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Original

Goiter size changes as an indicator of response to treatment following selenium intake, and its correlation with goiter type

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Abstract

Introduction: Goiter is a common problem in the world; however, it is more prevalent in countries with iodine deficiency. Goiter has different etiologies while one of them is Hashimoto's thyroiditis. Selenium is a trace element that has different important effects in the body. It has also some effects in the thyroid.

Objectives: This study aimed to evaluate the effect of selenium intake on goiter size and the correlation with goiter type.

Patients and Methods: In prospective observational study, 20 patients with Hashimoto's goiter and 40 patients with non-Hashimoto's goiter were evaluated for thyroid sizes. The nodule sizes were else evaluated. After the first evaluation, daily selenium supplement (200 mg) was prescribed for all patients for six months. After this time, the sizes of goiter and nodules were measured again.

Results: Results showed that the size of both goiter lobes in both Hashimoto's and non-Hashimoto's groups was significantly reduced before and after selenium intake ($P<0.001$). The reduction rate in left lobe size in patients with Hashimoto's goiter was 50.73% and in non-Hashimoto's goiter patients was 20.89% ($P<0.001$). The reduction rate in right lobe size in patients with Hashimoto's goiter was 53.37% and in non-Hashimoto's goiter was 20.46 ($P<0.001$).

Conclusion: We conclude that administration of selenium is effective in reducing the size of the goiter.

Keywords: Goiter type, Goiter size, Hashimoto's goiter, Selenium intake, Hashimoto's thyroiditis

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Introduction

Goiter is one of the most common thyroid disorders in the world and the prevalence of which often depends on the amount of iodine intake in different regions of the world. In countries with iodine deficiency, the rate of multinodular goiter is higher. In countries where people get enough iodine, the prevalence of nodular goiter is lower. In areas where goiter is not the result of iodine deficiency, it has been seen that the rate of goiter was 5.9%, which was the result of a study conducted in England (1-3).

Hashimoto's thyroiditis is the most common autoimmune disease of the thyroid, in which antibody against tyrosine peroxidase is produced. This disease can be accompanied by goiter, which is painless and may be accompanied by hypothyroidism like Hashimoto's disease (4-7).

Selenium as an element in the body and it has anti-inflammatory and antioxidant effects (8,9). Selenium inhibits oxidative stress. Depletion of selenium in the body is associated with various complications, including the increase of inflammatory factors and involvement with various diseases (10-12). In hypothyroidism and goiter, the level of selenium in the body of these people is lower than the mean level of selenium in the healthy population (11,13). It is observed that selenium intake has relationship with anti-thyroid peroxidase (anti-TPO) antibody reduction and improvement in sonographic features of thyroid (14).

In some studies, it is mentioned that selenium deficiency has been related to the etiology of Hashimoto's thyroiditis. In animal studies, reduced glutathione peroxidase and selenium deprivation may be responsible for thyroid

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Implication for health policy/practice/research/ medical education

In a prospective observational study on 60 patients with goiter, we found that administration of selenium is effective in reducing the size of the goiter.

cell oxidative damages, the start of fibrosis and poor tissue healing. Additionally, selenium deprivation may affect B-cell and T-cell-mediated immunity, underscoring the importance of selenium in the immune system. It is still unclear whether selenium deficiency can cause Hashimoto's thyroiditis, while it is difficult to prove a direct correlation among serum selenium with its tissue concentration (15-17).

Objectives

This study aimed to investigate the effect of selenium on the size of Hashimoto's goiter compared to non-Hashimoto's goiter in patients with goiter and explore its correlation with the goiter type.

Patients and Methods

Study design

In this prospective observational study, 20 patients with Hashimoto's goiter and 40 patients with non-Hashimoto's goiter were selected based on laboratory and sonographic findings from patients who were referred to the endocrinology clinic of Loghman hospital from 2019 to 2020.

After taking verbal consent, patients were assessed based on clinical and radiological evaluations. The inclusion criterion was presence of goiter based on the radiologist report. The exclusion criteria were having no consent to enter to the study, thyroid disorders without presence of goiter and hyperthyroidism involvement. Urinary iodine level was evaluated from all patients and patients with abnormal iodine levels were excluded.

All patients were evaluated by an expert endocrinologist in the hospital and laboratory tests included thyroid stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), anti-TPO antibody, and anti-thyroglobulin antibody were measured at the start of the study. Ultrasonographic measurement was conducted for thyroid size assessment by an expert radiologist in the hospital at first and the end of the study. During ultrasonography, presence of nodules in the thyroid was assessed. Thyroid volume greater than 9 cm^3 was considered abnormal for each lobe (18). The level of anti-TPO antibody was measured with DEIA05731 kit and the level above 9 IU/mL was abnormal based on the kit catalog. Goiter with accompanying anti TPO antibody level more than 9 IU/mL was considered as Hashimoto's goiter. If the level of anti TPO antibody was below 9 IU/mL, it was considered as non-Hashimoto's goiter.

The patients were divided into two groups; Hashimoto's goiter and non-Hashimoto goiter. Twenty people were in Hashimoto group and 40 people were in non-Hashimoto group. Daily using of selenium tablets (200 mg) were prescribed for both groups and continued for six months. After six months, thyroid ultrasonography was performed again and thyroid volume was evaluated. All data of the patients were recorded and compared between the two groups.

Statistical analysis

Categorical data were presented as frequency and percent and continuous data were presented as mean and standard deviation (SD) or median and interquartile range (IQR). Normal distributions of continuous data were assessed using Kolmogorov-Smirnov test. In order to compare patients' characteristics according to Hashimoto's goiter involvement, the chi-square test, independent *t* test, and Mann-Whitney U test were applied. To compare the treatment effect on the lobes and nodule sizes between the patients' groups, ANOVA was applied. Additionally, Wilcoxon test was employed to compare the lobes and nodule sizes within patients' groups. Meanwhile, the Pearson's correlation coefficient was calculated in order to assess the association between continuous variables. All statistical analysis was conducted by SPSS version 20. Moreover, *P* values less than 0.05 were considered significant.

Results

In this study, 60 patients with goiter who were undertreated with selenium (200 mg daily) were evaluated. Twenty patients (33.3%) had Hashimoto's goiter and 40 (66.67) were non-Hashimoto (Table 1). Out of 20 patients in the Hashimoto group, three patients were male and 17 were female, and in the non-Hashimoto group 8 patients were male and 32 were female, but this difference between the two groups was not significant. The mean age of all patients was 38.87 ± 12.24 years; In the Hashimoto group was 27.75 ± 5.72 and in the non-Hashimoto group was 44.42 ± 10.76 years old, and this difference was significant

Table 1. Demographic characteristics such as age and gender distribution of patients in the two groups

		Hashimoto's goiter		*P* value
		No (n = 40)	Yes (n = 20)	
Gender	Male, No. (%)	8 (20)	3 (15)	0.637[a]
	Female, No. (%)	32 (80)	17 (85)	
Age	Mean ± SD	44.42 ± 10.76	27.75 ± 5.72	<0.001[b]

[a] Chi-square; [b] Mann-Whitney U test.

between the two groups.

The sizes of the right and left lobes of the thyroid in the groups were measured before and after treatment, separately. The data are seen in Table 2.

In total, 26 patients (43.3%) had thyroid nodules. In the group of patients with Hashimoto's goiter 11 patients (55%) and in the other group 15 patients (37.5%) had thyroid nodules. There was no statistically significant difference between the two groups in terms of thyroid nodule presence (P = 0.197). In the Hashimoto's group before the treatment, the median, and IQR of nodule size were 16 mm^3 and 8 mm^3, respectively. After treatment, the mean and IQR of nodule size were 5 mm^3 and 12 mm^3, respectively. This decrease was statistically significant (P = 0.002). In addition, in non-Hashimoto's group before the treatment, the median and IQR of nodule size were 12 mm^3 and 18 mm^3 and after treatment were 9 mm^3 and 8 mm^3, respectively; therefore, these changes were statistically significant (P = 0.003; Table 3).

In patients without Hashimoto's goiter, no statistically significant relationship between patients' age and percentage of nodule size changes after treatment compared to before treatment was seen (r = -0.367; P = 0.178). In patients with Hashimoto's goiter, no statistically significant relationship was observed between patients' age and percentage of nodule size changes after treatment compared to before treatment (r = 0.139; P = 0.683). The mean percentage of nodule size changes, after treatment compared to before treatment, was -22.22% (37.31%) among men and -50% (72.73%) among women. The decrease in nodule size was statistically significantly greater among women than men (P = 0.035).

Discussion

In this study, 60 patients with goiter who were treated with selenium were studied. Around 33.3% of patients had Hashimoto's goiter. The mean age of patients with Hashimoto's goiter was 27.75 ± 5.72 years and this amount was 44.42 ± 10.76 years in non-Hashimoto's goiter patients and this difference between the two groups was statistically significant. Haraku Hashimoto first described "struma lymphomatosa", or an enlarged thyroid infiltrated with lymphocytes, in 1912; this is the basis for the name Hashimoto thyroiditis (19). According to estimates, there are 0.3–1.5 instances of HT for every 1000 people, with a 7–10:1 gender ratio for females (20,21). This disease mostly diagnosed in age of 30-50 years (4). As we observed in our study, patients with Hashimoto's disease were around 30 years old and the women with Hashimoto's goiter were more than men. The development of Hashimoto's thyroiditis begins with genetic susceptibility and progresses through environmental influences, the presence of detectable anti-TPO antibody in euthyroid people, subclinical disease, and clinical disease (22,23). This issue shows that the environmental factors can affect Hashimoto's goiter.

Goiter, or an enlarged thyroid, is an adapted response of thyroid follicular cells to any mechanism that prevents the generation of thyroid hormone. Hashimoto's thyroiditis is a significant cause in the development of goiter in

Table 2. The sizes of right and left lobes of thyroid in the groups were measured before and after the treatment

Hashimoto's goiter	Before treatment		After treatment		*P* value	Changes percentage	
	Median	IQR	Median	IQR		Median	IQR
Right lobe of the thyroid							
Yes	14186	9621	7758	4368	<0.001[b]	-53.37%	27.36%
No	15991	12118	11246	10546	<0.001[b]	-20.46%	14.79%
P value	0.875[a]		0.001[c]			<0.001[a]	
Left lobe of the thyroid							
Yes	10360	9587	5361	3212	<0.001[b]	-50.73%	24.23%
No	13869	10970	10600	8280	<0.001[b]	-20.89%	26.25%
P value	0.149[a]		0.633[c]			<0.001[a]	

[a] Mann-Whitney U test; [b] Wilcoxon test; [c] Covariance analysis.

Table 3. Nodule size before and after treatment according to the group of patients

Hashimoto's goiter	Pre-treatment		Post-treatment		*P*	Percentage of change	
	Mean	IQR	Mean	IQR		Mean	IQR
Yes	16	8	5	12	0.002[b]	-00.25%	31.42%
No	12	18	9	8	0.003[b]	-33.58%	67.66%
P value	0.507[a]		0.001[c]			0.005[a]	

[a] Mann-Whitney U test; [b] Wilcoxon test; [c] Covariance analysis.
IQR, Interquartile range.

both nations with and without iodine deficiency (24). Numerous studies have assessed how selenium affects thyroid disorders (25,26). Thyroid tissue may contain high levels of selenium. Selenium-containing proteins, or selenoproteins, play a significant role in thyroid tissue function. They too aid the thyroid's antioxidant defense against too much hydrogen peroxide exposure. They function as a component of the enzyme iodothyronine deiodinase, which affects how thyroid hormone is activated and deactivated. Consequently, a lack of selenium may lead to a drop in the level of active T3 hormone synthesis (27,28). Therefore, it seems that prescription of selenium, as a supplement can be useful in patients with goiter because selenium is an element for better function of thyroid.

According to research done in a Danish region with minor iodine deficiency, selenium deficiency associated with thyroid gland volume and nodule growth both before and after iodine supplementation (29). In some other studies, it was observed that selenium was low in patients with nodular goiter. Wu et al found that the prevalence of subclinical hypothyroidism, hypothyroidism, Hashimoto's thyroiditis, and goiter was significantly lower in patients who had sufficient selenium level (30). Turan and Turksoy concluded that selenium deficiency is associated with goiter involvement (31). In the present study we found that after selenium supplementation for 6 months, the volume of goiter was reduced. It seems that patients with goiter (Hashimoto's or non-Hashimoto's) suffer from selenium deficiency and prescription of selenium in these patients is a good method for reducing goiter size.

According to the study by Liu et al there was no correlation between thyroid-stimulating hormone and serum selenium or thyroid volume. Serum selenium levels did not significantly differ between people with and without goiter. There was no association between goiter risk and serum selenium (25). This study was evaluated the selenium in blood and its relationship with thyroid function and goiter. In the current study we evaluated the effect of selenium on goiter clinically. In fact, we evaluated the effect of selenium supplementation in patients with goiter and we observed that selenium had a significant relationship with reducing goiter size. As we mentioned above, selenium is a trace element and its concentration in thyroid should be assessed in future studies because may be thyroid has enough level of selenium however, the level of selenium in serum is not completely in normal value.

Winther et al found that selenium had no effect on Hashimoto's thyroiditis and thyroid volume (32). The findings of our study were in contrast with Winther and colleagues' study. We found that selenium using for six months can reduce goiter size significantly. We found selenium significantly reduced the nodule sizes in patients with Hashimoto thyroiditis and patients without Hashimoto thyroiditis. Winther and colleagues' study was a meta-analysis study but we conducted a clinical study. It seems that further studies should be performed clinically for assessment of selenium effect on goiter.

In study by Ventura et al, it was found that selenium has a protective effect on thyroid disease and improves symptoms, which was similar to the current study (14). We found that selenium can reduce goiter and nodule size. We else found that the effect of selenium in reduction of sizes of goiter or nodules were significantly higher in women than men. This finding may be coming from the higher rate of goiter and thyroid disorders in women however; it should be investigated more in further study.

Conclusion

Results showed that the size of the goiter significantly reduced following the intake of selenium in both groups of Hashimoto's and non-Hashimoto's goiter, while this reduction rate in Hashimoto's type was greater than non-Hashimoto's goiter; therefore, we conclude that taking selenium is effective in reducing the size of the goiter, and it is also associated with its type.

Limitations of the study

The lack of sample size and the unwillingness of some participants to participate in the study were the two limitations we faced with.

Authors' contribution

Conceptualization: AT and SK.
Methodology: SK.
Validation: SK, HM and AT.
Formal Analysis: SK.
Investigation: SK and AT.
Resources: AT and SA.
Data Curation: AT and SA.
Writing—Original Draft Preparation: HM, AT and SA.
Writing—Review and Editing: HM, AT and SA.
Visualization: AT and SA.
Supervision: AT, SK and SA.
Project Administration: All authors.
Funding Acquisition: AT.

Conflicts of interest

The authors declare that they have no competing interests

Ethical issues

The research was conducted in accordance with the tenets of the Declaration of Helsinki. The institutional ethical committee at Shahid Beheshti University of Medical Sciences approved all study protocols (IR.SBMU.MSP.REC.1399.202). Accordingly, informed consent was taken from all participants before any intervention. This study was extracted from the M.D., thesis of Alireza Tajik at this university. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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