检验,HUA组UA水平与身高、体重、腹围、BMI、WSR、FPG、FINS、TG、TC、UA、LDL-C、HDL-C、HbA1c、ISI等指标分别进行Pearson相关分析,列出直线方程。$P<0.05$ 为差异有统计学意义。

结　果

1. 两组患者各项指标比较:HUA组BMI、TG、TC、LDL-C、WSR、HOMA-IR 均高于NUA组,其中BMI、TG、TC、HOMA-IR 的差异有统计学意义($P<$0.05)。HUA组HbA1c明显低于NUA组,差异有统计学意义($P<0.05$)。见表1和图1。

表1　两组患者相关临床指标比较($\bar{x}\pm s$)

组　别	NUA组($n=81$)	HUA组($n=76$)
BMI(kg/m^2)	24.38±2.29	27.74±2.88
WSR	0.50±0.41	0.55±0.41
TC(mmol/L)	5.63±1.42	6.61±0.73
TG(mmol/L)	1.79±0.52	3.94±1.97
HDL-C(mmol/L)	1.74±0.33	1.13±0.22
LDL-C(mmol/L)	3.20±0.79	3.60±0.45
HOMA-IR	2.55±0.30	3.09±1.20
ISI	-2.50±0.38	-4.10±0.50
HbA1c	6.18±0.20	5.95±0.42
UA(μmol/L)	268.94±37.94	476.82±59.03

2. HUA组各项指标的Pearson相关分析:两组PDM患者UA水平与TG呈正相关($r=0.29, P<$0.05),直线方程为 $y=0.0105x-1.6115$;与TC呈正相关($r=0.33, P<0.05$),直线方程为 $y=0.0067x+2.3566$;与LDL-C)呈正相关($r=0.49, P<0.05$),直线方程为 $y=0.0058x+0.3866$;与HOMA-IR呈正相关($r=0.51, P<0.05$),直线方程为 $y=0.0452x-13.452$;与HbA1c呈负相关($r=-0.30, P<0.05$),直线方程为 $y=-0.0017x+6.7446$(图2)。

讨　论

高尿酸血症的原因主要分为体内尿酸产生过多和清除减少。据研究统计,有90%的患者是由于尿酸清除减少所致,包括肾小球重吸收增多、肾小球滤过率减少、肾小管分泌减少以及尿酸盐结晶沉积。PDM的高胰岛素状态可促进肾脏对UA的重吸收[7],同时排泄减少,血UA水平尿酸升高。高水平的血UA又可进一步激活肾素-血管紧张素系统,从而引发动脉平滑肌细胞增殖导致高血压,进而加重肾功能损害。Niskanen等[8]研究显示,体内高血尿酸与高胰岛素水平两者间存在紧密关系。在胰岛素抵抗
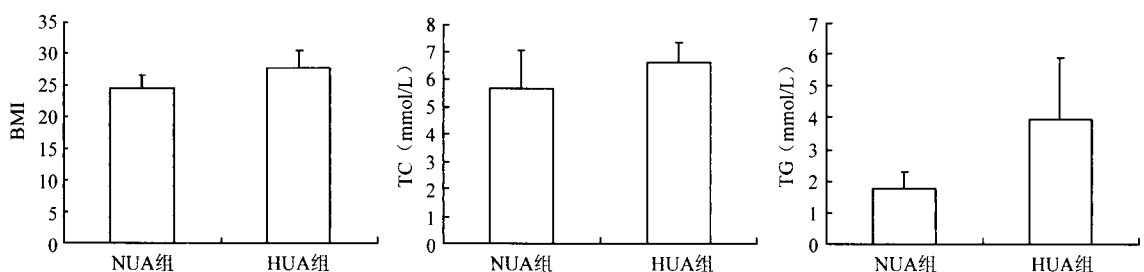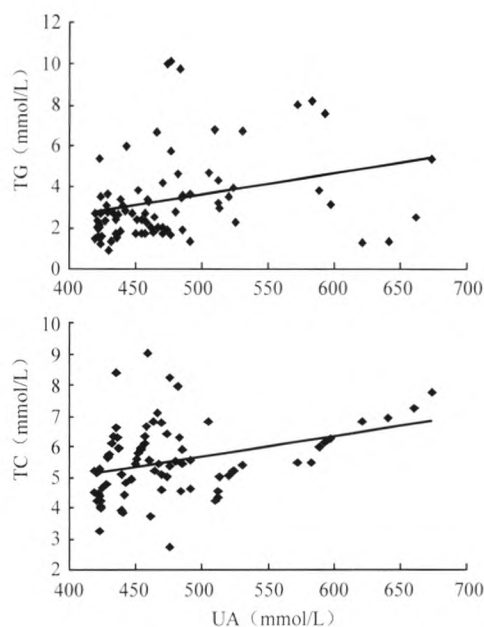

图1　两组患者BMI、TG和TC的比较

图2 两组患者TG、TC与UA的Pearson相关性分析

状态下，糖酵解中间产物向5-磷酸核糖及磷酸核糖焦磷酸转移，进而促进血UA的生成；胰岛素抵抗又可增加肝脏脂肪的合成，导致嘌呤代谢紊乱，血UA水平升高[9]。体内的高尿酸状态已知可引发多种病变，而生活习惯和饮食结构改变、肥胖、高胰岛素血症、胰岛素抵抗被认为是糖耐量异常的危险因素，也被认为与高尿酸血症密切相关。原发性高尿酸血症与代谢综合征关系密切[10,11]，在代谢紊乱的发病机制中，胰岛素抵抗被认为是最根本的病因[12]。

本研究中高尿酸血症患者（HUA组）占49.68%，且BMI、WSR、TG以及HOMA-IR指标均高于NUA组，与文献[13,14]结果相符，提示PDM人群血高尿酸水平与上述指标有显著关联。高尿酸血症既能直接影响PDM人群，又与血脂异常从而引发代谢综合征影响PDM[15]。本研究PDM患者UA水平与TG、TC、LDL-C及HOMA-IR呈正相关，提示应注意此四类指标超标人群的UA值，预防发生高尿酸血症。此外，本研究中HUA组HbA1c高于NUA组与目前多项研究相符。新近研究认为，血UA水平与PDM人群的联系要强于糖尿病人群，即在诊断糖尿病前，血UA水平随血糖的升高而上升，但是在新诊断的糖尿病患者中，其血UA水平则下降。提示如果血糖浓度高于一定水平，血UA与血糖浓度将呈负相关[16,17]。本研究存在不足，据以往研究证明，年龄、体重与UA水平呈正相关，男性比女性更易患高尿酸血症，但本研究并未提供有统计学意义的结果。

综上所述，高尿酸血症既能够促进动脉粥样硬化的形成，又能加重胰岛素抵抗，并与血脂异常、高血糖和高血压具有相辅相成的关系。因此，临床上应对高UA这一危险因素格外重视，控制和改善血UA水平对预防PDM具有积极意义。

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