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GENETIC INFLUENCE ON FACTOR VII ACTIVITY IS OVERWHELMED BY ENVIRONMENTAL FACTORS IN CHINESE NIDDM PATIENTS

KSL Lam, ED Janus, OCK Ma and C Bourke. Dept. of Medicine, Clinical Biochemistry and Pathology, University of Hong Kong, Hong Kong.

We studied the effects of genetic and environmental influences on factor VII coagulant activity (VIIc) in Chinese diabetic patients (264 NIDDM and 78 IDDM) and 143 normal controls. VIIc was measured by one-stage biological assay. The Arg→Glu mutation at residue 353 of the factor VII gene, which leads to loss of an MspI restriction site (M2 allele) and lower VIIc levels, was detected after MspI digestion of polymerase chain reaction-amplified genomic DNA. In both diabetic and control Chinese subjects the allele frequencies for M1 and M2 were 0.96 and 0.4 respectively, the corresponding reported frequencies in Caucasians being 0.89 and 0.11 respectively. As in Caucasians, VIIc levels were 22% lower in Chinese controls with M1M2 versus M1M1 genotype ($p<0.01$). The corresponding difference was 4% for NIDDM and 24% for IDDM patients respectively ($p=NS$). Despite similar genotypic distributions, NIDDM patients had higher mean VIIc levels than controls and IDDM patients ($p<0.01$); they were also older, and had higher serum creatinine, triglyceride, apo B (all $p<0.01$) and HbA1c ($p<0.01$ and <0.05 respectively), and lower HDL-cholesterol and apo A1 (both $p<0.01$). VIIc levels were similar between IDDM and controls. On multivariate regression analysis, serum triglyceride was the most significant independent determinant of VIIc ($p<0.0001$), contributing to over 25% of the variability in controls and diabetic patients. The contribution of the Arg_{353}→Glu genptype, although significant ($p<0.001$) was only 2.1 % for all subjects and 1% for diabetic patients. Other significant environmental determinants included age, female sex, total cholesterol, serum creatinine, mean albumin excretion rate and HbA1c. VIIc was higher in diabetic patients with macroangiopathy ($p<0.005$) and retinopathy ($p<0.0001$). In conclusion, the M2 allele is apparently less common in Chinese than in Caucasians. Plasma VIIc is determined by both genetic and environmental influences such that in NIDDM patients, the effect of environmental factors, particularly that of hypertriglyceridaemia predominates, almost negating the genetic influence. High VIIc may contribute to the development of macroangiopathic complications and perhaps also retinopathy in patients with NIDDM.

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CHOLESTERYL ESTER TRANSFER PROTEIN GENE POLYMORPHISMS IN CHINESE PATIENTS WITH NON-INSULIN-DEPENDENT DIABETES MELLITUS

KCB Tan, SWM Shiu and KSL Lam. Department of Medicine, University of Hong Kong, Hong Kong.

We determined the effect of variation at the cholesteryl ester transfer protein (CETP) gene locus on plasma lipid levels in 129 healthy volunteers and 191 Chinese patients with non-insulin-dependent diabetes mellitus (NIDDM). The TaqIA restriction fragment length polymorphism (RFLP) generates two alternative fragments of 7.5kb (A1) and 9.0kb (A2) whereas the TaqIB RFLP produces fragments of 4.4kb (B1) and 5.3kb (B2). There were no significant differences in the allele distribution at these polymorphic loci between the controls (A1=0.86, A2=0.14; B1=0.56, B2=0.44) and the diabetic patients (A1=0.91, A2=0.09; B1=0.65, B2=0.35) and the allele frequencies were similar to those described in Caucasian populations. Diabetic patients with the genotype 1-1 of the TaqIA polymorphism had significantly lower HDL cholesterol (HDL-C) than those with the genotype 1-2 (male: 1.05 ± 0.31 mmol/l vs 1.29 ± 0.45, $p<0.05$; female: 1.14 ± 0.30 vs 1.32 ± 0.42, $p<0.05$). No significant differences were observed in age, body mass index, total cholesterol, triglyceride, LDL cholesterol or HbA1c levels between the two genotypes. A similar association between TaqIA polymorphism and HDL-C was not seen in the controls. Fasting lipid levels between subjects with different genotypes of the TaqIB polymorphism were not significantly different in either the diabetic patients or the controls. In summary our data indicate that there is an association between TaqIA polymorphism of the CETP gene and plasma HDL-C concentration in Chinese patients with NIDDM.