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Genetic Control of Renin Angiotensin System and Extracellular Matrix-Related Protein Polymorphisms in Obese Preschool Children

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Background: We have recently shown that postnatal overnutrition in male rats leads to obesity and the acquired reset of the intra-renal renin angiotensin system (RAS) and of extracellular matrix (ECM)-linked molecules during renal maturation. Long-standing obesity, renal functional and structural impairment, and hypertension were programmed later in adulthood by early postnatal overnutrition. This study was designed to investigate whether genetic polymorphisms of RAS and ECM-linked proteins were associated with the susceptibility to obesity in childhood.

Methods: We performed the genotyping of angiotensin converting enzyme (ACE), angiotensinogen (AGT), angiotensin type 2 receptor (AT2), matrix metalloproteinase (MMP)-9, and plasminogen activator inhibitor (PAI)-1 proteins in 46 obese, 48 overweight, and 96 control children using PCR-restriction fragment length polymorphism analysis.

Results: The mean age was 22.3 ± 1.5 months in controls, 17.3 ± 2.19 months in overweight children, and 24.2 ± 2.96 months in obese children. No differences among the groups were found with respect to age, sex, gestational age, birth weight, blood pressure levels, and serum levels of glucose and cholesterol. Obese children showed a lower incidence of ACE II genotype, compared to the controls (Control 46.8% Vs. Obese 15.6%, $p < 0.05$). Overweight children had a higher incidence of MM genotype in the AGT M235T polymorphism (Control 2.1% Vs. Overweight 16.7%, $p < 0.05$). In overweight children, the MMP-9 C1562T polymorphism revealed an increase in CC genotype (Control 66.3% Vs. Overweight 90.7%, $p < 0.05$) and a decrease in CT genotype (Control, 30.5% Vs. Overweight 9.3%, $p < 0.05$). In the case of combination of overweight and obese children, a higher incidence of MM genotype in the AGT M235T polymorphism was found compared to the controls (Control 2.1% Vs. Overweight+Obese 10.6%, $p < 0.05$). There were no genotype differences of the AT2 C3123A and the PAI-1 4G/5G polymorphism among the groups.

Conclusions: The ACE I/D, AGT M235T, and MMP-9 C1562T polymorphisms could be suitable genetic markers for development of overweight or obesity of childhood.

Key Words: 레닌 안지오텐신 계, 세포외 기질, 비만

Renin angiotensin system, Extracellular matrix, Obesity