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Effects of lifestyle modification on metabolic parameters and carotid intima-media thickness in patients with type 2 diabetes

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Background and Aims: Lifestyle modification is known to have positive effects on glycemic control and cardiovascular risk factors. Diabetes is a risk factor for cardiovascular disease. The carotid intima-media thickness (IMT) is considered to be an index of the progression of atherosclerosis. The aim of this study was to evaluate the effect of a 6 month lifestyle modification intervention on metabolic parameters and carotid IMT in patients with type 2 diabetes.

Materials and Methods: Sixty five patients with type 2 diabetes were randomly assigned into 2 groups, the lifestyle modification (LSM) group and the control (CON) group. The patients in the LSM group attended an intensive lifestyle modification intervention program for 16 weeks and had monthly meetings after the program. Patients in the CON group had no change in their usual treatment. Fasting plasma glucose, 2 hour postprandial glucose, Hba1c, lipid profiles, hsCRP, fasting insulin level, carotid IMT, blood pressure, and body indices were measured at baseline and after 6 months.

Results: LSM group showed a significant reduction in Hba1c (-0.98 ± 1.22 vs. +0.05 ± 1.24%, p=0.002), fasting plasma glucose (-28.72 ± 26.44 vs. +6.15 ± 44.91 mg/dl, p=0.022), and 2 hour postprandial glucose (-37.63 ± 44.79 vs. +1.73 ± 7.63 mg/dl, p=0.003) after 6 months. Total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, HOMA2, and hsCRP levels showed no significant difference. Body weight (-2.01 ± 2.59 vs. +0.22 ± 1.73 kg, p=0.001), BMI (-0.80 ± 1.00 vs. +0.02 ± 0.80 kg/m², p=0.003), systolic blood pressure (-8.15 ± 15.92 vs. +0.42 ± 14.07 mmHg, p=0.041) were significantly decreased in the LSM group. Significant carotid IMT regression was seen in the LSM group after 6 months (mean IMT: -0.030 ± 0.144 vs. +0.083 ± 0.167 mm, maximum IMT: -0.084 ± 0.197 vs. +0.07 ± 0.199 mm, p=0.004, p=0.009, respectively).

Conclusion: Lifestyle modification in patients with type 2 diabetes had positive effects on glycemic control, weight loss, and prevention of carotid atherosclerosis progression.
PS 56
Regulation of weight and obesity

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Mutation analysis of small heterodimer partner (SHP, NROB2) gene among 596 Chinese subjects and identification of four novel variants

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Background and Aims: The atypical orphan nuclear receptor small heterodimer partner (SHP, NROB2) modulates the transcription activity of MODY1 gene HNF-4α. Mutations in SHP were associated with moderate obesity among Japanese. The purpose of the study was to evaluate the prevalence of SHP variants among obese Chinese men.

Materials and Methods: We screened the whole coding region and intron/exon boundaries for SHP in 324 unrelated Chinese obese subjects (BMI 27.8 ± 2.7, BMI ≥25 kg/m² is the cut off for obesity in this study) and 272 unrelated nondiabetic and nonobese control subjects (BMI 20.3 ± 2.5, BMI <23 kg/m²) by direct sequencing of the amplified polymerase chain reaction products.

Results: We identified six variants in 324 Chinese obese subjects, which included the previously reported mutations (H356del10, R34X) in Japanese obese subjects. The H356del10 was identified in seven separate obese carriers (2.2%) and R34X was identified in one carriers in this study. Additionally, a total of four novel mutations, including two missense mutations (G174A and G192E), one silent mutation (P10P) and one variants in intron1 (IVS1+10 C→T) were identified. The G174A and G192E variants were each identified in two separate obese carriers and P10P was identified in one carrier, the IVS1+10 C→T variants was also identified in one carrier. The overall frequency of the SHP mutations in Chinese obese objects in this study was 3.7% (12/324). All the mutations present in the heterozygous state. No mutations were identified in 272 nondiabetic lean controls (P>0.00068). Although, it was previously well documented that H356del10 and R34X mutation were associated with obesity among Japanese, whether the four novel mutations have any functional significance needs further investigation.

Conclusion: Genetic variation in the SHP gene may be a key genetic factor responsible for moderate obesity among Chinese.

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Genetic interaction between the IGF2 Apal polymorphism and the insulin variable number of tandem repeats in their associations with body mass index in children

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Background and Aims: The insulin (INS) gene variable number of tandem repeats (VNTR) and single nucleotide polymorphisms (SNPs) in the nearby IGF2 gene on chromosome 11 have been reported to be associated with weight gain. We therefore sought association between these genetic variants and weight at age 7 years in a normal population of children and explored possible gene–gene interactions.

Materials and Methods: Genomic DNA was extracted from blood and mouthwash samples from 1,400 children in the prospective Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) birth cohort (the Children in Focus and control sub-cohorts). Of these 621 also had microsatellite–validated DNA samples from both their parents for transmission disequilibrium testing. Plasma IGF-2 concentrations were measured at age 5 years and heights and weights were measured at age 7 years. Body mass index (BMI) was calculated as weight (kg) divided by height (m²), and was converted into a standard deviation score (SDS) by reference to the full ALSPAC cohort (n=14,000). All samples were genotyped for IGF2 Apal (rs680, G→A) and XcmI (rs3842759; A→G) (two IGF2 SNPs reported to be associated with BMI in adults), and HphI (rs689) as a surrogate for INS VNTR class. Genotyping was performed by PCR followed by restriction fragment length polymorphism analyses.

Results: The IGF2 XcmI SNP was associated with variation in plasma IGF-2 concentrations at age 5 years (geometric means: A/A 382 ng/ml, A/T 446; T/T 446; p=0.001) but not with markers of childhood obesity. In contrast both IGF2 Apal (p<0.05) and INS VNTR (p<0.05) were independently