

Osteoprotegerin and free T4 levels in subclinical hypothyroidism of childhood

Aristeidis Giannakopoulos, Alexandra Efthymiadou and Dionysios Chrysis

Division of Endocrinology, Diabetes and Metabolism, Department of Pediatrics, University of Patras Medical School, Rio Patras, Greece



INTRODUCTION AND OBJECTIVES

Osteoprotegerin (OPG) is a cytokine of the tumor necrosis factor receptor family, expressed in various cells types of the body including osteoblasts and endothelial cells. It acts as a soluble decoy receptor of RANK ligand preventing stimulation of osteoclastogenesis¹. In adults, subclinical hypothyroidism has been associated with cardiovascular complications². Furthermore several studies have linked OPG levels to increased cardiovascular risk³. In the present study we investigated the levels of OPG and other indices of bone metabolism such as tartrate-resistant acid phosphatase (TRAP) and bone alkaline phosphatase (BAP) in children and adolescents with **subclinical hypothyroidism (SH)**.

METHODS

The present study included 129 children and adolescents with SH (TSH between 5 μ IU/L and 10 μ IU/L with free T4 levels within normal range) and 346 healthy controls. In all subjects, age, gender and BMI were recorded and TSH, free T4, OPG, TRAP and BAP were measured. Regression analysis adjusted for age and BMI after appropriate log transformations was used and statistical significance was indicated with p value <0.05.

RESULTS

Summary of demographic elements and variables measured *

| | Euthyroid | Subclinical hypothyroidism |
|-----------------------------|-------------------|----------------------------|
| Individuals | 346 | 129 |
| Age (mean \pm SD) | 8,58 \pm 3,55 y | 7,75 \pm 3,75 |
| Gender (males) | 59 | 156 |
| BMI | 18 | 18,5 |
| BMI Z score (mean \pm SD) | 0,98 \pm 1,58 | 1,12 \pm 1,61 |
| OPG | 3,19 | 3,07 |
| Bone TRAP | 9,39 | 9,64 |
| TSH (mU/L) | 3,31 | 6,54 |
| Free T4 (μ g/dl) | 1,27 | 1,23 |
| BAP | 75 | 80,6 |

Results of data analysis

| Children with Subclinical Hypothyroidism (n=129) | | |
|--|------------|--|
| Partial Correlation | Covariance | Correlation Coefficient and statistical significance |
| Osteoprotegerin / free T4 | Age BMI | R= - 0,22 (p=0,015) |
| TRAP / free T4 | Age BMI | R= - 0,16 (p=0,002) |
| BAP / free T4 | Age BMI | R= - 0.065 (p=0,5) |

*In all variables the median is reported except from age and BMI Z score

- Age and BMI Z-score were no statistically different between SH and control group
- In children with subclinical hypothyroidism OPG and TRAP levels were negatively correlated to the serum free T4 levels with $r = -0,22$ (p=0,015) and $r = -0,16$ (p=0,002) respectively
- No correlation was found between BAP and free T4

CONCLUSIONS

OPG and bone TRAP levels in children and adolescents with SH are negatively correlated with free T4. Considering the probable effects of increased OPG in the vascular homeostasis, further research is needed to establish the role of childhood SH in the long-term cardiovascular risk.

REFERENCES

- 1) Simonet, W. et al(1997). Osteoprotegerin: A Novel Secreted Protein Involved in the Regulation of Bone Density. *Cell*.
- 2) Nagasaki, T.et al (2005). Increased levels of serum osteoprotegerin in hypothyroid patients and its normalization with restoration of normal thyroid function. *European Journal of Endocrinology*, 152(3), 347–353.
- 3) Lieb, W.et al (2010). Biomarkers of the osteoprotegerin pathway: Clinical correlates, subclinical disease, incident cardiovascular disease, and mortality. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 30(9), 1849–1854.

