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Letters to the editor

Glucose tolerance in Japanese subjects with S20G mutation of the amylin gene

Dear Sir,
Amylin is a 37 amino acid peptide which is the main constituent of islet amyloid deposits [1]. The peptide is synthesized by the pancreatic beta cells and co-secreted with insulin [2]. It has been suggested that amyloid formation in the pancreas may be a cause of islet cell dysfunction in non-insulin-dependent diabetes mellitus (NIDDM) [3]. At pharmacological doses, infusion of amylin causes peripheral insulin resistance [4]. Sakagashira et al. [5] have reported the S20G missense mutation of the amylin gene in Japanese NIDDM patients. They found the mutation in 12 out of 294 patients with NIDDM (4.1 %), whereas none of a group of non-diabetic subjects and insulin-dependent diabetic patients had the mutation. To further elucidate the association between the mutation and NIDDM, we analysed the S20G mutation in 184 subjects aged 56.6 ± 5.4 years (range 50--79) who had normal glucose tolerance by 75 g oral glucose tolerance test (OGTT) by World Health Organization criteria, and 86 patients with NIDDM aged 54.5 ± 7.5 years (range 35--69) in Japan. The normal group consisted of 119 men and 65 women, and the diabetic group of 76 men and 10 women. We recruited normal subjects aged 50 years or more to exclude pre-diabetic subjects. The A → G substitution was detected by polymerase chain reaction amplification of the gene followed by Msp I digestion as described previously [5]. The missense mutation was found in 4 out of 86 NIDDM patients (4.7 %) and 3 out of 184 individuals with normal glucose tolerance (1.6 %). None of the subjects was homozygous for the missense mutation. Table 1 shows the clinical characteristics and OGTT data of individuals with the S20G mutation. One of three non-diabetic persons had high body mass index (BMI), whereas none of four diabetic patients was obese. One diabetic subject showed a low and delayed insulin response; OGTT was not performed in three other diabetic men because of fasting hyperglycaemia. Glucose-induced insulin secretion was apparently normal in the non-diabetic subjects with the mutation. Although the variant allele was more common in diabetic patients than in normal subjects, the difference did not reach statistical significance. Our results also indicate that the mutation does not necessarily result in the development of diabetes. Other genetic and environmental factors may be essential for individuals with the mutation to develop overt diabetes.

Table 1. Glucose and insulin levels of subjects heterozygous for the S20G mutation of the amylin gene during 75 g oral glucose tolerance tests

Age (years)	Sex	BMI	Glucose (mmol/l)			Insulin (pmol/l)		
			0	60	120	0	60	120 min
68	M	21.5	5.2	6.6	6.1	27	232	167
55	F	34.8	5.6	7.8	5.5	67	647	431
52	M	24.1	5.2	5.4	5.6	42	317	110
53	M	21.3	6.4	12.5	12.2	17	55	113
49	M	19.5	9.8			17		
57	M	23.5	10.7			38		
57	M	20.2	8.0			48		

Yours sincerely,
K. Yamada, X. Yuan, S. Ishiyama, K. Nonaka

Corresponding author: Dr. K. Yamada, Division of Endocrinology and Metabolism, Department of Medicine, Kurume University School of Medicine, 67 Asahimachi, Kurume 830, Japan

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