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Height and glucose tolerance in adult subjects

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Summary. In a prospective study concerning the pathogenesis of impaired glucose tolerance and Type 2 (non-insulin-dependent) diabetes mellitus, 346 subjects with no clinical history of diabetes were given a standard 75 g oral glucose tolerance test. The expected positive associations between 120-min plasma glucose concentration and age and body mass index were observed in both sexes and between 120-min plasma glucose and waist/hip ratio in male subjects. An unexpected negative correlation was found between 120-min plasma glucose and height in both sexes ($r = -0.23$, (95% confidence interval, -0.38–-0.07) $p < 0.007$ for male subjects and $r = -0.24$, (-0.37–-0.11) $p < 0.006$ for female subjects). These negative associations with height remained significant after controlling for age and body mass index in male subjects but not in female subjects. In the latter a highly significant negative relationship of height with age was recorded ($r = -0.33$, (-0.45–-0.20) $p < 0.0001$). Comparison between individuals with impaired glucose tolerance and control subjects matched for sex, age and body mass index showed that subjects with impaired glucose tolerance are significantly shorter. Mean (± SEM) height in the male subjects with impaired glucose tolerance ($n = 29$) was 173.4 ± 1.1 cm vs 176.9 ± 1.3 cm in control subjects, $p = 0.02$. In the female subjects ($n = 39$) mean (± SEM) height was 159.4 ± 1.0 cm vs 162.4 ± 1.0 cm in control subjects, $p = 0.02$. The negative relationship between height and glucose tolerance is a new epidemiological observation which has not been previously reported. One possible reason for this is that the most commonly used anthropometric index, body mass index, eliminates height as an independent analytical variable.

Key words: Type 2 (non-insulin-dependent) diabetes mellitus, impaired glucose tolerance, glucose tolerance, oral glucose tolerance test, epidemiology, height, body mass index, waist/hip ratio.

A pilot study for a prospective study concerning the pathogenesis of Type 2 diabetes mellitus suggested that subjects with impaired glucose tolerance (IGT) are shorter than age-matched control subjects [1]. This observation has important implications for the pathogenesis of IGT and hence Type 2 diabetes. We have been unable to find any data specifically relating height to IGT or Type 2 diabetes in the literature. The prospective study has already revealed 12 subjects with newly diagnosed diabetes and 73 with IGT giving further opportunity to determine whether there is a significant difference in height between IGT subjects and those with normal glucose tolerance and also to study the relationship between several anthropometric measures, including height, and glucose tolerance as a continuous variable. We have, therefore, carried out a preliminary analysis of the data collected thus far.

Subjects and methods

In the Isle of Ely Diabetes Project subjects aged 40–64 years, registered with the only general practice in Ely, are invited by letter to attend for a standard 75 g oral glucose tolerance test (OGTT) after an overnight fast. Subjects with known Type 1 (insulin-dependent) diabetes are excluded from the study and those with known Type 2 diabetes have only one (non-fasting) sample taken. The subjects give informed written consent and the study has been approved by the Cambridge District Ethical Committee. For subjects with no clinical history of diabetes, venous blood samples, fasting and at 30 and 120 min after oral administration of glucose, are taken through an indwelling needle kept patent by injecting 1–1.5 ml of heparin solution, containing 100 IU/ml of heparin in a solution of NaCl (128 mmol/l) with 0.5% chlorbutol as preservative. Samples are immediately placed on ice and then separated in a cooled centrifuge kept of 4 °C. All samples are kept on ice during transport to the laboratory. Plasma glucose is measured by a standard laboratory method [2].

Table 1. Characteristics (mean ± SD) of 346 subjects tested

Age (years)	*n*	Weight (kg)	Height (cm)	BMI	WH	120-min blood glucose
Male subjects (n = 145)						
40–49	49	79.0 ± 10.6	175.3 ± 5.3	25.70 ± 3.2	0.89 ± 0.05	5.9 ± 1.3
50–54	28	80.1 ± 9.0	175.5 ± 5.0	26.05 ± 3.1	0.90 ± 0.05	6.7 ± 1.9
55–59	19	81.3 ± 12.4	177.0 ± 6.7	25.90 ± 3.7	0.91 ± 0.06	6.4 ± 1.6
60–64	49	80.6 ± 10.0	174.2 ± 6.8	26.50 ± 2.6	0.92 ± 0.06	7.8 ± 2.6
Female subjects (n = 201)						
40–49	75	67.6 ± 13.8	163.6 ± 6.6	25.2 ± 4.8	0.76 ± 0.05	5.9 ± 1.6
50–54	28	66.2 ± 10.7	163.7 ± 6.5	24.7 ± 3.9	0.76 ± 0.05	5.9 ± 1.1
55–59	35	68.5 ± 12.5	160.7 ± 5.3	26.6 ± 5.0	0.79 ± 0.05	7.3 ± 2.8
60–64	63	65.6 ± 12.8	158.7 ± 5.7	26.0 ± 4.8	0.78 ± 0.07	7.9 ± 2.6

WH = waist/hip ratio

Between taking the 30 and 120-min blood samples, the subjects answer a detailed questionnaire on diet, alcohol and smoking habits, and brief medical and family histories are recorded. Measurements of height, weight, hip and waist circumference are taken with the subjects wearing light-weight clothing.

Statistical analysis

Univariate and multiple regression analyses of plasma glucose concentrations on age and the anthropometric measurements (for those with normal glucose tolerance, IGT and newly diagnosed diabetes) have been performed using the Statistical Package for the Social Sciences (SPSSX). Comparison of the IGT and the control subjects is by paired *t*-tests using the one-tail test.

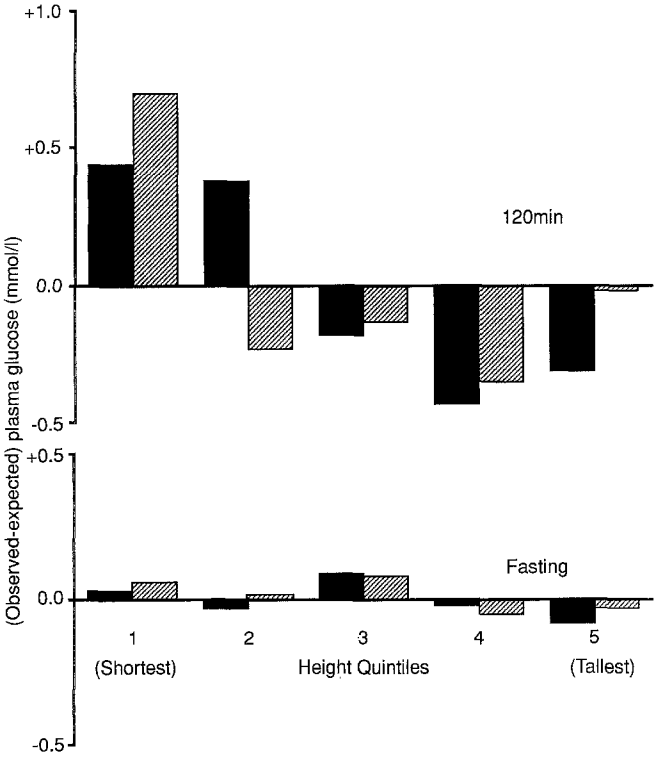

Fig. 1. Differences between observed and expected plasma glucose concentrations at fasting and 120 min in male and female subjects for quintiles of height with expected values adjusted for age and body mass index. ■ = male subjects, ▨ = female subjects

Results

A total of 346 subjects have complete OGTT results thus far. The characteristics of the group are shown in Table 1. We identified 12 subjects with previously undiagnosed Type 2 diabetes and 73 subjects with IGT (both as defined by the World Health Organisation [3]). Of these 73 subjects, 68 could be satisfactorily matched with control subjects and are described below.

We found a positive association between the 120-min plasma glucose and age for both male subjects and female subjects; r = 0.34, (95% confidence interval, 0.19–0.48) $p < 0.0001$ and r = 0.38, (0.25–0.49) $p < 0.0001$ respectively. A similar positive association was found with body mass index (BMI); r = 0.28, (0.12–0.42) $p < 0.0006$ for male subjects and r = 0.38, (0.26–0.49) $p < 0.0001$ for female subjects. In female subjects there was a positive association with weight; r = 0.26, (0.12–0.38) $p < 0.0004$ but in male subjects this did not reach statistical significance. In male subjects the waist/hip ratio correlated positively with the 120-min plasma glucose; r = 0.40, (0.25–0.53) $p < 0.0001$. In female subjects the association was weaker but present; r = 0.15, (0.01–0.29) $p < 0.026$. In contrast, there was a negative association between the 120-min glucose and height in both male subjects and female subjects; r = −0.23, (−0.38– −0.07) $p < 0.007$ for the former and r = −0.24, (−0.37– −0.11) $p < 0.0006$ for the latter.

In female subjects (but not in male subjects) a highly significant reduction in height was found in association with age; r = −0.33, (−0.45– −0.20) $p < 0.0001$. In male subjects the negative association of 120-min plasma glucose with height was significant after second-order partial correlation analysis controlling for age and BMI; r = −0.20, (−0.35– −0.03) p = 0.021. Figure 1 shows, for male subjects and female subjects separately, the observed and expected values for fasting and 120-min plasma glucose by increasing quintiles of height. Expected values for each height quintile have been calculated taking into account the effects of age and BMI and of interactions between age and BMI.

Comparison between the IGT group and an equal number of control subjects matched for sex, age (within two years) and BMI (within 2 kg/m^2) showed that the IGT subjects were significantly shorter than the control group. The mean (± SEM) height for the IGT males (n = 29) was 173.4 ± 1.1 cm compared to 176.9 ± 1.3 in the control group (p = 0.02). In female subjects the difference was less marked but still significant. The mean (± SEM) height of the IGT subjects (n = 39) was 159.4 ± 1.0 cm vs 162.4 ± 1.0 cm, p = 0.02. In both comparisons for male subjects and female subjects the mean waist/hip ratio of the IGT and control groups as matched were virtually identical (0.93 and 0.92 for male subjects; 0.77 and 0.77 for female subjects respectively).

Discussion

The association between 120-min plasma glucose concentration and age has been reported previously [4]. This is secondary to impaired insulin response to a glucose load and peripheral insulin resistance [5]. The correlation with

BMI and waist/hip ratio has been established in other studies [6, 7]. BMI is a measurement of general obesity, while the waist/hip ratio is an index of abdominal adiposity. Both conditions are characterised by insulin resistance and associated with IGT and an increased risk of developing Type 2 diabetes [8].

In the present investigation male and female IGT subjects were found to be significantly shorter than matched control subjects from the same population. This finding confirms the observation made in our small pilot study in which individuals from a different population were tested [1]. Furthermore, the present study shows that there is a general negative association between height and 120-min plasma glucose irrespective of the classification of individuals into discrete categories (normal, IGT and diabetic).

We have been unable to find any previous studies which have reported such a negative association of height with glucose tolerance. It seems strange that such an association could have been missed in the many studies of glucose tolerance which have been conducted and in which height has been measured. There are at least three explanations. Firstly, the determinants of adult height are numerous and in some populations may have obliterated the relationship which we observed. Severe, chronic childhood infections may operate in this way, for example. Secondly, in virtually all studies in which glucose tolerance has been measured, the main anthropometric index used has been BMI. Thus, height is eliminated as an independent analytical variable. Thirdly, as the present data show, height in postmenopausal females is very strongly and negatively age related (presumably due to the effect of spinal osteoporosis causing height loss). Without recognising and allowing for this confounding effect of age, the association with the 120-min glucose might be obscured. Prentice et al. [9] have shown a similar decline in height in association with age in British females.

The significance of the association of short stature and glucose intolerance can only be speculative at present.

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