MELANOCORTIN 4 RECEPTOR GENE POLYMORPHISM AND ASSOCIATION WITH CHOLESTEROL LEVELS IN MALAYSIAN MALAYS

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Melanocortin-4 receptor (MC4R) is a G-protein coupled receptor which regulates appetite and body weight. Mutations in the MC4R gene cause the monogenic form of obesity. MC4R mutations result in early onset of obesity. This study was aimed to investigate the MC4R rs2229616 polymorphism (Val101Ile) and its association with obesity-related parameters in a Malaysian Malay population. This study involved 649 subjects. Obesity-related parameters were collected. Buccal swabs were collected for extraction of genomic DNA. The genotyping was performed using real-time PCR system. The results showed that 3% of the non obese and obese groups were GA heterozygotes respectively. The frequencies of GG homozygote in non obese and obese groups were 95% in both. No AA homozygote mutant was found in both non obese and obese groups. The genotypes were in Hardy-Weinberg equilibrium. Significant associations were observed between MC4R rs2229616 SNP with LDL cholesterol (age and gender adjusted) (additive model: p=0.032, R=0.140) and with total cholesterol (age and gender adjusted) (additive model: p=0.002, R=0.179). There was no significant association between the MC4R rs2229616 SNP with BMI. In summary, the MC4R rs2229616 polymorphism is associated with cholesterol levels in Malaysian Malays but not with any other obesity parameters.

ASSOCIATION OF CHROMOSOME 9P21 POLYMORPHISM WITH CORONARY ARTERY DISEASE IN WESTERN INDIANS

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Indians have a high propensity to develop Coronary Artery Disease (CAD) and it has been estimated that 60% of the world’s cardiac population will be in India by the year 2020. In this context it is very important to evaluate the new markers especially genetic variants in the Indian population, which is a heterogeneous group. Genome-wide studies have implicated SNPs in 88kb region of chromosome 9p21 to be associated with CAD. In the current study we have evaluated the association of SNP rs10757278 at the 9p21 locus with CAD in Western Indians. Genotyping for rs10757278A/G was done by direct sequencing in 215 cases with confirmed CAD and 150 controls. Significantly higher frequency of the G allele was seen in cases as compared to controls 0.64 vs 0.53. The G allele showed association with risk of CAD (OR 1.589; 95% CI 1.177-2.146; P 0.003). The association is explained by the recessive model of inheritance. Addition of the 9p21 allele to Framingham risk score FRS, resulted in a shift of 17% of individuals from the low risk category to the intermediate-low (>5% to <10% 10-year risk) and 7% from intermediate-low to intermediate-high (>10% to <20% 10-year risk) categories. In conclusion the rs10757278 A/G SNP at the 9p21 locus is significantly associated with the risk of CAD in Western Indians.

APOLIPOPROTEIN E POLYMORPHISM IN GENERAL POPULATION AND IN PATIENTS OF ISCHEMIC AND HEMORRHAGIC STROKE IN CONSTANTINE CITY

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Apolipoprotein E has been one of the most thoroughly studied genetic polymorphism, particularly for its effects on lipid profiles. Several epidemiological studies have identified that plasma concentrations of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, and triglycerides (TG) are important predictors of myocardial infarction MI and coronary heart disease. Apolipoprotein E, a 299-amino acid, 34-kDa molecular weight is polymorphic and exist in three protein isoforms designated E2, E3, and E4 encoded by three alleles e2, e3, and e4. These three apoE isoforms differ from each other by amino acid substitution at either amino acid 112 or 158. These three isoforms determine the six genotypes (e2/e2, e2/e3, e2/e4, e3/e3, e4/e3, and e4/e4). ApoE is a component of several classes of plasma lipoprotein: very low-density lipoproteins (VLDL), high-density lipoprotein (HDL), intermediate density lipoproteins (IDL), and Chylo-microns, and plays a key role in regulating plasma cholesterol and triglyceride homeostasis functioning as ligand for LDL-receptors, LDL-receptor related protein. However there are no reports investigating apoE gene polymorphisms in Algerian patients. We therefore done the present study to estimate the frequency of apoE genotype and alleles in healthy subjects and in patients with cerebrovascular disease as well the prevalence of disease associated with particular apoE genotypes and alleles. Mean level of lipid, as well as genetic of Apolipoprotein E (apoE) were determined in control (509) and in CVD (205) including cerebral infarction (63%) and cerebral hemorrhage (37%) in subjects in Constantine, a selected population of east of Algeria. The apoE allele frequencies of patients (ICV and controls were 3.1% vs. 5.0% for e2, 81.8% vs. 84.3% for e3, and 15.1% vs. 10.5% for e4. The patients compared with control subjects had statistically significantly higher mean cholesterol (1.96 + 0.47 mg/dl vs. 1.82 ± 0.40 mg/dl p = 0.05) and LDL-C (1.28 ± 0.43 mg/dl, vs. 1.09 ± 0.27 mg/dl, p < 0.01), and lower HDL cholesterol with mean values of (0.37 ± 0.11 mg/dl vs. 0.44 mg/dl p = 0.01). Those patients who carried the apoE4 allele, had an association with cerebral infarction but not with cerebral hemorrhage, the carriers of allele e4 and e3/e4 subjects compared with e3/e3 are associated with an increased incidence of ICVD with odds.