Original Article

Effect of *Selenomethionine*- Enriched Yeast on Hypothyroidism Patients

Hajyasini, A[1], Dehnad, A[2*], Farzi, A[3], Mobasseri, M[4], Ostadrahimi, A[5], Kafili, B[5]

1. *Higher education institute of Rab-Rashid, Tabriz, Iran.*
2. *Department of Bacterial Diseases Research, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension Organization (AREEO), Karaj, Iran.*
3. *Faculty of Chemical and Petroleum Engineering, University of Tabriz, Tabriz, Iran.*
4. *Endocrine Research Center Tabriz University of Medical Sciences.*
5. *Nutrition Research Center, Tabriz University of Medical Sciences.*

How to cite this article: **Hajyasini A, Dehnad A, Farzi A, Mobasseri M, Ostadrahimi A, Kafili B. Effect of *Selenomethionine*-Enriched Yeast on Hypothyroidism Patients. Archives of Razi Institute. 2025;80(1):257-261.** DOI: 10.32592/ARI.2025.80.1.257

Article Info:
Received: 17 November 2023
Accepted: 20 June 2024
Published: 28 February 2025

Corresponding Author's E-Mail:
a.dehnad@rvsri.ac.ir

ABSTRACT

Selenium (Se) is a trace mineral that plays a critical role in public health. It is a vital component of numerous enzymes and proteins called selenoproteins, thus affecting a wide range of biological activities. Hashimoto's disease is the most common cause of hypothyroidism. In addition to being a critical micronutrient for thyroid health, selenium has a direct association with liver health. The objective of this study is to examine the impact of Selenium on lipid factors, thyroid factors (anti-TPO and TSH), and liver enzymes. A double-blind, randomized clinical trial was conducted, enrolling 40 patients with Hashimoto's thyroiditis in two equal control (placebo) and intervention (Selenium) groups. Participants received 200 micrograms of Selenium over 60 days, with blood samples collected before and after the intervention. The spectrophotometric method was employed to measure total blood catalase, anti-TPO, TSH, malondialdehyde, serum lipid profile, and liver factors. The results were then subjected to statistical analysis. The study revealed a significant decrease in plasma MDA levels in response to selenium consumption. Additionally, a notable increase in hemoglobin levels was observed in the experimental group following the intervention, reaching a statistical significance of $P<0.05$. However, catalase enzyme, lipid profile components, and liver enzymes in the intervention group remained largely unchanged compared to the pre-intervention and control groups ($P>0.05$).TSH and anti-TPO levels exhibited a relative decrease in the intervention group ($P>0.05$). The findings of this study suggest a potential association between selenium consumption and improved serum lipid factors, liver enzymes, anti-thyroid peroxidase antibody, MDA, and HGB levels in individuals diagnosed with Hashimoto's thyroiditis.

Keywords: Hashimoto's Disease, Selenium, Lipid Factors, Liver Enzymes, Thyroid Factors.

1. Introduction

Selenium (Se) is a trace mineral that plays a critical role in public health. It is a vital component of numerous enzymes and proteins, called selenoproteins, and thus affects a wide range of biological activities, including anti-inflammation, thyroid function, fertility, DNA synthesis, and reproduction (3, 4). Selenium is also known for its potent antioxidant function (5, 6). A substantial proportion of the population exhibits inadequate intake of Se, attributable to the limited bioavailability of Se in soil and the low concentrations of Se present in vegetables (7). A prevalent approach to augmenting the Se content of food products involves the enrichment of foods with the organic form of Se. In this regard, live yeast cells have been observed to absorb Se and convert it into L (+) selenomethionine (8). It is noteworthy that selenomethionine, a derivative of Se, is considered toxic in its inorganic form when consumed in high doses (mg) (9).Moreover, there is a prevalent report of abnormal levels of serum liver enzymes in hypothyroid patients (10).The relationship between thyroid and liver health is intricate, with the activation of thyroid hormones being contingent on the liver's role (10).Reports indicate that maintaining an average level of Se is essential for averting thyroid disorders. Conversely, studies have indicated a heightened risk of developing thyroid cancer in cases of Se deficiency (11, 12). A direct relationship has been demonstrated between selenium (Se) levels in serum and low-density lipoprotein (LDL) cholesterol, triglycerides, and total cholesterol concentrations in populations with high Se levels (13, 14). In this study, we examined the effects of Se on liver enzymes, lipid factors, hemoglobin (HGB), malondialdehyde (MDA), total antioxidant, and glutathione reductase levels under a double-blinded clinical trial performed on patients with Hashimoto's disease.

2. Materials and Methods

2.1. Study Population

A prospective randomized, double-blind, placebo-controlled clinical trial was conducted on 40 patients with subclinical hypothyroidism symptoms aged 18–60. The study was conducted from July 2019 to October 2019 in the outpatient ward of the Endocrine Clinic at Emam Reza Hospital in Tabriz City. Patients were enrolled in the study after providing written consent and receiving a brief description of the study's importance. Diagnoses were made based on TSH levels in two consecutive tests and were subsequently reviewed by an expert endocrinologist. The patients were stratified into two groups: a control group and an intervention group. Patients who had consumed trace element and antioxidant supplements in the previous six months, suffered from renal failure, proteinuria, acute or chronic liver disease, were pregnant, or had heart problems were excluded from the study.

2.2. Sample Size

The sample size was determined based on the findings of a preliminary study (i.e., TSH changes were calculated as the primary outcome before and after the intervention for five subjects per group). The sample size was calculated to be 20 per group using a standard formula for a randomized controlled trial based on the first type error (α) of 0.05 and 80% power, anticipating an approximate dropout rate of 10% during the study. Consequently, 20 participants were enrolled in each group.

2.3. Trial Procedure

Forty patients were randomly allocated to one of the groups (control and treatment) using a randomized block method, in which both participants and investigators were blinded to allocations. The participants' data, including age, gender, weight, and height, were recorded before the study began. The height and weight of the participants were measured without shoes and with minimal clothing via a calibrated scale and stadiometer.BMI was calculated as weight (kg)/height (m2). The subjects in the treatment group were administered 200 µg of selenium in the form of a capsule containing selenium-enriched yeast once daily for eight weeks. The control group received a placebo capsule. Selenium-enriched yeast was produced at the Nutrition Research Center, Tabriz University of Medical Sciences, Iran, through the cultivation of Saccharomyces cerevisiae in selenium-rich media (15, 16). During the study, the participants maintained their usual physical activity, dietary, and medication intake. The effects of Se consumption were monitored weakly in participants.

2.4. Metabolic Parameters

Venous blood samples were obtained from each participant before and after Se supplementation consumption. The following parameters were measured: TSH (normal range: 5.0 milli-international units per liter (mIU/L)), anti-TPO (normal range: less than 34 international units per millimeter (IU/ml)), total blood catalase, malondialdehyde (MDA), serum cholesterol level, liver enzymes (ALT and AST), glutathione reductase (GR), and total antioxidant capacity (TAC) were measured by commercial methods. The spectrophotometric method was used to measure the blood MDA, TCA, HGB, and GR. The serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), ALT, and AST were measured via an auto analyzer.

2.5. Statistical Analysis

A comprehensive set of descriptive parameters was obtained for all the study variables in each group. The Kolmogorov-Smirnov test was then employed to assess the normality of these variables.

3. Results

The present study randomly classified patients into two groups: the intervention group (mean age: 39.36 ±2.41) and the control group (mean age: 45.38 ±3.29). The levels of TSH and Anti-TPO were examined in both groups. The results indicated a relative decrease in TSH and Anti-TPO levels; however, no significant difference existed between the intervention and placebo groups at the baseline and after treatment. Furthermore, the mean levels of GR, TAC, ALT,

AST, total cholesterol, HDL-C, LDL-C, VLDL, TG, MDA, and HGB were evaluated in both groups at the baseline and following treatment, as illustrated in Table 1. The findings of the study demonstrated that the catalase level experienced an increase in the intervention group during the 60-day treatment period with Se capsules. Additionally, the HDL, LDL, TG, total cholesterol, and VLDL values exhibited a significant reduction during the treatment phase with Se capsules. The within-group comparison revealed a statistically significant reduction in the mean MDA level (P = 0.004) and a substantial increase in the mean HGB level (P=0.038) in the intervention group following treatment with the Se supplement. In contrast, the placebo group exhibited no statistically significant variation in MDA (P=0.794) or HGB (P=0.798) levels. The findings revealed that none of the metabolic factors were influenced by demographic factors, except for HDL and HGB levels, which exhibited a significant dependency on gender (P=0.074) and BMI (P=0.019), respectively (Table 2).

Table1. Mean (standard deviation) level of metabolic factors under treatment of selenium for 60 days.

Variables	Before Se Treatment	After Se Treatment	Before Placebo Treatment	After Placebo Treatment	*P. value in treatment group*	*p.value in placebo group*
GR	13.1±0.1	13.19±0.15	13.05±0.09	13.04±0.08	0.752	0.912
TAC	1.52±0.03	1.64±0.02	1.59±0.02	1.67±0.07	0.06	0.273
ALT	35.36±0.64	33.93± 0.67	35.54±0.31	35.78±0.42	0.804	0.533
AST	34.6±1.13	33.07±0.82	34.31±0.48	34.14±0.58	0.816	0.823
CAT	69.64±11.82	122.91±11.95	92.15±6.57	83.07±10.88	0.62	0.462
HGB	13.64±0.37	13.82±0.2	13.57±0.33	13.46±0.26	**0.038**	0.798
MDA	1.97±0.18	1.09±0.01	1.75±0.08	1.1±0.01	**0.049**	0.794
Total Cholesterol	190.8±9.1	180.6±12.67	197.8±8.08	210.5±14.3	0.347	0.468
HDL-C	23.83±2.19	21.56±1.89	28.17±1.68	25.97±1.82	0.544	0.339
LDL-C	128.95±5.1	123.34±5.38	140.02±8.79	152.32±13.8	0.916	0.462
V-LDL	31.38±4.88	28.2±4.33	28.84±4.68	32±4.24	0.229	0.623
TG	156.9±24.41	141.4±21.94	144.2±23.41	160±21.2	0.952	0.633
TSH	8.31±4.2	7.7±2.32	8.09±0.93	6.56±1.18	0.467	0.269
Anti-TPO	457.06±139.26	396.82±142.16	483.49±144.06	521.79±128.84	0.399	0.395

Table2. The effect of demographic factors on metabolic parameters levels.

Variables	Gender	Age	Waist	Height	Weight	BMI
HDL-C	**0.074**	0.919	0.756	0.254	0.426	0.351
VLDL	0.134	0.526	0.958	0.338	0.474	0.46
LDL-C	0.9	0.927	0.647	0.351	0.322	0.328
TG	0.134	0.526	0.958	0.338	0.474	0.46
Total Cholesterol	0.443	0.435	0.567	0.384	0.268	0.269
MDA	0.109	0.843	0.676	0.238	0.439	0.371
HGB(g/dL)	0.233	0.777	0.373	**0.011**	**0.021**	**0.019**
Catalase	0.887	0.968	0.556	0.664	0.702	0.692
GR	0.826	0.451	0.252	0.324	0.3	0.315
TAC	0.183	0.13	0.354	0.684	0.815	0.809
ALT	0.566	0.838	0.621	0.295	0.328	0.286
AST	0.887	0.474	0.157	0.417	0.517	0.504

4. Discussion

In light of the escalating prevalence of thyroid disease and the deleterious side effects of thyroid disorders on public health, the introduction of effective control and prevention strategies is imperative. For instance, there is a direct relationship between thyroid diseases and liver disorders (18). This study examined the effect of selenium, a confirmed dietary supplement, on thyroid hormones, liver enzymes, and lipid factors. The findings of the study indicated a decline in lipid factors (TGD, VLDL, LDL, HDL, and total cholesterol) in the selenium group, though the differences observed between the two groups were not statistically significant. The study concluded that selenium exerts no significant influence on plasma lipid profiles; however, it did modify lipid factor values in comparison with the placebo group. These observations are consistent with a recent meta-analysis study that reported a marginal effect on reducing TG levels and an absence of effect on total cholesterol and HDL-C levels (19). However, the reduction of MDA level was found to be significantly dependent on selenium ($P<0.05$), as indicated by the GR, CAT, and TAC enzymes, which demonstrated a slight increase compared with the placebo group (20, 21).In this study, liver enzymes, including ALT and AST, were also evaluated, indicating a relative reduction compared to the placebo group, consistent with findings from similar studies (22, 23). The study also noted a relative decrease in TSH and anti-TPO values, though this difference was not statistically significant between the two groups. These results align with previous studies that have observed the weak effect of selenium in patients with autoimmune hypothyroidism (24) and its lack of effect on TPO Ab levels in women with autoimmune hypothyroidism (25). The present study found that Selenium consumption in Hashimoto's thyroiditis was associated with improved serum lipid factors, liver enzymes, anti-thyroid peroxidase antibody, MDA, and HGB levels. The findings underscore the significant effect of selenium supplementation on serum MDA and HGB levels in subclinical hypothyroidism patients. However, given the conflicting results related to the impact of selenium supplements on serum lipid factors and liver enzymes, further research with larger sample sizes and varying doses of selenium is recommended to achieve more precise conclusions.

Acknowledgment

This study was supported by the Nutrition Research Center at Tabriz University of Medical Sciences, Tabriz, Iran.

Authors' Contribution

A.H. and A.D. designed the study and performed the data analysis and interpretation; A.F. and M.M. revised the manuscript. A.O. wrote the first draft. B.K. discussed the results. The authors read and approved the final manuscript.

Ethics

The study was conducted subsequent to ethical approval by the ethics committee of Tabriz University of Medical Sciences, Tabriz, Iran (reference number: IR. TBZMED. REC.1398.339). The study was also registered on the website of the Iranian Registry of Clinical Trials (IRCT20190212042686N2), which is available at the following address: https://www.irct.ir/.

Conflict of Interest

The authors have no conflict of interest.

Data Availability

The datasets utilized and/or examined during the present study are available upon reasonable request to the corresponding author.

References

1. Genchi G, Lauria G, Catalano A, Sinicropi MS, Carocci A. Biological activity of selenium and its impact on human health. International Journal of Molecular Sciences. 2023;24(3):2633.
2. Kieliszek M, Bano I, Zare H. A comprehensive review on selenium and its effects on human health and distribution in Middle Eastern countries. Biological Trace Element Research. 2022;200(3):971-87.
3. Boitani C, Puglisi R. Selenium, a key element in spermatogenesis and male fertility. Molecular Mechanisms in Spermatogenesis. 2009:65-73.
4. Lyons M, Papazyan T, Surai P. Selenium in food chain and animal nutrition: lessons from nature-review. Asian-Australasian Journal of Animal Sciences. 2007;20(7):1135-55.
5. Bjørklund G, Shanaida M, Lysiuk R, Antonyak H, Klishch I, Shanaida V, et al. Selenium: An antioxidant with a critical role in anti-aging. Molecules. 2022;27(19):6613.
6. Zoidis E, Seremelis I, Kontopoulos N, Danezis GP. Selenium-dependent antioxidant enzymes: Actions and properties of selenoproteins. Antioxidants. 2018;7(5):66.
7. Saha U, Fayiga A, Sonon L. Selenium in the soil-plant environment: A review. International Journal of Applied Agricultural Sciences. 2017;3(1):1-18.
8. Fagan S, Owens R, Ward P, Connolly C, Doyle S, Murphy R. Biochemical comparison of commercial selenium yeast preparations. Biological trace element research. 2015;166:245-59.
9. Yu Q, Xia C, Han F, Xu C, Rombenso A, Qin JG, et al. Effect of different dietary selenium sources on growth performance, antioxidant capacity, gut microbiota, and molecular responses in pacific white shrimp Litopenaeus vannamei. Aquaculture Nutrition. 2022;2022:1-16.
10. Piantanida E, Ippolito S, Gallo D, Masiello E, Premoli P, Cusini C, et al. The interplay between thyroid and liver: implications for clinical practice. Journal of endocrinological investigation. 2020;43:885-99.

11. Schomburg L. The other view: The trace element selenium as a micronutrient in thyroid disease, diabetes, and beyond. Hormones. 2020;19(1):15-24.
12. Kazi Tani LS, Dennouni-Medjati N, Toubhans B, Charlet L. Selenium Deficiency—From Soil to Thyroid Cancer. Applied Sciences. 2020;10(15):5368.
13. Obeid O, Elfakhani M, Hlais S, Iskandar M, Batal M, Mouneimne Y, et al. Plasma copper, zinc, and selenium levels and correlates with metabolic syndrome components of lebanese adults. Biological trace element research. 2008;123:58-65.
14. Yang K-C, Lee L-T, Lee Y-S, Huang H-Y, Chen C-Y, Huang K-C. Serum selenium concentration is associated with metabolic factors in the elderly: a cross-sectional study. Nutrition & metabolism. 2010;7(1):1-7.
15. Esmaeili S, Khosravi-Darani K, Pourahmad R, Komeili R. An experimental design for production of selenium-enriched yeast. World Appl Sci J. 2012;19(1):31-7.
16. Suhajda A, Hegoczki J, Janzso B, Pais I, Vereczkey G. Preparation of selenium yeasts I. Preparation of selenium-enriched Saccharomyces cerevisiae. Journal of Trace Elements in Medicine and Biology. 2000;14(1):43-7.
17. Xin C, Niu L, Fan H, Xie J, Sun X. Increased incidence of thyroid disease in patients with sarcoidosis: a systematic review and meta-analysis. Endocrine Connections. 2023;1(aop).
18. Kyriacou A, McLaughlin J, Syed AA. Thyroid disorders and gastrointestinal and liver dysfunction: a state of the art review. European Journal of Internal Medicine. 2015;26(8):563-71.
19. Hasani M, Djalalinia S, Sharifi F, Varmaghani M, Zarei M, Abdar ME, et al. Effect of selenium supplementation on lipid profile: a systematic review and meta-analysis. Hormone and Metabolic Research. 2018;50(10):715-27.
20. Khalaf A, Ahmed W, Moselhy W, Abdel-Halim B, Ibrahim M. Protective effects of selenium and nano-selenium on bisphenol-induced reproductive toxicity in male rats. Human & experimental toxicology. 2019;38(4):398-408.
21. Ahmad H, Tian J, Wang J, Khan MA, Wang Y, Zhang L, et al. Effects of dietary sodium selenite and selenium yeast on antioxidant enzyme activities and oxidative stability of chicken breast meat. Journal of agricultural and food chemistry. 2012;60(29):7111-20.
22. Reja M, Makar M, Visaria A, Marino D, Rustgi V. Increased serum selenium levels are associated with reduced risk of advanced liver fibrosis and all-cause mortality in NAFLD patients: National Health and Nutrition Examination Survey (NHANES) III. Annals of Hepatology. 2020;19(6):635-40.
23. Lin Y, He F, Lian S, Xie B, Liu T, He J, et al. Selenium status in patients with chronic liver disease: a systematic review and meta-analysis. Nutrients. 2022;14(5):952.
24. Moncayo R, Moncayo H, Kapelari K. Nutritional treatment of incipient thyroid autoimmune disease. Influence of selenium supplementation on thyroid function and morphology in children and young adults. Clinical Nutrition. 2005;24(4):530-1.
25. Karanikas G, Schuetz M, Kontur S, Duan H, Kommata S, Schoen R, et al. No immunological benefit of selenium in consecutive patients with autoimmune thyroiditis. Thyroid. 2008;18(1):7-12.