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 titers of antibodies and increased inflammatory disease activity. These effects were detected especially on the titer of antibodies against thyroid peroxidase (anti-TPO).
- Data obtained from pediatric populations are scarce and inconclusive.
- Selenocytoine is found in enzymes of thyroid tissue:
  - Glutathione peroxidases (GPx) and Thioredoxin reductases (TR) 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-Whitney U 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: Tables 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 ClicialTrials.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

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>11.8±0.3 (8.8-16.4)</td>
<td>11.3±0.5 (4.5-17.8)</td>
<td>0.42</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>4/29</td>
<td>7/23</td>
<td>0.24</td>
</tr>
</tbody>
</table>
| 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

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TPO (U/ml)</td>
<td>765.4±125.9</td>
<td>761.8±132.0</td>
<td>+0.6±49.2**</td>
</tr>
<tr>
<td>Control group</td>
<td>702.0±156.0</td>
<td>878.6±215.4</td>
<td>+176±95.8***</td>
</tr>
<tr>
<td>Anti-Tg (U/ml)</td>
<td>289.8±61.3</td>
<td>265.6±43.2</td>
<td>-24.2±65.0**</td>
</tr>
<tr>
<td>Control group</td>
<td>182.9±24.3</td>
<td>273.1±96.7</td>
<td>+94.3±84.5**</td>
</tr>
</tbody>
</table>
| *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<0.03. ***P<0.003. §P<0.005

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

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid Volume (ml)*</td>
<td>8.8±0.5</td>
<td>7.0±1.2</td>
<td>+0.7±1.0**</td>
</tr>
<tr>
<td>Control group</td>
<td>7.1±1.0</td>
<td>12.4±2.3</td>
<td>-0.3±0.4**</td>
</tr>
</tbody>
</table>
| *Data are described as mean value (x) ± Standard 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)

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