EVALUATION OF SERUM CYTOKINES IL-6 AND OSTEOPROTEGERIN (OPG) MEASUREMENTS IN THE DIAGNOSIS OF CHRONIC AUTOIMMUNE THYROIDITIS AND GRAVES’ DISEASE IN CHILDREN

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INTRODUCTION

Chronic autoimmune thyroiditis (cAIT) and Graves’ disease (GD) are the most common autoimmune disorders in children. Osteoprotegerin (OPG) is a soluble glycoprotein that belongs to the tumor necrosis factor TNF receptor superfamily (TNFR) and plays an important role in bone homoeostasis and in vasculature. It acts as a decoy soluble receptor for the receptor activator of nuclear factor κB ligand (RANKL) in inhibiting osteoclastogenesis. OPG acts as a decoy receptor for the TNF-related apoptosis inducer ligand (TRAIL). Thus OPG acts as a potential counter-regulatory and anti-apoptotic factor.

PROINFLAMMATORY CYTOKINE IL-6 has been associated with the induction of inflammation and autoimmunity. IL-6 is released by fibroblasts, T-cells, endothelial cells and monocytes. It is a pleiotropic cytokine exerting multiple biologic activities on different types of target cells including induction of B-cell differentiation, activation of T-cells, induction of acute phase proteins, stimulation of hemopoietic precursor cell growth and differentiation, pyrogenic action as well as inhibition of cell growth and apoptosis.

AIM OF THE STUDY

The aim of the study was to determine concentrations IL-6 and OPG in autoimmune thyroid disease (AITD) in children.

MATERIAL AND METHODS

1. Studied groups and analyzed markers: 64 children, 3 subgroups: 22 children with hypothyroidism (hypoT), 22 children with hyperthyroidism (hyperT) (newly diagnosed patients) and 20 healthy subjects as an euthyroid control.

2. Inclusion criteria: clinical, hormonal and autoimmune: TRAb+ in GD: ATPO+/ ATG+ in cAIT.

3. Methods: thyroid hormones - MEIA tests (Abbott, AxSym); OPG and IL-6 - ELISA tests (Biomedica and BenderMedSystem, Vienna, Austria), antibodies TRAb/ATG/ATPO – RIA tests (Brahms, Berlin, Germany).

4. Serum concentrations of IL-6 and OPG in groups of patients with hypo- and hyperthyroidism (vs control) were evaluated at the onset of disease (before treatment introduction).

5. Statistical analysis was carried out in SPSS 17.0 for Windows (SPSS, Chicago, IL). Shapiro-Wilk normality test, ANOVA (Newman-Keuls post-test), nonparametric Kruskal-Wallis (Dunn’s post-test) and Spearman’s rank correlation were used.

RESULTS

1. No significant difference was observed between IL-6 serum concentrations in studied groups (p=0.48; Kruskal-Wallis test).

2. OPG concentrations were significantly higher (ANOVA p=0.013; Newman-Keuls p<0.01) in children with GD: (mean ± SD: 4.48 ± 2.01 pmol/L) compared to control group (3.02 ± 1.17 pmol/L), whereas no significant difference between children with cAIT (3.79 ± 1.28 pmol/L) vs control group (Newman-Keuls p>0.05) and cAIT vs GD (Newman-Keuls p>0.05) was observed. (Fig. 1).

3. In children with hyperthyroidism we identified significant positive correlation between OPG and IL-6 (r=0.51; p<0.05). (Fig. 2.)

4. ROC curve indicates good efficacy of OPG to discriminate groups of hyperthyroid and healthy children (AUC=0.716; p=0.017) at cut-off point of 4.54 pmol/L with low sensitivity (54.5%) but high specificity (95%). (Fig. 3.)

5. In these groups of children (hyperT vs control) AUC of IL-6 based on ROC curve did not differ significantly from 0.5 (p=0.435).

CONCLUSION

Based on performed study we suggest that OPG may be considered as a marker of hyperthyroidism in children with GD.

Table 1. Descriptive statistics and significance of differences - hyperT, hypoT and control group (ANOVA - analysis of variance, KW - Kruskal-Wallis non-parametric test)