Apolipoprotein B signal peptide polymorphism in relation to lipids and diabetes in male CAD patients

Previous studies reported inconsistent data concerning an association between the apolipoprotein B (apo B) signal peptide insertion/deletion (Ins/Del) polymorphism and coronary artery disease (CAD) or myocardial infarction [1]. Our group found an association between the Del allele and CAD in non-diabetic Czech males under 55 years of age [2]. In addition to problems posed by the selection of control groups, as well as by differences in the disease definition and in ethnic background discussed by Marshall et al. [3], other factors such as the presence or absence of type 2 diabetes mellitus might also partially explain some inconsistencies of the previous association studies, e.g. the apo B Ins/Del polymorphism was associated with 2-h and fasting plasma glucose level [4,5].

To test the possible influence of type 2 diabetes, we analyzed a group of male patients with angiographically proven CAD according to the standard criteria [6]. Subjects were recruited consecutively from the Center of Cardiovascular Surgery and Transplantation in Brno and from the Department of Cardiopulmonary Testing, University Hospital Brno-Bohunice in a period from August 1996 to October 1998. Allele frequencies of the polymorphism mentioned above were ascertained by PCR methods [7] in 515 patients [Caucasians, mean age 57.65 ± 8.25 years, 348 (67.6%) of them with hypertension, 135 (26.2%) with type 2 diabetes mellitus, without valvular diseases or cardiomyopathies]. In order to contribute to the still open question of a relationship of the studied polymorphism with CAD, fasting plasma concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides (TG), apo B and apo AI were measured as described elsewhere [8]. The data for TC, TG, LDL, HDL were available from 252 patients without hypolipidemic therapy, and for apo B and apo AI from 219 of these patients.

Allele frequencies (genotypes) in the total sample were 65.6% for Ins and 34.4% for Del alleles. We found a significant association between this polymorphism and the plasma concentration of TC [P = 0.05, Kruskal–Wallis ANOVA (K-W ANOVA)], LDL (P < 0.05, K-W ANOVA) and apo B (P < 0.05, K-W ANOVA) in patients without hypolipidemic therapy. The respective mean plasma concentration values in patients with Ins/Ins, Ins/Del and Del/Del genotypes were 5.61 ± 0.89; 5.74 ± 1.11; 6.16 ± 1.28 mmol/l for TC, 3.40 ± 0.84; 3.52 ± 0.91; 3.91 ± 1.05 mmol/l for LDL, and 1.13 ± 0.21; 1.16 ± 0.26; 1.27 ± 0.25 g/l for apo B. In agreement with previous studies, our results thus confirm the relation between the Ins/Del polymorphism in the signal peptide of the apo B gene and variations in plasma lipoprotein and apolipoprotein levels [1].

In the whole sample, we observed that allele frequencies of the polymorphism studied tended to be different between CAD patients with and without type 2 diabetes mellitus, with a higher frequency of the Ins allele in the diabetics (69.7 vs. 64.2%; P = 0.06, Fisher’s exact test). This finding is consistent with the studies of Kammerer et al. and Boerwinkle et al. who reported associations between this polymorphism and 2-h or fasting plasma glucose levels [4,5], suggesting a potential link between this polymorphism and glucose metabolism. In addition, we can not, as well, exclude the possibility that diabetes might affect the apo B signal peptide polymorphism-related risk of CAD.

Contrary to the study of Gardemann et al. [9], we did not find any difference in the apo B allele frequencies between patients with and without MI history (65.2% for the Ins, 34.8% for the Del alleles-148 Ins/Ins, 159 Ins/Del, 42 Del/Del in patients with MI history, and 66.6% for the Ins, 33.4% for the Del alleles-72 Ins/Ins, 77 Ins/Del, 17 Del/Del in patients without MI history, NS, Fisher’s exact test).

In conclusion, our findings show that the apo B Ins/Del polymorphism affects plasma lipoprotein and apolipoprotein levels in male CAD patients and that the Ins allele is associated with the type 2 diabetes mellitus in these patients with a marginal significance.

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