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LETTER TO THE EDITOR

Vitamin D and selenium for type 2 diabetes mellitus with Hashimoto's thyroiditis: Dosage and duration insights

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Abstract

This letter discusses the publication by Feng *et al*. Iodine, selenium, and vitamin D are closely associated with thyroid hormone production in humans; however, the efficacy of selenium and vitamin D supplementation for type 2 diabetes mellitus (T2DM) patients with Hashimoto's thyroiditis (HT) remains controversial. In the retrospective study we discuss herein, the authors highlighted significant improvements in thyroid function, thyroid antibodies, blood glucose, and blood lipid in T2DM patients with HT following addition of vitamin D and selenium to their antidiabetic regimens, underscoring the value of these supplements. Our team is currently engaged in research exploring the relationship between micronutrients and HT, and we have obtained invaluable insights from the aforementioned study. Based on this research and current literature, we recommend a regimen of 4000 IU/day of vitamin D and 100-200 μg/day of selenium for over three months to six months for patients with HT, particularly for those with concurrent T2DM.

Key Words: Vitamin D; Selenium; Type 2 diabetes mellitus; Hashimoto's thyroiditis; Dosage; Duration

Core Tip: Supplementation with vitamin D and selenium shows promise in improving the prognosis of type 2 diabetes mellitus (T2DM) and Hashimoto's thyroiditis (HT). Despite controversies surrounding their efficacy, a retrospective study discussed in this letter reveals significant benefits from adding these supplements to antidiabetic regimens. Based on this research and current literature, we recommend a regimen of 4000 IU/day of vitamin D and 100-200 μg/day of selenium for over three to six months for patients with HT, particularly for those with concurrent T2DM.

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TO THE EDITOR

We are fortunate to have read the article, which was written by Feng *et al*[1] and published in the *World Journal of Diabetes*. We extend our felicitations to the authors for completing the aforementioned retrospective study and providing new insights into treating type 2 diabetes mellitus (T2DM) patients with Hashimoto's thyroiditis (HT). The study by Feng *et al* [1] revealed that, compared with antidiabetic drugs alone, the supplementation of 4000 IU vitamin D and 200 μg selenium daily for three to six months, in combination with standard antidiabetic drugs, significantly improved thyroid function, thyroid antibodies, blood glucose, and blood lipid in T2DM patients with HT. In this letter, therefore, we discuss the ideal dosage and duration of vitamin D and selenium administration in treatment of HT, taking into account the study by Feng *et al*[1] as well as previous literature.

DOSE AND DURATION OF VITAMIN D

The optimal dosage and duration of vitamin D supplementation in HT patients is controversial. An early randomized controlled trial from Türkiye revealed that vitamin D supplementation of 1000 IU per day for one month significantly reduced thyroid peroxidase antibodies (TPOAb) and thyroglobulin antibodies (TGAb) in patients with autoimmune thyroid disease[2]. A prospective study from Greece indicated that vitamin D supplementation of 1200-4000 IU per day for four months significantly reduced TPOAb in HT patients, although they observed no significant effects on TGAb or thyroid-stimulating hormone (TSH)[3]. Additionally, a study from Iran found that a vitamin D supplementation of 50000 IU per week for three months significantly reduced TGAb and TSH levels in female patients, compared to those who received a placebo, with no significant effect on TPOAb[4]. Although these studies reported different results on the benefits of vitamin D supplementation, they are all in concordance that vitamin D supplementation is beneficial for HT patients. Taken in combination, the results of these studies suggest that an average daily vitamin D supplementation ranging from 1000 to 7143 IU is effective for treating HT. Of note, the study by Feng *et al*[1] demonstrated that, in addition to thyroid function and thyroid antibodies, 4000 IU of vitamin D per day improved blood glucose and lipid levels in T2DM patients with HT, suggesting that high-dosage vitamin D may have the additional benefit of modulating glucose and lipid metabolism in such patients. In light of this additional evidence, therefore, we recommend supplementation with 4000 IU of vitamin D daily for HT patients, particularly those HT patients with T2DM.

With regard to the appropriate duration of vitamin D supplementation, a clinical study from Turkey discovered that a one-month duration allowed for reduction of TPOAb and TGAb levels in patients with autoimmune thyroid disease[2], which is the lowest effective duration reported to date. A subsequent meta-analysis indicated that vitamin D supplementation for more than three months reduced TPOAb and TGAb levels in HT patients, whereas treatment for three months or less reduced only TGAb levels[5]. A recent meta-analysis further indicated that vitamin D supplementation for longer than three months not only reduced TPOAb and TGAb, but also increased free triiodothyronine (FT3) and free thyroxine (FT4) in HT patients[6]. In contrast, treatments lasting three months only resulted in a reduction of TGAb[6]. These findings, therefore, demonstrate that vitamin D supplementation for longer than three months provided additional benefits for HT patients. Of note, the study by Feng *et al*[1] revealed that vitamin D supplementation for six months was more effective in improving FT3, FT4, TSH, TPOAb, and TGAb in T2DM patients with HT compared with a three-month regimen. With regard to treatment duration, therefore, we recommend that HT patients take vitamin D for 3-6 months or more.

DOSE AND DURATION OF SELENIUM

As with vitamin D, the optimal dosage and duration of selenium supplementation in the treatment for HT remain unclear. With regard to dosage, a recent meta-analysis of 35 studies revealed that a daily selenium supplementation of 100 μg or more reduced TSH and TPOAb in HT patients[7]. Unfortunately, it did not compare the benefits of various selenium dosages. In fact, most previous clinical studies set the daily intake of selenium at 200 μg, regardless of the

selenium type, emphasizing that 200 μg/day of selenium improved the prognoses of HT patients[8,9]. Similarly, the study by Feng *et al*[1] demonstrated that a daily supplementation of 200 μg selenium, in addition to the standard anti-diabetic drugs and vitamin D, effectively improved thyroid function and antibodies in T2DM patients with HT. However, a high dosage of selenium may be associated with potential adverse events. It has been reported that selenium dosages exceeding 400 μg/day can lead to acute toxic symptoms in the gastrointestinal and nervous systems[10], and supplementation of 200 μg/day selenium may increase the risk of developing T2DM[11]. Therefore, we recommend that the daily selenium supplementation for HT patients be maintained between 100 and 200 μg.

With regard to the duration of selenium treatment, an early meta-analysis indicated that a three-month duration of selenium supplementation significantly reduced TPOAb and TGAb levels in patients with autoimmune thyroiditis, while supplementation for six or twelve months did not have a significant effect on TPOAb or TGAb[12]. Subsequently, another meta-analysis found that selenium supplementation led to reduced levels of TPOAb and TGAb after three months, while only TGAb was reduced after six months, and no reduction in thyroid antibodies was seen after twelve months[13]. In contrast, Feng *et al*[1] demonstrated that selenium supplementation for both three and six months reduced TPOAb and TGAb levels. We speculate that this difference may be attributable to the synergistic effect of supplemental selenium and vitamin D in HT patients, as the selenium supplementation by Feng *et al*[1] was based on concurrent vitamin D supplementation. As it has been shown that selenium treatment for three or six months is beneficial, despite concerns about its long-term effects, we recommend that the duration of selenium supplementation should be set at 3-6 months. In summary, combined with research by Feng *et al*[1] and the current literature, we recommend a regimen of 4000 IU/day of vitamin D and 100-200 μg/day of selenium for over three months to six months for patients with HT, particularly for those with concurrent T2DM.

SYNERGISTIC EFFECT OF VITAMIN D AND SELENIUM

In addition to the optimal dosage and duration, the existence of synergy between vitamin D and selenium remains unclear, as does its mechanism. Evidence suggests that selenium enhances the effects of vitamin D in the treatment of HT. Krysiak *et al*[14] included 47 female patients with HT who had normal thyroid function and vitamin D deficiency. Of these, 23 had been treated with selenomethionine for 12 months prior to treatment, while the other 24 had not received selenium treatment. After six months of vitamin D treatment, the levels of TPOAb and TGAb in patients with HT significantly decreased, and these changes were more pronounced in patients who had received selenomethionine[14]. This indicates that selenium supplementation may enhance the therapeutic effects of vitamin D on HT. Although a nutritional study indicated that vitamin D promotes selenium absorption, it is unclear whether vitamin D enhances the efficacy of selenium in the treatment of HT[15]. In summary, there may be a synergistic effect between vitamin D and selenium; however, its strength and formation mechanisms require further exploration.

LIMITATIONS AND PROSPECTS

Although the study by Feng *et al*[1] provided clinical evidence for a supplementation regimen of vitamin D combined with selenium in the treatment of T2DM with HT, it did have some limitations. First, it was a retrospective case-control study with a lack of randomization and blinding of patients, leading to potential selection and implementation biases. Second, as there was no treatment group with selenium-only supplementation, it is unclear whether selenium and vitamin D play a synergistic role in the treatment of T2DM with HT. Third, it is unclear whether the long-term effects of vitamin D combined with selenium are observed in the treatment of T2DM with HT, as the study by Feng *et al*[1] only assessed these effects at three- and six-month timepoints. Considering these limitations, it is too early to conclude that a com-bination of vitamin D and selenium has a significant clinical effect in the treatment of T2DM with HT. In the future, multicenter, randomized controlled, double-blind clinical trials should be conducted to further evaluate the short- and long-term effects of vitamin D alone, selenium alone, and a combination of vitamin D and selenium in the treatment of T2DM with HT.

Finally, we wish to express our appreciation to Feng *et al*[1] for sharing their research and novel finding addressing the clinical effects of vitamin D and selenium in specific HT patients. In addition to increasing confidence in our practice, the aforementioned study provides new insights and evidence for clinicians to gain a deeper understanding of the combination of vitamin D and selenium, ultimately enriching our treatment of T2DM with HT.

CONCLUSION

In conclusion, this study highlights the potential benefits of vitamin D and selenium supplementation in improving thyroid function, reducing thyroid antibody levels, and optimizing blood glucose and lipid levels in patients with T2DM and HT. Based on current research, we recommend a daily regimen of 4000 IU of vitamin D and 100-200 μg of selenium for three to six months. Although our findings are promising, they require validation in larger, randomized controlled trials to confirm their efficacy and safety. Future research should focus on the potential synergistic effects of these supplements and elucidate their long-term effects in patients with concurrent T2DM and HT.

FOOTNOTES

Author contributions: Yu YF, Shangguan XL, Tan DN, Qin LN, Yu R Yu YF and Shangguan XL analyzed the literature and wrote the letter; Tan DN and Qin LN performed the research mentioned in the letter; Yu R proposed the idea and revised the letter; All authors have read and approved the final manuscript. Yu YF and Shangguan XL have made equal contributions to this work as co-first authors for two reasons. Firstly, Yu YF and Shangguan XL made contributions of equal significance throughout the research process. The choice of these researchers as co-first authors acknowledges and respects this equal contribution. Secondly, the research was a collaborative effort, and co-first authorship accurately reflects the distribution of responsibilities and the substantial time and effort invested in completing the study and the resulting paper. In summary, designating Yu YF and Shangguan XL as co-first authors are appropriate for our manuscript as it faithfully reflects our team's collaborative ethos, equal contributions, and diversity.

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REFERENCES

1 **Feng F**, Zhou B, Zhou CL, Huang P, Wang G, Yao K. Vitamin D, selenium, and antidiabetic drugs in the treatment of type 2 diabetes mellitus with Hashimoto's thyroiditis. *World J Diabetes* 2024; **15**: 209-219 [PMID: 38464371 DOI: 10.4239/wjd.v15.i2.209]
2 **Simsek Y**, Cakır I, Yetmis M, Dizdar OS, Baspinar O, Gokay F. Effects of Vitamin D treatment on thyroid autoimmunity. *J Res Med Sci* 2016; **21**: 85 [PMID: 28163731 DOI: 10.4103/1735-1995.192501]
3 **Mazokopakis EE**, Papadomanolaki MG, Tsekouras KC, Evangelopoulos AD, Kotsiris DA, Tzortzinis AA. Is vitamin D related to pathogenesis and treatment of Hashimoto's thyroiditis? *Hell J Nucl Med* 2015; **18**: 222-227 [PMID: 26637501]
4 **Chahardoli R**, Saboor-Yaraghi AA, Amouzegar A, Khalili D, Vakili AZ, Azizi F. Can Supplementation with Vitamin D Modify Thyroid Autoantibodies (Anti-TPO Ab, Anti-Tg Ab) and Thyroid Profile (T3, T4, TSH) in Hashimoto's Thyroiditis? A Double Blind, Randomized Clinical Trial. *Horm Metab Res* 2019; **51**: 296-301 [PMID: 31071734 DOI: 10.1055/a-0856-1044]
5 **Zhang J**, Chen Y, Li H, Li H. Effects of vitamin D on thyroid autoimmunity markers in Hashimoto's thyroiditis: systematic review and meta-analysis. *J Int Med Res* 2021; **49**: 3000605211060675 [PMID: 34871506 DOI: 10.1177/03000605211060675]
6 **Tang J**, Shan S, Li F, Yun P. Effects of vitamin D supplementation on autoantibodies and thyroid function in patients with Hashimoto's thyroiditis: A systematic review and meta-analysis. *Medicine (Baltimore)* 2023; **102**: e36759 [PMID: 38206745 DOI: 10.1097/MD.0000000000036759]
7 **Huwiler VV**, Maissen-Abgottspon S, Stanga Z, Mühlebach S, Trepp R, Bally L, Bano A. Selenium Supplementation in Patients with Hashimoto Thyroiditis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Thyroid* 2024; **34**: 295-313 [PMID: 38243784 DOI: 10.1089/thy.2023.0556]
8 **Mazokopakis EE**, Papadakis JA, Papadomanolaki MG, Batistakis AG, Giannakopoulos TG, Protopapadakis EE, Ganotakis ES. Effects of 12 months treatment with L-selenomethionine on serum anti-TPO Levels in Patients with Hashimoto's thyroiditis. *Thyroid* 2007; **17**: 609-612 [PMID: 17696828 DOI: 10.1089/thy.2007.0040]
9 **Wang W**, Mao J, Zhao J, Lu J, Yan L, Du J, Lu Z, Wang H, Xu M, Bai X, Zhu L, Fan C, Wang H, Zhang H, Shan Z, Teng W. Decreased Thyroid Peroxidase Antibody Titer in Response to Selenium Supplementation in Autoimmune Thyroiditis and the Influence of a Selenoprotein P Gene Polymorphism: A Prospective, Multicenter Study in China. *Thyroid* 2018; **28**: 1674-1681 [PMID: 30398407 DOI: 10.1089/thy.2017.0230]
10 **Institute of Medicine (US) Panel on Dietary Antioxidants and Related Compounds**. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington (DC): National Academies Press (US); 2000 [PMID: 25077263]
11 **Stranges S**, Marshall JR, Natarajan R, Donahue RP, Trevisan M, Combs GF, Cappuccio FP, Ceriello A, Reid ME. Effects of long-term selenium supplementation on the incidence of type 2 diabetes: a randomized trial. *Ann Intern Med* 2007; **147**: 217-223 [PMID: 17620655 DOI: 10.7326/0003-4819-147-4-200708210-00175]
12 **Wichman J**, Winther KH, Bonnema SJ, Hegedüs L. Selenium Supplementation Significantly Reduces Thyroid Autoantibody Levels in Patients with Chronic Autoimmune Thyroiditis: A Systematic Review and Meta-Analysis. *Thyroid* 2016; **26**: 1681-1692 [PMID: 27702392 DOI: 10.1089/thy.2016.0256]
13 **Qiu Y**, Xing Z, Xiang Q, Yang Q, Zhu J, Su A. Insufficient evidence to support the clinical efficacy of selenium supplementation for patients with chronic autoimmune thyroiditis. *Endocrine* 2021; **73**: 384-397 [PMID: 33774780 DOI: 10.1007/s12020-021-02642-z]
14 **Krysiak R**, Kowalcze K, Okopień B. Selenomethionine potentiates the impact of vitamin D on thyroid autoimmunity in euthyroid women with Hashimoto's thyroiditis and low vitamin D status. *Pharmacol Rep* 2019; **71**: 367-373 [PMID: 30844687 DOI: 10.1016/j.pharep.2018.12.006]
15 **Schwalfenberg GK**, Genuis SJ. Vitamin D, Essential Minerals, and Toxic Elements: Exploring Interactions between Nutrients and Toxicants

in Clinical Medicine. *ScientificWorldJournal* 2015; **2015**: 318595 [PMID: 26347061 DOI: 10.1155/2015/318595]

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