血清脂联素与载脂蛋白 A5 及 2 型糖尿病的关系 *

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摘要 目的:检测血清脂联素(APN)水平,分析血清 APN 浓度与血脂、血清载脂蛋白 A5(apoA5)及 2 型糖尿病的关系。方法:收集 2 型糖尿病(T2DM) 210 例,健康体检者 112 例,采用 ELISA 法检测血浆脂联素水平,双抗体夹心 ELISA 法检测血清载脂蛋白 A5(apoA5)水平,7600-020E 全自动生化分析仪检测总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)等,放射免疫分析仪检测血胰岛素水平。结果:T2DM 患者血清 APN 浓度明显低于健康对照组,LDL-C、TG 及 TC 均高于对照组(P<0.05)。T2DM 患者血清 apoA5 浓度(200.3±51.2)ng/ml,显著低于健康对照组(229.8±56.5)ng/ml,P<0.05。Pearson 相关分析显示经年龄、性别校正后 APN 水平与 LDL-C、TG 呈负相关,与 HDL-C 呈正相关;T2DM 组 APN 与 apoA5 呈正相关(P<0.05)。结论:T2DM 患者血清 APN 水平显著降低,本研究证实低水平血清 APN 和 apoA5 不仅与血脂代谢密切相关,还可作为 T2DM 患者早期监测的指标,对其预后评价具有积极的意义。

关键词:脂联素;载脂蛋白 A5;冠心病

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The Relationship Among Plasma Adiponectin, Apolipoprotein A5 and Type 2 Diabetic Patients*

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ABSTRACT Objective: To test plasma adiponectin of type 2 diabetic patients (T2DM) and evaluate whether plasma adiponectin (APN) was associated with T2DM. Methods: Plasma APN were measured using adiponectin ELISA kit in 223 cases T2DM patients and 112 cases healthy examinations, apolipoproteinA5 (apoA5) concentration were tested by sandwich enzyme-linked immunosorbent assay. Plasma total cholesterol (TC), triglycerin (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were measured by 7600-020E automatic biochemistry analyzer, The serum insulin were measured by using RIA. Results: Plasma APN in T2DM were significantly lower than those in the control subjects, and the level of LDL-C, TG, Lp (a) are higher than the comparison group (P<0.05) Serum apoA5 concentrations (200.3±52.6)ng/ml of T2DM were lower than healthy control (229.8±56.5) ng/ml, P<0.05. Pearson correlation analysis showed that adiponectin was significantly negatively correlated with LDL-C and TG, and positively correlated with HDL-C after adjustment for age and sex, APN was positively correlated with apoA5 in T2DM. Conclusion: Serum APN of T2DM patients were apparently decreased, this research lower APN and apoA5 not only correlated with lipid metolism, but also as a early index for monitoring of T2DM patients, have active significance for Prognostic evaluation.

Key words: Adiponectin; ApolipoproteinA5;T2DM

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前言

糖尿病的发病率呈逐年增高趋势,已经成为继肿瘤、心脑血管病之后第三位严重危害人类健康的慢性疾病。脂联素(adiponectin,APN)是脂肪组织特异性分泌的多种脂肪细胞因子之一,大量前瞻性和多学科研究已经证实,血清 APN 浓度变化与人类多种疾病密切相关。因此,本文旨在研究 T2DM 患者血清 APN、apoA5 及血脂水平的关系,并进一步探讨血清 APN 浓度变化对 T2DM 早期诊断、预后评价的影响。

1 材料与方法

1.1 研究对象

选择 2011 年 4 月~11 月鼓楼医院内分泌科收治的 T2DM 患者血清共 210 例,男性 108 例,女性 102 例,年龄 53.9±13.2 岁,排除各种急慢性感染性疾病及肿瘤等,均符合 WHO 的糖尿病诊断标准[1]。112 例健康人来自本院体检中心,

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男性 60 例，女性 52 例，年龄为 55.2±11.9 岁，均排除心血管疾病，肾病，感染性疾病及糖尿病等。

1.2 检测方法

1.2.1 生化指标的检测 所有对象清晨空腹抽取肘静脉血 5ml，室温放置 30mim 后，分离血清用于生化指标检测（日立 7600-020E 全自动生化分析仪），试剂由日本第一化学株式会社提供。血清 apoA5 浓度的检测采用本课题组前期建立的双抗体夹心 ELISA 法 [2]。血清 FINS 水平由 GC-911γ 放免计数仪测定，检测试剂由 Roche 公司提供。

1.2.2 脂联素的检测 具体操作参照说明书。以 A492 平均值为纵坐标，Log(APN 蛋白浓度)为横坐标绘制标准曲线。

1.3 统计学处理

利用 SPSS 17.0 统计软件对所获数据进行处理，计量资料以 $\bar{x}\pm s$ 表示，Logistic 多元回归分析相关危险因素对 T2DM 风险度可能产生的影响；不符合正态分布的指标经对数转换达到近似正态分布后进行数据分析，两组间差异比较采用独立样本 t 检验，两组以上资料比较采用 q 检验，不同影响因素进行 pearson 相关性分析，以 P＜0.05 为具有统计学意义。

2 结果

2.1 T2DM 组与对照组一般资料的比较

研究对象基本资料的比较如表 1 所示。与健康对照组比较，T2DM 组患者的 HDL、ApoⅠ/ApoB 水平显著低于对照组，LDL-C、TG、TC 均高于对照组（均 P＜0.05）。根据公式 HOMA-IR=[空腹胰岛素(μU/mL)× 空腹血糖(mg/dL)]/22.5，计算胰岛素抵抗指数。

表 1 T2DM 组与对照组一般资料的比较 ($\bar{x}\pm s$)

Table1 Comparison of general information betweenT2DM group and control($\bar{x}\pm s$)

Index	Control(n=112)	T2DM (n=210)
Age (y)	55.2± 11.9	53.90± 13.20
Gender (m/f)	60/52	108/102
BUN(mmol/L)	4.94± 1.13	6.69± 1.90*
LDL-C(mmol/L)	1.16± 0.39	2.18± 0.57*
HDL-C(mmol/L)	1.55± 0.32	1.08± 0.52*
TC(mmol/L)	3.72± 0.61	4.51± 0.86*
TG(mmol/L)	1.18± 0.46	1.79± 0.61*
ApoⅠ(mmol/L)	1.32± 0.37	1.20± 0.19
ApoB(mmol/L)	0.78± 0.21	0.88± 0.22
ApoⅠ/ ApoB	1.69± 0.31	1.36± 0.31*
FBG(mmol/L)	10.16± 2.31	4.38± 1.04
FINS(mU/L)	16.82± 4.34	11.34± 4.12
HOMA-IR	7.60± 1.58	2.21± 1.32*

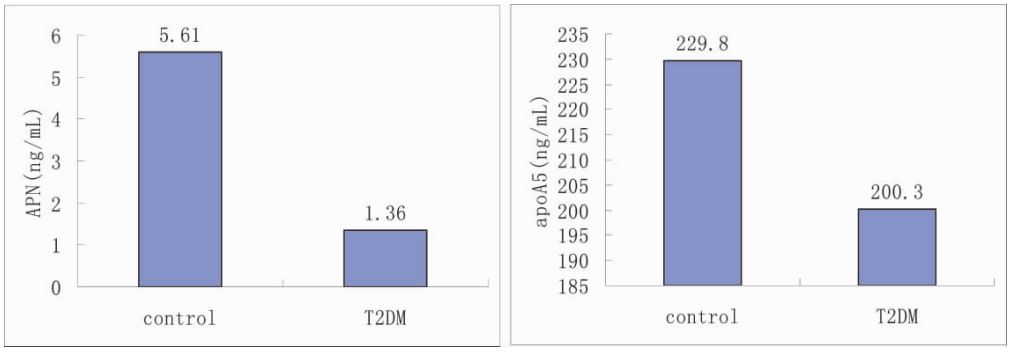
注：* 与对照组比较，P＜0.05

Note: *Comparison with control group, P＜0.05

2.2 血清脂联素和 ApoA5 水平的比较

T2DM 患者血清 APN 浓度明显低于健康对照组（P＜0.05）。T2DM 患者血清 apoA5 浓度低于健康对照组，差别有统计学意义(P＜0.05)见图 1。

Fig.1 Comparison of APN and apoA5 betweenT2DM group and control($\bar{x}\pm s$)



Note: * Comparison with control, P＜0.05

2.3 血清 APN 浓度与血脂水平的相关性分析

T2DM 组中，血清 APN 浓度与 LDL-C 和 TG 均呈负相关（r 分别为 -0.201 和 -0.224，P＜0.05）；APN 与 apoA5、HDL-C 呈正相关(r 分别为 0.35，0.29，P＜0.05)。

2.4 T2DM 危险因素分析

logistic 回归分析结果表明低 APN 血症、低 apoA5 血症和高 TC 血症是与高血糖共同作用促进 T2DM 发生发展，见表 2。

表 2 T2DM 相关危险因素的多元回归分析

Table 2 Type 2 diabetes mellitus risk factors related to multiple regression analysis

	Regression coefficient	Standard error	P value	ORvalue	95%CI
APN	-0.307	0.114	0.018	0.906	0.313～1.912
TC	1.399	0.428	0.021	3.211	1.810～7.537
HOMA-IR	1.217	0.402	0.020	3.019	1.726～9.223
ApoA5	-0.246	0.119	0.015	1.121	0.845～1.950

3 讨论

APN 是肥胖相关激素家族的新成员，实体证据已经揭示了 APN 在人类健康和疾病中的重要作用，潜在的分子机制研究结果证实了血清 APN 浓度变化与致病机制之间的复杂关系[3-5]。正常人 APN 血浆浓度范围为 3.0～30.0μg/mL，随着年龄增加而增加，女性血清 APN 水平明显高于男性。研究发现 APN 具有增加胰岛素敏感性和保护胰岛 β 细胞的功能，在 2 型糖尿病的发生、发展中起双重保护性作用[6-9]。

在本研究中，与健康对照组比较，T2DM 患者血清 TG、TC 和 LDL-C 明显升高，血清 HDL-C 显著降低（均 P＜0.05）。APN 基因中包含调节糖脂代谢的主要调节因子（过氧化物酶体增殖物激活受体 PPARγ）的反应元件，循环中低浓度 APN 降低脂蛋白脂肪酶(LPL)活性水平，导致 HDL-C 水平降低[10-12]。T2DM 患者血清 APN 浓度明显低于健康对照组（1.36±0.41 vs 5.61±0.25 ng/ml, P＜0.05），差异有显著性。临床研究表明，以异常脂肪因子和炎症调节因子为特征的慢性低度炎症状态可通过多种机制损伤胰岛 β 细胞功能，T2DM 常伴有多种炎症因子（白细胞计数，IL-6,TNF-α 等）和急性时向反应蛋白(hs-CRP)升高，APN 通过抑制应激信号途径和细胞内皮信号途径干扰 TNF 的生成[13-15]；APN 抑制粘附因子表达、通过核因子 κB 途径阻止单核细胞与内皮细胞表面结合，抑制受损血管内皮的炎症反应，消耗增加，导致低 APN 血症[16-17]。在 T2DM 组，血清 apoA5 浓度显著低于对照组(P＜0.05)，急性炎症状态时，虽然 apoA5 表达增加，但免疫荧光显示 apoA5 呈核周和弥散性细胞浆染色，其主要定位在内质网，表明 apoA5 不能有效的从内质网运输到高尔基体，即 apoA5 释放效率低[18-20]。相关性研究显示，T2DM 患者血清 APN 浓度与 LDL-C、TG 呈负相关（r分别为 -0.201,-0.224，P＜0.05）；APN 与 apoA5、HDL-C 呈正相关（r 分别为 0.35，0.29，P＜0.05）；大量前瞻性研究证实血清低 APN 水平不仅与肥胖、胰岛素抵抗密切相关，而且作为独立危险因子早期监测 T2DM 发生[15]。

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