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Effectiveness of Selenium Supplementation in the Treatment of Graves–Basedow Disease: A Scoping Review

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ADMINISTRATIVE INFORMATION

Support - Universidad del cauca.

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 August 2025 and was last updated on 30 August 2025.

INTRODUCTION

Review question / Objective The objective of this scoping review is to evaluate the effectiveness of the use of selenium in patients with GBD (or with GBD orbitopathy), who are under usual treatment for the disease (or who have previously been treated), in relation to different clinical and/or biochemical outcomes.

Background Graves-Basedow disease (GBD) is an autoimmune thyroid disorder characterized by loss of tolerance to the thyrotropin receptor, with clinical manifestations such as a hyperadrenergic state, goiter, orbitopathy, and myxedema, among others. Selenium is a micronutrient, essential for the synthesis of selenoproteins. Selenium deficiency has been linked to an increased risk and exacerbation of GBD and GBD orbitopathy; therefore, it has been suggested that supplementation with this micronutrient could modify some outcomes associated with both conditions.

Rationale Selenium is an essential micronutrient for the biosynthesis of selenoproteins containing selenocysteine, the thyroid contains the highest amount of selenium per gram of tissue and most of the selenoproteins are expressed in the thyroid and participate in the metabolism of thyroid hormones.
Selenium deficiency has been associated with an increased risk of AITD, an effect that could be explained by several mechanisms, such as decreased synthesis and secretion of interferon gamma and other cytokines, accompanied by an alteration in the cellular immune response, with increased activity of autoreactive T lymphocytes (TL) and low activity of regulatory TL (Treg).
Selenium deficiency has also been documented to be associated with AITD; in fact, multiple studies have shown that selenium supplementation in areas deficient in this micronutrient decreases thyroid Ab concentrations, suggesting that it could modify the natural course of AITD.
Previously, several studies have documented that serum selenium concentrations are significantly lower in individuals with GBD, which has led to the

consideration of selenium deficiency as a risk factor for the development of GBD.
This has led to the suggestion that selenium supplementation could have a favorable effect not only in the prevention of AITD (and in this sense, GBD), but also in the fact that it could positively modify different biochemical outcomes (e.g., TSH, FT4, FT4 concentrations, and thyroid Ab titers) or clinical outcomes associated with the disease.
These concepts led to the design and conduct of clinical studies that evaluated the effectiveness of selenium supplementation in patients with GBD with or without ophthalmopathy, with different (and sometimes discordant) findings. However, despite the evidence from these clinical studies, there is still no universally accepted criterion for the use of selenium in such patients.

METHODS

Strategy of data synthesis Using modified versions of the Population, Interventions, Comparators, and Outcomes (PICO) framework, we formulated the research question and selected the eligibility criteria for the scoping review.

Eligibility criteria The following data were collected in the review: design type, country, inclusion criteria, interventions, selenium dose, number of participants, follow- up time, and clinical and/or biochemical outcomes. Only adult participants (>18 years) diagnosed with GBD or GBD orbitopathy were considered.

Source of evidence screening and selection A structured literature search was carried out in PubMed/Medline, Scopus, Biosis, ProQuest, Web of Science, and Google Scholar for articles published from January 2000 to March 2025 (human trials, clinical trials, meta–analyses, reviews, scoping reviews, and systematic reviews).
The search terms used were: 'Graves-Basedow disease' or 'Graves' disease' or 'hyperthyroidism' or 'Graves' hyperthyroidism' or 'selenium or selenium supplementation' and 'effectiveness', detailing the search strategy as follows: Graves-Basedow disease [Title/Abstract] OR Graves' disease [Title/Abstract] OR hyperthyroidism [Title/Abstract] OR Graves' hyperthyroidism [Title/Abstract] OR Selenium intake [Title/Abstract] OR Selenium supplementation AND Effectiveness [Title/Abstract] OR Outcomes [Title/Abstract].
Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a total of 15 studies were included, 11 in individuals with GBD, and 4 in patients with GBD orbitopathy. The titles and abstracts of all studies were independently reviewed by three investigators using the Rayyan web tool. Full texts for the studies that met the initial inclusion criteria were obtained and reviewed, and the data were extracted through a standardized template, using a predefined data form created in Excel.
In the presence of discrepancies in data extraction, the investigators collaboratively conducted a second round of analysis and extraction to validate the information obtained.

Data management The titles and abstracts of all studies were independently reviewed by three investigators (H.V.–U., A.C.–P., and H. V.–S) using the Rayyan web tool (this further helped reduce selection bias). Full texts for the studies that met the initial inclusion criteria were obtained and reviewed, and the data were extracted through a standardized template, using a predefined data form created in Excel.
In the presence of discrepancies in data extraction, the investigators collaboratively conducted a second round of analysis and extraction to validate the information obtained. Each article was scrutinized according to the JBI Critical Appraisal Checklist; only those written in English were considered.

Reporting results / Analysis of the evidence In patients with GBD, the benefits were achieved in six clinical scenarios (hyperthyroidism due to GBD; GBD treated with methimazole; newly diagnosed GBD; untreated hyperthyroid patients with GBD; recurring GBD; and patients with GBD after radioactive iodine treatment), with favorable outcomes in relation to: increased TSH levels and decreased FT4, FT3, TPOAb, TgAb, and TRAb levels.
Clinical scenarios where selenium supplementation has been shown to be effective (in patients with GBD orbitopathy)
Meanwhile, in patients with GBD orbitopathy, benefits were achieved in four major clinical scenarios (mild GBD orbitopathy with euthyroidism; mild and active GBD orbitopathy (CAS >3); inactive moderate-to-severe GBD orbitopathy; and mild-to-moderate GBD orbitopathy); with favorable outcomes in relation to: quality of life, reduced ocular involvement, and slowed progression of the disease (in mild Graves' orbitopathy); differences in palpebral fissure and CAS score, eyelid aperture (even in inactive moderate-to-sever.

Presentation of the results Production of graphs, figures, and tables; and publication in an indexed journal.

Language restriction English.

Country(ies) involved Colombia.

Other relevant information None

Keywords Graves-Basedow; Selenium; Thyroid; Autoimmunity; Orbitopathy.

Dissemination plans indexed journals, webinars, instagram.

Contributions of each author

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