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L-selenomethionine supplementation in children and adolescents with autoimmune thyroiditis: preliminary results of a randomized double-blinded placebo-controlled clinical trial

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Introduction

- Selenium treatment has been documented to have beneficial effects in adult patients with autoimmune thyroiditis, especially in those with a higher titer of antibodies and increased inflammatory disease activity. These effects were detected especially on the titer of antibodies against thyroid peroxidase (anti-TPO)[1]
- Data obtained from pediatric populations are scarce and inconclusive[2,3]

- Selenocysteine is found in enzymes of thyroid tissue
  - **Glutathione peroxidases (GPXs)** and **Thioredoxin reductases (TRs)** that have anti-oxidative actions, protect cell molecules from ROS and regulate expression of transcriptional factors
  - **Triiodothyronine deiodinases (TDs)** that catalyze T3 production

- *Potential Mechanisms*:
  1. **Increased oxidative stress- and cell death** may lead to expression of different epitopes that are recognized by the immune system
  2. **Cytokine production** is influenced by lymphocytic infiltration of the thyroid gland
  3. **Peripheral conversion of T4 to T3**

Objectives

To investigate whether daily supplementation of organic selenium at a high dose (200μg in the form of L-selenomethionine) has any effect on the titer of thyroid autoantibodies

Methods

Protocol: 100 children and adolescents with a diagnosis of autoimmune thyroiditis (under the age of 18ys) are randomized to blindly receive daily either 200μg of organic selenium (in the form of L-selenomethionine) or placebo for 6 months

- FT4, TSH, anti-TPO, anti-Tg autoantibodies are determined at 0, 3, 6 months
- Ultrasound of the thyroid gland is performed at 0, 6 months
- Follow-up every 3 months. To increase compliance: 1) phone contact once monthly, 2) blisters of tablets are requested to be returned during the next visit
- Sample size calculation: Number of patients needed in each arm to detect a difference of 10% in the percentage decrease in the titer of antibodies, with a statistical power of 80% and at the level of statistical significance 5% were found to be 35.3
- Statistical analysis: A mixed between-within subjects analysis of variance model was implemented. T-test and Mann-WhitneyU tests were also used appropriately.

Study characteristics:

- Single-center
- Two study groups: Intervention (L-selenomethionine) and Control (Placebo)
- Randomization using a random number table
- Double-blinded: Tablets are identical in terms of appearance and taste but differ in terms of their active ingredients. Obtained from the INTERMED Pharmaceutical Laboratories
- Patients' guardians gave their written and informed consent
- Protocol Submitted to CliicalTrials.gov [Identifier: NCT02644707]

Results*

Here is presented the analysis of the data obtained from **63 patients that completed 3 months (33 and 30 patients in the two study groups respectively) and **43 patients that completed 6 months of treatment** (24 and 19 patients in the two study groups respectively)*

***Table 1.** Baseline characteristics*

	Intervention group	Control group	P
Age (years)	11.8±0.3 (8.8-16.4)	11.3±0.5 (4.5-17.8)	**0.42**
Sex (M/F)	4/29	7/23	**0.24**

Data are described as mean value (x) ± Standard Error (SE) (range) (for age) or frequencies (for sex)

***Table 2.** Differences in the titer of autoantibodies between groups*

		0	3 mo.	Dif.	6 mo.	Dif.
Anti-TPO (U/ml) *	**Intervention group**	755.4±125.9	761.8±132.0	**+6.3±49.2****	664.1±112.2	**+58.5±41.5*****
	Control group	702.0±156.0	878.6±215.4	**+176.6±95.8****	666.3±246.6	**+213.7±148.3*****
Anti-Tg (U/ml) *	**Intervention group**	289.8±61.3	265.6±43.2	**-24.2±65.0§**	172.3±34.3	**-120.4±80.2§§**
	Control group	182.9±24.3	277.3±96.7	**+94.3±84.5§**	184.4±33.2	**-1.1±26.8§§**

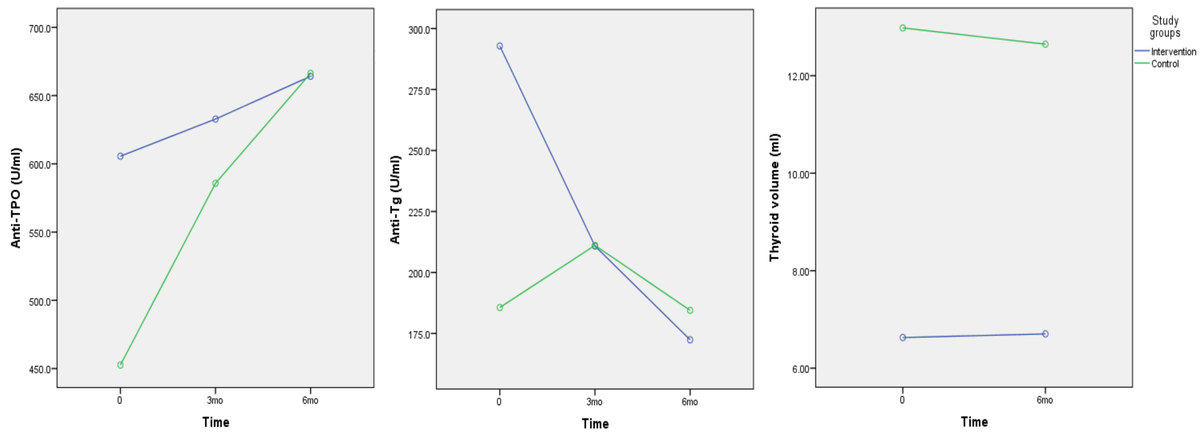
**Data are described as mean value (x) ± Standard Error (SE). Titer of antibodies did not differ between the two groups at the beginning (data not shown). **p=0.37, *** p=0.83, § p=0.36, §§ p=0.05*

***Table 3.** Differences in the thyroid volume between groups (included only those patients who completed 6 months of treatment)*

		0	6 mo.	Dif.
Thyroid Volume (ml)*	**Intervention group**	6.8±0.5	7.0±1.2	**+0.07±1.0****
	Control group	7.1±1.0	12.4±2.3	**-0.3±0.4****

**Data are described as mean value (x) ± Error (SE) . Thyroid volume did not differ between the two groups at the beginning (data not shown). **P=0.81.*

***Figures 1-3.** Differences in the titer of autoantibodies and thyroid volume between groups (included only those patients who completed 6 months of treatment)*



- No side-effects were described in both study groups
- No patient refusal of compliance or drop-out from the study were observed in both study groups

Conclusions

A. Based on these results, selenium supplementation for a 6-month period:
   - **decreases the levels of antibodies against thyroglobulin but not thyroid peroxidase**
   - **doesn't appear to delay the increase in thyroid volume (that also occurs, at least to an extent, as result of physiological growth) in children and adolescents with autoimmune thyroiditis**

B. The completion of the study, after the inclusion of all patients and for the whole study period, is needed to confirm and enhance these preliminary results.

References

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