The association between rs4684677 T/A polymorphism in preproghrelin gene and predisposition to autoimmune thyroid diseases in children.

**BACKGROUND**

Ghrelin and obestatin are two gastrointestinal peptides obtained by post-translational processing of a common precursor, preproghrelin. Ghrelin is an orexigenic and adipogenic peptide and a potent growth hormone secretagogue (GHS) modified by the enzyme ghrelin-O-acyl-transferase to bind and activate its receptor, the GHS-R [1].Obestatin was initially identified as an anorexogenic peptide and as the cognate ligand for GPR39, but its effect on food intake and its ability to activate orphan G protein–coupled receptor GPR-39 (GPR39) are still controversial. The preproghrelin is a gene responsible for generation of ghrelin and obestatin [2,3]. mRNA expression for preproghrelin was found inAITDs in previous studies [4]. There are papers, where a role of preproghrelin polymorphism on various immunological diseases was determined, but nothing is known about its influence on the autoimmune thyroid diseases (AITDs). The aim of our study was to estimate the association of two polymorphism of preproghrelin gene with the predisposition to GD and HT in children.

**DESCRIPTION OF METHODS**

The study was performed in the group of 145 patients with GD (mean age, 16.5±2.2) and 87 patients with HT (mean age, 15.2±2.2) at 161 healthy volunteers (mean age, 16.3±3). DNA was extracted from the peripheral blood leukocytes using a classical salting out method. The two SNPs rs696217 and rs4684677 in the ghrelin/obestatin prepropeptide gene were genotyped by TaqMan SNP genotyping assay (Applied Biosystems, USA). For all studied polymorphisms were used ready to use fluorogenic TaqMan assays: rs696217 (C.3151003.20) and rs4684677 (C.25607748.10). Reactions were carried out in a 7900HT Fast Real-Time PCR System (Applied Biosystems, USA) under the following conditions: 10 min at 95°C for starting AmpliTaq Gold activity, 40 cycles of 95°C for 15 s and 60°C for 1 min. As a negative control, we used a sample without template. The negative control was helpful for measuring any false positive signal caused by contamination. All SNPs were analyzed in duplicates. The levels of thyroid hormones, TSH and anti-thyroid autoantibodies were determined using chemiluminescence method.

**RESULTS AND CONCLUSION**

In our study, rs4684677 T alleles was more frequent in patients with HT in comparison to healthy subjects (p=0.002) with OR = 8.0 and 95% confidence interval for OR: 1.8-20.67, what means that risk for development of HT is eight higher for T allele in comparison to A allele when considering CG as a point of reference. Also when considering only women group rs4684677 T alleles was more frequent in HT in comparison to healthy subjects (p=0.02) with OR = 6.7 and 95% confidence interval for OR: 1.2-168.37. Frequency of the SNP rs696217 is not different between the groups. There was significant relationship between rs4684677 polymorphisms and IT4 concentration (p=0.02) stated in women with HT and GD. When considering all patients (men and women with GD or HT) relationship between rs4684677 polymorphisms in preproghrelin gene could contribute to autoimmune thyroid diseases development in children and T allele is the main risk factor.

**REFERENCES**

