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Effects of GLP-1 receptor polymorphisms on adolescent obesity

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To address the possibility that genetic variation of GLP-1R gene could affect obesity according to the genotypes, we tried to detect the mutation/SNP in GLP-1R. In accordance with our aims, subgroups with and without NAFLD and also subgroups with and without insulin resistance were compared with each other and with the control group. Genomic DNA was extracted from 162 overweight/obese patients and 100 controls and full exon sequencing and association study for GLP-1R gene were carried out. Three polymorphisms and one mutation were detected in fourth and fifth exons of GLP-1R gene. There were no significant differences in allele frequencies of these polymorphisms between groups with NAFLD (non-alcoholic fatty liver disease) or insulin resistance, and also there were no significant differences in BMI, weight, height and other obesity related factors among the wild type, heterozygote and homozygote of these variants in patients ($p>0.05$). RI3IQ variation was detected in three cases from which 1/3 had fatty liver but none showed insulin resistance. There were also statistically meaningful results for 'Odds Ratio' among different genotypes and allele frequencies in groups with fatty liver and/or insulin resistance. One of our polymorphisms was rs6918287 for which in heterozygote group, we detect double risk of insulin resistance. Patients with A allele also show approximately doubled risk for fatty liver occurrence. However, for rs3765468, we got tripled risk for insulin resistance in homozygous individuals and around double probability for fatty liver disease in heterozygous ones. The other SNP was rs6923761. In heterozygous individuals, there is an increase in risk for fatty liver and a decrease in risk for insulin resistance. In homozygous group also the prospect of insulin resistance is double declined. Patients with A allele of this polymorphism show a drop in risk for insulin resistance as well. GLP-1R polymorphisms could influence effects of GLP-1 on obesity and diabetes and thus the functional analysis of the GLP-1R polymorphisms is expected. Full exon sequencing and function analysis also remain to be examined.

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