Selenium supplementation and autoantibody titers in Graves’ disease

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Abstract

Objectives: To evaluate the efficacy of Se supplementation in patients with GD and GO in terms of changes in ocular and systemic signs and symptoms, health-related quality of life (HRQoL), and selenoprotein, thyroid tropin, thyroid hormone, and autoantibody levels.

Methods: RTCs evaluating the efficacy of Se supplementation in adult patients with GD and active GO, versus placebo or no active therapy, were included. A literature search was performed by two independent authors with eligible studies undergoing a validation screen. Data extraction of selected studies was done using a data extraction form, with statistical analysis using RevMan 5.1 software. Results were presented as mean differences, standard errors, and 95% confidence intervals, and graphically presented as forest plots. Estimates were calculated using the inverse variance method for continuous variables and pooled using the fixed effects model. If and Chi² tests were used to assess heterogeneity.

Results: Fourteen studies were initially retrieved for consideration, but only two trials were ultimately included. Both had good methodological quality and totaled 197 patients with GD and non-severe GO. The only available common outcomes of interest were changes in TRAB and TPOAb titers. No statistically significant difference was found in Se supplementation versus placebo. No significant heterogeneity was found in either the TRAB (I²=36%) or TPOAb (I²=0%) analysis.

Conclusions: This is the first meta-analysis summarizing the current available data on the efficacy of Se supplementation in patients with GD and active non-severe GO. Se supplementation in these patients was not associated with statistically significant differences in both TRAB and TPOAb titers on follow up. Larger studies are recommended to strengthen these findings.

Background

Selenium (Se), a trace mineral with antioxidant properties, has been proposed by studies to be potentially beneficial in patients with Graves’ disease (GD), especially those with active Graves’ ophthalmopathy (GO).

Objectives

General: To evaluate efficacy of Se supplementation in patients with GD and GO
Specific: To evaluate changes in:
1. Ocular and systemic signs and symptoms
2. Health-related quality of life
3. Selenoprotein, thyroid tropin, thyroid hormone, and autoantibody levels

Methods

Databases:
- MEDLINE, Embase, ClinicalTrials.gov,
- Google Scholar, Cochrane Central Register of Controlled Trials
- References of articles and individual authors

Keywords:
- selenium, “selenite”, “selenoprotein”
- thyroid, “orbiotropathy”, “oophalmopathy”
- hyperthyroidism, “Graves’ disease”, “thyrotoxicosis”
- thyroid-related eye disease”, “Basedow disease”

Inclusion Criteria:
- RTCs evaluating efficacy of Se supplementation on top of standard therapy in adult GD patients with active GO
- Versus either placebo or alternative comparator
- Outcomes: clinical activity of GO as measured via objective examination or symptom scores; levels of selenium or selenoproteins, TSH, thyroid hormones, TRAB and TPOAb
- No restrictions on language, ethnicity or gender

Exclusion Criteria:
- Pregnancy
- Comorbid systemic or ocular disease
- Severe GO requiring steroid use at outset
- Previous or ongoing use of Se supplements

Flowchart

Figure 1. Flowchart of methodology used to arrive at the studies included in the analysis.

Table 1. Methodological assessment of the quality of studies included in the review.

<table>
<thead>
<tr>
<th>Study</th>
<th>Se supplementation</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calleger 2015</td>
<td>64.2 ± 7.2</td>
<td>19.3 ± 3.8</td>
<td>7.7 ± 3.8</td>
<td>0.03 ± 0.02</td>
</tr>
<tr>
<td>Marconi 2011</td>
<td>6.7 ± 5.6</td>
<td>10.4 ± 3.8</td>
<td>7.7 ± 3.8</td>
<td>0.03 ± 0.02</td>
</tr>
</tbody>
</table>

Figure 2. Mean difference in TRAB titers between the Se and placebo groups.

Table 3. List of excluded studies and reasons for exclusion.

Study | Reason for Exclusion
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Watt 2013 | Ongoing trial, no data yet available
Wartenbruch 2007 | Case control design, no intervention
Khong 2014 | Case control design, no intervention
Petersen 2013 | Cross-sectional design, no intervention
Vicia 2005 | Different intervention and outcome measures
Smith 2011 | Review article
Dantas 2011 | Review article
Dharmasena 2014 | Editorial
Stumilo 2013 | Different disease population
Tosi 2010 | Different disease population
Fan 2014 | Different disease population
Xu 2011 | Animal study

Figure 3. Mean difference in TPOAb titers between the Se and placebo groups.

Conclusions

- Se supplementation in patients with GD and non-severe GO was not associated with significant differences in TRAB and TPOAb titers.
- More studies with larger populations and more clinical outcomes are recommended.