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Plasma homocysteine in polycystic ovary syndrome: does it correlate with insulin resistance and ethnicity?

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Summary

BACKGROUND Polycystic ovary syndrome (PCOS) is associated with insulin resistance and premature coronary artery disease (CAD). Hyperhomocysteinaemia is a recognized risk factor for atherosclerosis, particularly among migrant South Asians, and has recently been shown to be correlated positively with the degree of insulin resistance/hyperinsulinaemia.

OBJECTIVES To compare total plasma homocysteine (Hcy) in PCOS with controls from ethnic groups at high and low risk of insulin resistance.

METHODS Case control study of three ethnic groups, Sri Lankans (SL), British Asians (BA) and white Europeans (C), with and without PCOS at specialist centres in Sri Lanka and Yorkshire, UK. Fasting total plasma Hcy concentration was analysed by fluorescence polarization immunoassay and examined for any correlation with age, body mass index (BMI), central obesity, fasting insulin and insulin sensitivity [calculated by the Quantitative Insulin Sensitivity Check Index (QUICKI) method], lipids and testosterone in each ethnic group.

RESULTS Eighty SL with PCOS and 45 controls, 47 BA with PCOS and 11 controls, and 40 C with PCOS and 22 controls were studied. Both Asian groups with PCOS were younger than affected Europeans ($P = 0{\cdot}008$). Sri Lankans with PCOS had significantly lower BMI values than other affected groups: mean ± SEM (SL) 26·3 ± 0·95; (BA) 30·59 ± 7·54; (C) 32·1 ± 5·95 kg/m^2 ($P = 0{\cdot}006$). However, waist : hip ratios (WHR) of Sri Lankans with PCOS were similar to others: mean ± SEM (SL) 0·97 ± 0·01 (BA) 1·04 ± 0·02 (C) 0·92 ± 0·01, $P = 0{\cdot}33$. Mean plasma Hcy was significantly higher in all PCOS groups than in their ethnically matched controls (Student's *t*-test): (SL) 10·2 ± 1·9 *vs* 9·0 ± 3·8, $P = 0{\cdot}01$; (BA) 7·9 ± 1·9 *vs* 6·8 ± 2·5, $P < 0{\cdot}0001$; (C) 8·3 ± 2·3 *vs* 6·8 ± 1·5, $P = 0{\cdot}0007$ μmol/l. Sri Lankans with PCOS had significantly greater Hcy concentrations than British Asians and Europeans with PCOS [$P = 0{\cdot}001$; single-factor analysis of variance (ANOVA)] and also significantly greater fasting insulin concentrations [(SL) 242·9 ± 38·9; (BA) 89·4 ± 8·9; (C) 48·6 ± 4·8 pmol/l ($P = 0{\cdot}0003$)] and significantly lower QUICKI [(SL) 0·308 ± 0·004; (BA) 0·335 ± 0·005; (C) 0·375 ± 0·002 ($P = 0{\cdot}0007$)]. Fasting plasma Hcy correlated best with fasting insulin ($r = 0{\cdot}56$, $P = 0{\cdot}0001$) and QUICKI ($r = -0{\cdot}53$, $P < 0{\cdot}0001$) in Sri Lankans with PCOS. Hcy in PCOS subjects from all three ethnic groups correlated significantly with fasting insulin following adjustment for age, BMI and WHR ($r = 0{\cdot}45$, $P = 0{\cdot}0001$), but this was not evident in the controls ($r = -0{\cdot}32$, $P = 0{\cdot}1$).

CONCLUSIONS Elevation of fasting plasma homocysteine in PCOS varies with ethnicity and correlates significantly with fasting insulin. High homocysteine in young Sri Lankans with PCOS has major implications for their long-term risk for atherosclerosis.

Introduction

The polycystic ovary syndrome (PCOS) is the most common endocrine disorder of women of reproductive age worldwide (Franks, 1995; Balen, 1999), is associated with insulin resistance and the metabolic syndrome (Dunaif *et al*., 1987), and has an increased risk for premature coronary artery disease (CAD) (Talbot *et al*., 1995). Elevation of plasma homocysteine (Hcy) is associated with premature atherosclerosis (Clarke *et al*., 2001; Knekt *et al*., 2001; Van den Brandhof *et al*., 2001). Homocysteine has recently been correlated with insulin resistance/hyperinsulinaemia of the metabolic syndrome (Meigs *et al*., 2001), and also with androgens in a study of transsexuals (Giltay *et al*., 1998). Concurrently, PCOS has been associated with elevated plasma Hcy (Yarali *et al*., 2001; Loverro *et al*., 2002;

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