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EFFECTS OF *FTO* RS9939906 AND *MC4R* RS17782313 ON OBESITY, TYPE 2 DIABETES MELLITUS AND BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION

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Background: *FTO* rs9939609 A/T and *MC4R* rs17782313 C/T SNPs have been associated with overall obesity in general population, and associations with type-2 diabetes are not clear. Individuals with mutations in *MC4R* gene have lower levels of blood pressure, independently of obesity.

Objectives: To investigate the association between *FTO* rs9939609, *MC4R* rs17782313 polymorphisms with anthropometric indicators, blood pressure and type-2 diabetes mellitus among hypertensive patients.

Methods: 217 individuals (86 men and 131 women) with hypertension (systolic and/or diastolic blood pressure \geq 140/90 mmHg or use of lowering BP agents) were genotyped [TaqMan-based assays (Applied Biosystems Inc., Foster City, CA)]. Type-2 diabetes was diagnosed according to the American Diabetic Association. Weight (kg), height (m), waist, hip and neck circumferences (cm) were measured and body mass index (BMI, kg/m²) was calculated. BAI (%) was evaluated according to formula: hip (cm) / [height (m)]^{1.5}-18. Data were expressed as mean \pm SD or frequencies (%). Analysis of covariance models (ANCOVA) and modified Poisson's regression were used to analyze associations with genotype, blood pressure and type-2 diabetes.

Results: Mean age of all participants was 59.8 \pm 11.2 years, systolic blood pressure 152.1 \pm 20.6 mmHg and diastolic blood pressure of 87.7 \pm 13.0 mmHg. Prevalence of type-2 diabetes mellitus was 44.7%. Rare allele frequencies were 0.40 for A for *FTO* rs9939609 and 0.18 for C for *MC4R* rs17782313 (Hardy-Weinberg equilibrium $P=0.8$ for both). After adjustment for age and BMI, risk allele C for *MC4R* was associated with type-2 diabetes in women [RR 1.5 (95% CI 1.1 – 2.2); $P=0.03$]. We found a positive effect of *FTO* rs9939609 on neck circumference among men and women and on BAI among women; *MC4R* rs17782313 has a positive effect on neck among women. In contrast, we found a negative effect of *MC4R* rs17782313 on systolic (TT 154.2 \pm 20.3, TC/CC 144.2 \pm 20.3; $P=0.05$) and diastolic (TT 90.1 \pm 12.2, TC/CC 83.2 \pm 12.1; $P=0.03$) blood pressure in men, independently of age and BMI.

Conclusions: Common genetic variants in *FTO* and *MC4R* have positive effects on obesity and type-2 diabetes mellitus and a negative one over blood pressure among patients with hypertension.