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IAA、ICA 及 GADA 联合检测对糖尿病分型的诊断价值

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摘要 目的:探讨胰岛素自身抗体(IAA)、胰岛细胞抗体(ICA)及谷氨酸脱羧酶抗体(GADA)联合检测对糖尿病分型的诊断价值。**方法:**选择 2015 年 6 月~2016 年 6 月在我院进行诊治的 1 型糖尿病患者 30 例为 A 组, 2 型糖尿病患者 60 例为 B 组, 同期在我院进行体检健康者 50 例为 C 组, 采用酶联免疫吸附法(ELISA)检测三组的 IAA、ICA 及 GADA, 比较三组的阳性检出率。**结果:**A 组空腹血糖为 (10.12 ± 3.68) mmol/L, B 组空腹血糖为 (11.23 ± 3.26) mmol/L, A 组和 B 组的空腹血糖均明显高于 C 组 (4.35 ± 1.42) mmol/L ($P < 0.05$), 但 A 组和 B 组的空腹血糖相比无明显差异 ($P > 0.05$); A 组和 B 组的 IAA、ICA 及 GADA 单独和联合检测的阳性率均明显高于 C 组 ($P < 0.05$), 且 A 组的 IAA、ICA 及 GADA 单独和联合检测的阳性率明显高于 B 组 ($P < 0.05$); IAA、ICA 及 GADA 联合检测对 1 型和 2 型糖尿病的敏感性和特异性均明显高于单独检测 ($P < 0.05$)。**结论:**IAA、ICA 及 GADA 联合检测对糖尿病分型具有较高的临床诊断价值。

关键词:胰岛素自身抗体; 胰岛细胞抗体; 谷氨酸脱羧酶抗体; 糖尿病分型

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Diagnostic Value of Combined Detection of IAA, ICA and GADA in the Classification of Diabetes Mellitus

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ABSTRACT Objective: To study the diagnostic value of combined detection of IAA, ICA and GADA in the classification of diabetes mellitus. **Methods:** 30 cases of patients with type 1 diabetes who were treated in our hospital from June 2015 to June 2016 were selected as A group, 60 cases of patients with type 2 diabetes were selected as B group, 50 cases of healthy people were selected as C group. The IAA, ICA and GADA of the three groups were detected by ELISA, and the positive rate of the three groups were compared. **Results:** The fasting glucose of A group was (10.12 ± 3.68) mmol/L, B group was (11.23 ± 3.26) mmol/L, A group and B group were significantly higher than that of C group ($P < 0.05$), but there was no significant difference between A group and B group ($P > 0.05$); the positive rates of GADA, ICA and IAA in A group and B group were significantly higher than those in C group ($P < 0.05$), and the positive rates of GADA, ICA and IAA in A group were significantly higher than those in B group ($P < 0.05$); the sensitivity and specificity of combined detection of IAA, ICA and GADA in type 2 and type 1 diabetes mellitus were significantly higher than that in the single test ($P < 0.05$). **Conclusions:** The combined detection of IAA, ICA and GADA has a high diagnostic value in the classification of diabetes mellitus, which is worth clinical application.

Key words: IAA; ICA; GADA; Classification of diabetes mellitus

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前言

糖尿病是一种临床较为常见的以糖代谢紊乱及血糖升高为主要特征的慢性代谢性疾病^[1]。按照发病机制的不同,糖尿病可以分为 1 型糖尿病和 2 型糖尿病。糖尿病早期分型对患者进行早期免疫干预以及胰岛素治疗具有重要的临床意义,可有效改善预后^[2]。糖尿病患者机体内还有多种可以破坏胰岛 β 细胞功能的抗体,其中胰岛素自身抗体(IAA)、胰岛细胞抗体(ICA)

以及谷氨酸脱羧酶抗体(GADA)是最为重要的三种抗体^[3,4]。临床上已有关于 IAA、ICA 及 GADA 对糖尿病的诊断价值的研究,但关于其对糖尿病分型的诊断机制的报道较为少见。本研究主要探讨了 IAA、ICA 及 GADA 联合检测对糖尿病分型的诊断价值。

1 资料和方法

1.1 一般资料

选择 2015 年 6 月~2016 年 6 月我院诊治的 1 型糖尿病患者 30 例为 A 组, 2 型糖尿病患者 60 例为 B 组, 同期在我院进行体检健康者 50 例为 C 组。其中, A 组 30 例, 男 18 例, 女 12 例; 年龄 5~42 岁, 平均 (25.31 ± 8.24) 岁。B 组 60 例, 男 32

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例,女 28 例;年龄 32~82 岁,平均(51.23± 11.76)岁。C 组 50 例,男 26 例,女 24 例;年龄 21~58 岁,平均(36.12± 8.35)岁。本研究获得我院伦理委员会的批准,所有患者均签署知情同意书。

1.2 研究方法

三组研究对象均于清晨空腹采集 3 mL 非抗凝血,离心后取上层血清,用免疫印迹法检测三组的 IAA、ICA 及 GADA,试剂盒均购自深圳亚辉龙生物科技有限公司,比较三组的 IAA、ICA 及 GADA 阳性检出率。结果判定以 S/CO≥ 1.0,即 IAA 和 ICA(样本 A405 nm/ 阴性对照 A405 nm)≥ 2.50、GADA(样本 A405 nm/ 阴性对照 A405 nm)≥ 3.0 为阳性。然后计算分析 IAA、ICA 及 GADA 单独和联合检测对 1 型糖尿病及 2 型糖尿病的敏感性和特异性。

1.3 统计学分析

采用 SPSS15.0 软件进行统计学分析,计量资料以 $\bar{x} \pm s$ 表

示,组间对比用 t 检验,计数资料用 χ^2 检验,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 三组空腹血糖水平对比

A 组空腹血糖为 (10.12± 3.68) mmol/L, B 组空腹血糖为 (11.23± 3.26) mmol/L, A 组和 B 组的空腹血糖均明显高于 C 组的 (4.35± 1.42) mmol/L ($P < 0.05$),但 A 组和 B 组的空腹血糖相比无明显差异 ($P > 0.05$)。

2.2 三组 IAA、ICA 及 GADA 阳性检出率对比

A 组和 B 组的 IAA、ICA 及 GADA 单独和联合检测的阳性率均明显高于 C 组 ($P < 0.05$),且 A 组的 IAA、ICA 及 GADA 单独和联合检测的阳性率明显高于 B 组 ($P < 0.05$),见表 1。

表 1 三组 IAA、ICA 及 GADA 阳性检出率对比[例(%)]

Table 1 Comparison of the positive detection rate of IAA, ICA and GADA between three groups [n(%)]

Group	n	IAA	ICA	GADA	Combined detection
A group	30	5(16.67) **	8(26.67) **	9(30.00) **	23(76.77) **
B group	60	3(5.00) #	7(11.67) #	8(13.34) #	19(31.67) #
C group	50	1(2.00) *	1(2.00) *	0(0) *	2(4.00) *

Note: Compared with B group, * $P < 0.05$; compared with C group, # $P < 0.05$.

2.3 IAA、ICA 及 GADA 单独和联合检测对 1 型糖尿病的敏感性和特异性

IAA、ICA 及 GADA 联合检测对 1 型糖尿病的敏感性和特异性均明显高于单独检测 ($P < 0.05$),见表 2。

表 2 IAA、ICA 及 GADA 单独和联合检测对 1 型糖尿病的敏感性和特异性(%)

Table 2 Comparison of the sensitivity and specificity of IAA, ICA, and GADA alone and combined detection of type 1 diabetes (%)

	IAA	ICA	GADA	Combined detection
Sensitivity	56.67 ⁺	63.33 ⁺	60.00 ⁺	80.00
Specificity	80.00 ⁺	83.33 ⁺	76.67 ⁺	93.33

Note: Compared with combined detection, ⁺ $P < 0.05$.

2.4 IAA、ICA 及 GADA 单独和联合检测对 2 型糖尿病的敏感性和特异性

IAA、ICA 及 GADA 联合检测对 2 型糖尿病的敏感性和特异性均明显高于单独检测 ($P < 0.05$),见表 3。

表 3 IAA、ICA 及 GADA 单独和联合检测对 2 型糖尿病的敏感性和特异性(%)

Table 3 Comparison of the sensitivity and specificity of IAA, ICA, and GADA alone and combined detection of type 2 diabetes (%)

	IAA	ICA	GADA	Combined detection
Sensitivity	65.00 ⁺	61.67 ⁺	66.67 ⁺	88.33
Specificity	83.33 ⁺	85.00 ⁺	86.67 ⁺	95.00

Note: Compared with combined detection, ⁺ $P < 0.05$.

3 讨论

糖尿病是由于胰岛素分泌相对或绝对不足而引发的一种代谢性疾病^[9]。1 型糖尿病的发病机制为机体自身的免疫系统发生紊乱,对胰岛 β 细胞的功能进行攻击,出现自身的免疫功能紊乱,造成胰岛 β 细胞受损,导致机体胰岛素的合成及分泌量降低甚至完全缺乏,患者具有异常的体液免疫及细胞免疫^[6-8];2 型糖尿病则主要以胰岛素抵抗为主要临床特征,并伴有

胰岛素分泌不足^[9]。目前临床上主要通过患者的临床症状、发病年龄、酮症倾向、胰岛素 C 肽检测,胰岛素检测、胰岛素和 C 肽释放曲线等对糖尿病进行分型^[10-12]。

本研究结果显示 A 组和 B 组的空腹血糖均明显高于 C 组,但 A 组和 B 组的空腹血糖相比无明显差异,提示检测空腹血糖虽可以诊断糖尿病,但却不能对糖尿病分型进行鉴别诊断。IAA 可以通过和胰岛素进行结合,继而形成抗原抗体复合物,导致胰岛素的生物活性丧失,是评价药用胰岛素治疗效果

的理想指标^[13-15]。ICA 作为一种特异性的免疫球蛋白,可以对胰岛 β 细胞的胞浆成分发挥细胞毒效应,可以反映机体的胰岛功能^[16-18]。GADA 是胸腺、胃、卵巢、睾丸和胰岛 β 细胞等非神经组织合成酶,可以对特异性自身免疫反应进行抑制,从而诱导免疫耐受。GADA 水平的高低能在一定程度上反映患者胰岛 β 细胞损害的严重程度^[19,20]。本研究中,A 组和 B 组的 IAA、ICA 及 GADA 单独和联合检测的阳性率均明显高于 C 组,且 A 组的 IAA、ICA 及 GADA 单独和联合检测的阳性率明显高于 B 组,提示 IAA、ICA 及 GADA 联合检测对糖尿病及时、准确的分型具有重要的临床意义。此外,IAA、ICA 及 GADA 联合检测对 1 型糖尿病及 2 型糖尿病的敏感性和特异性均明显高于单独检测($P<0.05$)。准确地对 1 型糖尿病的发生进行鉴别诊断有利于减慢及阻止自身免疫系统对胰岛 β 细胞的破坏,更好地对胰岛 β 细胞功能进行保护。

综上所述,IAA、ICA 及 GADA 联合检测对糖尿病分型具有较高的临床诊断价值,值得推广应用。

参考文献(References)

- [1] Schauer P R, Bhatt D L, Kirwan J P, et al. Bariatric Surgery versus Intensive Medical Therapy for Diabetes - 3-Year Outcomes - NEJM [J]. New England Journal of Medicine, 2014, 371(7): 680-681
- [2] Zinman B, Wanner C, Lachin J M, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes [J]. New England Journal of Medicine, 2015, 373(22): 2117-2128
- [3] Min W, Yang H, Huang S, et al. The role of combinedly detecting GADA, ICA and IAA in screening LADA in newly diagnosed type 2 diabetes patients[J]. Chinese Journal of Diabetes, 2013, 21(11): 1018-1020
- [4] Singla R, Homko C, Schey R, et al. Diabetes-Related Autoantibodies in Diabetic Gastroparesis [J]. Digestive Diseases & Sciences, 2015, 60(6): 1733-1737
- [5] Association A D. Executive summary: Standards of medical care in diabetes-2014[J]. Diabetes Care, 2014, 37 Suppl 1(2): S4-S36
- [6] Gubitosiklug R A. Kidney disease and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study[J]. Diabetes Care, 2014, 37(1): 9-16
- [7] Bodin J, B?lling A K, Becher R, et al. Transmaternal Bisphenol A Exposure Accelerates Diabetes Type 1 Development In NOD Mice [J]. Toxicological Sciences, 2014, 137(2): 311-323
- [8] Kowalewska B, Kawko M, Zorena K, et al. Yeast-like fungi in the gastrointestinal tract in children and adolescents with diabetes type 1 [J]. Pediatric Endocrinology, 2015, 20(4): 170-177
- [9] Udell JA, Bhatt DL, Braunwald E, et al. Saxagliptin and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Moderate or Severe Renal Impairment: Observations From the SAVOR-TIMI 53 Trial[J]. Diabetes Care, 2014, 38(4): 696-705
- [10] Cryer P E. Hypoglycemia-Associated Autonomic Failure in Diabetes: Maladaptive, Adaptive, or Both?[J]. Diabetes, 2015, 64(7):2322-2323
- [11] Althouse A D, Abbott J D, Forker A D, et al. Risk factors for incident peripheral arterial disease in type 2 diabetes: results from the Bypass Angioplasty Revascularization Investigation in type 2 Diabetes (BARI 2D) Trial[J]. Diabetes Care, 2014, 37(5): 1346-1352
- [12] Laura M, Reinaldo Sousa D S, Tina F, et al. TYK2, a Candidate Gene for Type 1 Diabetes, Modulates Apoptosis and the Innate Immune Response in Human Pancreatic β -Cells. [J].Diabetes,2015, 64 (11): 3808-3817
- [13] Sun C, Sedimbi S K, Ashok A K, et al. CRYAB-650 C>G (rs2234702) affects susceptibility to type 1 diabetes and IAA-positivity in Swedish population [J]. Human Immunology, 2015, 73 (7): 759-66
- [14] Strollo R, Vinci C, Arshad M H, et al. Antibodies to post-translationally modified insulin in type 1 diabetes [J]. Diabetologia, 2015, 58(12): 2851-2860
- [15] Miyahara M, Nagano C, Nakanishi S, et al. A Case of Fulminant Type 1 Diabetes Mellitus with Plural Islet-related Autoantibodies [J]. Journal of the Japan Diabetes Society, 2014, 58(3): 205-211
- [16] Pörksen S, Laborie L B, Nielsen L, et al. Disease progression and search for monogenic diabetes among children with new onset type 1 diabetes negative for ICA, GAD- and IA-2 Antibodies [J]. BMC Endocrine Disorders, 2010, 10(1): 16
- [17] Andersson C, Kolmodin M, Ivarsson S A, et al. Islet cell antibodies (ICA) identify autoimmunity in children with new onset diabetes mellitus negative for other islet cell antibodies [J].Pediatric Diabetes, 2014, 15(5): 336-344
- [18] Singla R, Homko C, Schey R, et al. Diabetes-Related Autoantibodies in Diabetic Gastroparesis [J]. Digestive Diseases & Sciences, 2015, 60 (6): 1733-1737
- [19] Ché ramy M, Skoglund C, Johansson I, et al. GAD-alum treatment in patients with type 1 diabetes and the subsequent effect on GADA IgG subclass distribution, GAD 65, enzyme activity and humoral response [J]. Clinical Immunology, 2010, 137(1): 31-40
- [20] Kordonouri O, Charpentier N, Hartmann R. GADA positivity at onset of type 1 diabetes is a risk factor for the development of autoimmune thyroiditis [J]. Pediatric Diabetes, 2011, 12(1): 31-33