

# Selenium Supplementation in Patients with Hashimoto Thyroiditis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

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## Abstract

**Background:** Hashimoto thyroiditis (HT) is the most common cause of hypothyroidism in iodine-sufficient areas. Selenium is an essential trace element required for thyroid hormone synthesis and exerts antioxidant effects. Therefore, it may be of relevance in the management of HT.

**Methods:** We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the effect of selenium supplementation on thyroid function (thyrotropin [TSH], free and total thyroxine [fT4, T4], free and total triiodothyronine [fT3, T3]), thyroid antibodies (thyroid peroxidase antibodies [TPOAb], thyroglobulin antibodies [TGAAb], thyrotropin receptor antibody [TRAb]), ultrasound findings (echogenicity, thyroid volume), immune markers, patient-reported outcomes, and adverse events in HT. The study protocol was registered on PROSPERO (CRD42022308377). We systematically searched MEDLINE, Embase, CINHAL, Web of Science, Google Scholar, and the Cochrane CENTRAL Register of Trials from inception to January 2023 and searched citations of eligible studies. Two independent authors reviewed and coded the identified literature. The primary outcome was TSH in patients without thyroid hormone replacement therapy (THRT); the others were considered secondary outcomes. We synthesized the results as standardized mean differences (SMD) or odds ratio (OR), assessed risk of bias using the Cochrane RoB 2 tool, and rated the evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

**Results:** We screened 687 records and included 35 unique studies. Our meta-analysis found that selenium supplementation decreased TSH in patients without THRT (SMD -0.21 [confidence interval, CI -0.43 to -0.02]; 7 cohorts, 869 participants; I<sup>2</sup> = 0%). In addition, TPOAb (SMD -0.96 [CI -1.36 to -0.56]; 29 cohorts; 2358 participants; I<sup>2</sup> = 90%) and malondialdehyde (MDA; SMD -1.16 [CI -2.29 to -0.02]; 3 cohorts; 248 participants; I<sup>2</sup> = 85%) decreased in patients with and without THRT. Adverse effects were comparable between the intervention and control groups (OR 0.89 [CI 0.46 to 1.75]; 16 cohorts; 1339 participants; I<sup>2</sup> = 0%). No significant changes were observed in fT4, T4, fT3, T3, TGAAb, thyroid volume, interleukin (IL)-2, and IL-10. Overall, certainty of evidence was moderate.

**Conclusions:** In people with HT without THRT, selenium was effective and safe in lowering TSH, TPOAb, and MDA levels. Indications for lowering TPOAb were found independent of THRT.

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