

EVALUATION OF SERUM CONCENTRATIONS OF SELECTED CYTOKINES OPG AND sRANKL IN THE DIAGNOSIS OF AUTOIMMUNE THYROID DISEASE IN CHILDREN

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Introduction:

Chronic autoimmune thyroiditis (cAIT) and Graves' disease (GD) are the most common autoimmune disorders in children, associated with induction of inflammation and autoimmunity process. OPG, a cytokine receptor which mediates suppressive effect on osteoclastogenesis and its soluble ligand RANKL (sRANKL) are regulators of inflammation and may constitute a link between bone, autoimmune disease, and vasculature.

Objective:

We hypothesized that cytokines OPG and sRANKL play a crucial role in modulating an immune response in both, thyroid disorders in children. The aim of study was to evaluate the concentrations of OPG and sRANKL in these two opposite clinical and hormonal thyroid diseases: cAIT and GD.

Tables and Figures:

	Hypothyroidism (hypoT) n=22	Hyperthyroidism (hyperT) n=22	Control group n=20	s
n	22	22	20	
sex	18 girls/4 boys	16 girls/6 boys	11 girls/9 boys	ns
Age [years]	11.39 ± 2.68	12.68 ± 4.62	11.57 ± 4.86	ns
BMI [kg/m ²]	19.18 ± 4.54	18.25 ± 3.42	18.17 ± 3.50	ns
BMI SDS	0.33 ± 1.54	-0.38 ± 1.05	-0.17 ± 1.04	ns
Cole index	1.05 ± 0.22	0.95 ± 0.13	0.9 ± 0.14	ns
TSH [0.5-5.0 μIU/mL]	46.76 ± 47.59 ↑	0.01 ± 0.01 ↓	2.28 ± 0.99	p<0.001 (K-W)
ft4 [0.7-1.85 ng/dL]	0.54 ± 0.31 ↓	4.24 ± 1.06 ↑	1.03 ± 0.12	p<0.001 (ANOVA)
ft3 [1.7-3.5 pg/mL]	2.10 ± 0.97	19.01 ± 5.30 ↑	2.70 ± 0.56	p<0.001 (ANOVA)
TRAb [<1 IU/L]	0.7 ± 0.3	24 ± 20 ↑	0.5 ± 0.3	p<0.001 (K-W)
ATG [<60 IU/mL]	533 ± 770 ↑	426 ± 649 ↑	18 ± 9	p<0.001 (K-W)
ATPO [<60 IU/mL]	2597 ± 912 ↑	2280 ± 1080 ↑	13 ± 12	p<0.001 (K-W)
OPG [pmol/l] [mean ± SD median (IQR)]	3.79 ± 1.28 3.77(1.79)	4.48 ± 2.01 4.68 (2.86)	3.02 ± 1.17 3.00 (1.98)	p=0.013 (ANOVA)
sRANKL [pmol/l] [mean ± SD median (IQR)]	0.38 ± 0.45 0.23 (0.35)	0.39 ± 0.58 0.20 (0.33)	0.27 ± 0.34 0.09 (0.48)	ns p=0.33 (K-W)

Table 1. Descriptive statistics and significance of differences (ANOVA – analysis of variance, K-W – Kruskal-Wallis nonparametric test)

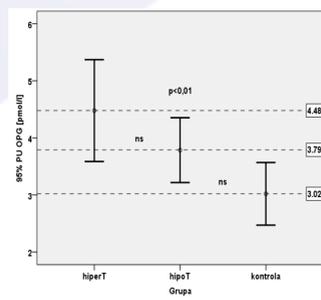


Fig. 1. Boxplot of OPG serum concentrations in studied groups

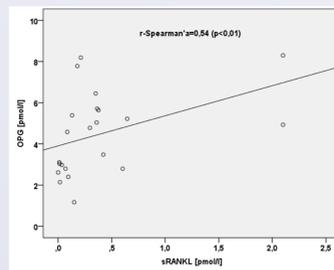


Fig. 2. Positive correlation of OPG and sRANKL in GD (Spearman's $r=0.54$; $p<0.01$)

Material and Methods:

- The study group consisted of 64 children, 44 newly diagnosed, untreated children with cAIT (n=22; with hypothyroidism) and GD (n=22; hyperthyroidism), and the control group of 20 healthy children. (Table 1.)
- Cytokine concentrations were evaluated using the ELISA technique (Bender MedSystems GmbH, Vienna, Austria).
- 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:

- The studied groups of children did not differ significantly in concentrations of sRANKL ($p=0.33$).
- We observed significantly higher concentrations of OPG in children with GD ($p<0.01$) (mean±SD; 4.48 ± 2.01 pmol/L) compared to control (3.02 ± 1.17 pmol/L); whereas no significant difference between children with cAIT (3.79 ± 1.28 pmol/L) vs control ($p>0.05$) and cAIT vs GD ($p>0.05$) was observed. (Fig.1)
- In children with hyperthyroidism we found positive correlation between both cytokines sRANKL and OPG ($r=0.54$); ($p<0.01$). (Fig. 2.) and in hyperthyroid children sRANKL correlated positively with ATPO ($r=0.46$); ($p<0.05$). (Fig.3.)
- In hypothyroid children sRANKL correlated positively with ft4 and ft3 ($r=0.53$; $r=0.52$) and ($p<0.05$; $p<0.05$), respectively (Fig.4.;5.) and negatively correlated with TSH ($r= -0.51$);($p<0.05$). (Fig.6.)
- ROC analysis indicates that OPG may be a marker of hyperthyroidism, exhibiting a good discriminatory efficacy between group of hyperthyroid children 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.7.)

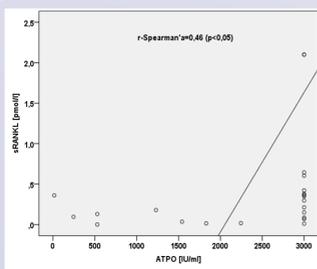


Fig. 3. Positive correlation of sRANKL and ATPO in GD (Spearman's $r=0.46$; $p<0.05$)

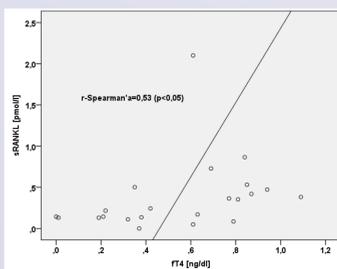


Fig. 4. Positive correlation of sRANKL and ft4 in cAIT (Spearman's $r=0.53$; $p<0.05$)

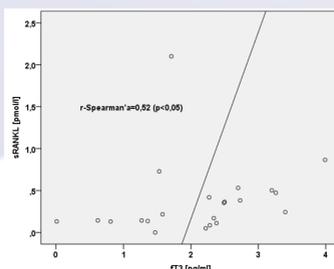


Fig.5. Positive correlation of sRANKL and ft3 in cAIT (Spearman's $r=0.52$; $p<0.05$)

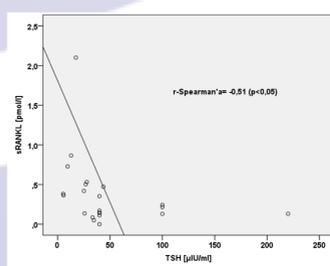


Fig.6. Negative correlation of sRANKL and TSH in cAIT (Spearman's $r= -0.51$; $p<0.05$)

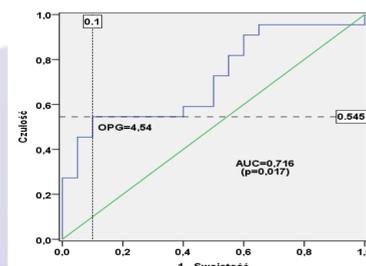


Fig. 7. ROC curve of OPG GD vs control ($AUC=0.716$, $p=0.017$, cut-off=4.54 pmol/l, sensitivity: 54.5%, specificity: 95%)

Conclusion:

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

Poster Number: P1-P267

There was no conflict of interest related to this study
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57th ESPE 2018 Meeting
ATHENS, GREECE
27th-29th September 2018

