Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 62; Numer/Number 4/2011
ISSN 0423–104X

The role of vitamins in the prevention and treatment of thyroid disorders

Rola witamin w zapobieganiu i leczeniu chorób tarczycy

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Abstract

Although vitamin deficiencies are uncommon in Poland or other developed countries, many patients take vitamin supplements. Despite the widespread availability of vitamins and the universal belief that vitamins offer health benefits, few publications have addressed their role in the prevention and treatment of thyroid diseases. There is some evidence to suggest that the administration of vitamins with anti-oxidant properties in patients with hyperthyroidism can decrease the severity of clinical symptoms, and that vitamin D supplementation can have a beneficial effect on the bone system for these patients. It has also been suggested that patients with autoimmune thyroid diseases should be periodically screened for vitamin B_{12} deficiency. There has been no data to support vitamin supplementation in the primary or secondary prevention of thyroid malignancies. **(Pol J Endocrinol 2011; 62 (4): 340–344)**

Key words: *hyperthyroidism, thyroid neoplasms, autoimmune thyroid disorder, vitamins*

Streszczenie

Chociaż niedobory witamin w Polsce i krajach rozwiniętych zdarzają się rzadko, bardzo duża grupa pacjentów spożywa suplementy witaminowe. Pomimo powszechnego przekonania o korzystnym wpływie na stan zdrowia oraz szerokiej dostępności niewiele jest publikacji określających ich rolę w zapobieganiu i leczeniu chorób tarczycy. Dane z piśmiennictwa sugerują, że u pacjentów z nadczynnością tarczycy witaminy o działaniu antyoksydacyjnym mogą zmniejszać nasilenie objawów klinicznych, zaś stosowanie witaminy D może korzystnie wpływać na stan kośćca w tej grupie chorych. Sugeruje się także, aby pacjentów z autoimmunologiczną chorobą tarczycy okresowo badać w kierunku niedoboru witaminy B_{12}. Nie ma danych uzasadniających suplementację witamin w prewencji pierwotnej czy wtórnej nowotworów tarczycy. **(Endokrynol Pol 2011; 62 (4): 340–344)**

Słowa kluczowe: *nadczynność tarczycy, nowotwory tarczycy, autoimmunologiczna choroba tarczycy, witaminy*

Introduction

Although primary vitamin deficiencies are infrequently diagnosed nowadays, sales figures for vitamin supplements in Poland are high, and continue to rise. According to "The healthcare and pharmacy market in Poland 2009. Anticipated development for the years 2009–2011", Poland's pharmacy market volume in terms of retail prices exceeds 24 billion zloty, 34% of which is generated by over-the-counter medications [1]. It is universally accepted that the use of vitamin supplements prevents many diseases (e.g. infections or malignancies), increases vitality, improves mood and enhances treatment of many disorders. Despite this belief, and the widespread availability of vitamins, their health impact and role in the prevention and treatment of diseases remain insufficiently understood.

Aim of the study

We aimed to review the current state of knowledge on the possible role of vitamins in patients with thyroid disorders. This undertaking has proven exceedingly difficult, as few publications have addressed this issue in the Polish or the international scientific literature, and only a few of those that have done so meet current standards of quality and reliability.

Material and methods

To identify suitable literature, an electronic search was performed using PubMed. We used the search string "(*vitamin*[Title] OR antioxidant*[Title]) AND (*thyroid*[Title] OR goiter*[Title])". PubMed identified 117 articles written in English or Polish published up to 2010. Titles and abstracts were screened, and 36 publica-

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tions that were consistent with the study's objectives were selected for a full-text reading.

Vitamins with antioxidant properties (A, C and E)

Cell homeostasis is maintained in part with the help of the oxidoreductive system which limits the damage caused by the so-called reactive oxygen species — by-products of the normal metabolism of oxygen. Its depletion leads to oxidative stress which results in structural and functional damage. Oxidative stress is responsible for ageing and plays a role in the development of atheromatosis, cancer and Alzheimer's disease.

Both hyper- and hypothyroidism have been proven to promote cellular oxidative stress by influencing the intensity of oxygen reactions. Hyper- and hypothyroidism have both been shown to affect concentrations of the vitamins involved in scavenging of free radicals (usually decreasing their concentrations, although study results differ) i.e. vitamins A, C and E. The concentrations of those vitamins return to normal after the achievement of euthyreosis [2–8].

Is supplementation of these vitamins or other antioxidants therefore indicated in patients with thyroid disorders? That the answer is 'yes' has been suggested by the results of animal studies where administration of vitamin E in individuals with hyper- or hypothyroidism reduced oxidative stress, decreased sensitivity to thyroid hormones, and prevented peroxidation of circulating LDL lipoproteins [9–11].

In a group of patients with hyperthyroidism due to Graves' disease, treated solely with a combination of antioxidants (vitamin C, vitamin E, beta-carotene, selenium, zinc, copper), clinical symptoms were reduced to a similar extent as in patients treated with thyreostatic medications. Moreover, in patients treated with antioxidants, the symptoms of hyperthyroidism subsided more rapidly, paralleled by decreased markers of oxidative stress. Given that normalization of thyroid hormone levels was not observed in this group, the authors suggested that the clinical symptoms of hyperthyroidism may reflect free radical toxicity and oxidative stress [12]. The beneficial effects of antioxidant supplementation (with a preparation similar to that used by Guerra) were also seen in a different study. Patients receiving antioxidants concomitantly with thyreostatic medications achieved euthyreosis more rapidly compared to patients treated with thyreostatics alone [13]. It seems therefore that supplementation of vitamins C and E, and possibly other antioxidants, may have beneficial effects in patients with hyperthyroidism. This issue requires further study and definitive resolution, especially in view of other reports suggesting that supplementation of vitamins A and E may be associated with increased patient mortality [14].

Conversely, it appears that using antioxidants in the prevention of thyroid cancer is not justified. Although results of a retrospective analysis showed decreased incidence of thyroid cancer in patients taking beta-carotene, vitamin E or vitamin C [15], recent meta-analyses and systematic reviews of prospective studies unequivocally deny anti-neoplastic effects of antioxidant vitamins [16, 17].

Vitamin A

The metabolism of vitamin A seems fairly closely connected to the activity of the hypothalamic-pituitary-thyroid axis. Animal studies show that vitamin A deficiency is associated with decreased thyroid iodine uptake, limited synthesis and secretion of hormones, as well as thyroid enlargement. The total serum triiodothyronine and thyroxine concentrations increase (common transport proteins e.g. transthyretin bind both thyroid hormones and the retinol-binding protein, the synthesis of which decreases in vitamin A deficiency). The rate of hepatic conversion of thyroxine to triiodothyronine is also decreased. Normally, the secretion of thyroid-stimulating hormone (TSH) is regulated by the thyroid-hormone-activated receptor and the retinoid X receptor. The latter, after binding the ligand (vitamin A) binds with its promoter region of DNA encoding the beta-subunit of TSH, limiting its expression. Vitamin A deficiency is thus associated with increased TSH secretion [18].

This issue has not been as well studied in humans. Studies conducted in areas of endemic iodine deficiency have shown that children with goiter and concomitant vitamin A deficiency were at less risk of developing hypothyroidism. They also had higher levels of TSH and thyroxine compared to children without vitamin A deficiency. A strong correlation was found between goiter size and severity of vitamin A deficiency [19]. Monotherapy with vitamin A led to a decrease in TSH concentrations and reduction in goiter size, with unchanged serum concentrations of thyroid hormones [20].

Vitamin B_6

Vitamin B_6 is a co-enzyme participating in more than 100 enzymatic reactions in the human body. Clinically, vitamin B_6 is essential for the production of neurotransmitters, myelin sheaths, hemoglobin, myoglobin, and the metabolism of homocysteine. Its deficiency leads to dysfunction of the central nervous system (manifesting as irritability, mood disturbance,

impaired consciousness and seizures), peripheral nervous system (polyneuropathy), as well as anemia and hyperhomocysteinemia.

There are numerous publications in the medical literature regarding the role of vitamin B_6 in the pathogenesis and treatment of neurologic, psychiatric and hematologic diseases, but few on the subject of vitamin B_6 in the context of thyroid dysfunction.

The activity of the hypothalamic-pituitary-thyroid axis in the setting of vitamin B_6 deficiency has been studied in rats. Well-conducted experiments have shown that vitamin B_6 deficiency leads to hypothyroidism resulting from decreased TRH synthesis in the hypothalamus. The reversal of vitamin B_6 deficiency has led to normalization of thyroid hormone levels [21]. Over-supplementation of vitamin B_6 in human and animal studies has led to decreased concentrations of the thyroid-stimulating hormone [22, 23].

No studies have looked at whether hyperthyroidism or hypothyroidism may lead to vitamin B_6 deficiency. Similarly, there have been no studies on the usefulness of vitamin B_6 supplements in patients treated with antithyroid agents. According to some physicians, such treatment may prevent leucopoenia, a fairly common adverse effect of antithyroid agents. We have not found a single publication addressing the efficacy of this measure.

Conversely, there are reports of possible adverse effects of higher than physiologic doses of vitamin B_6. The daily requirement for vitamin B_6 is 2 mg, a level more than sufficiently provided by the typical diet. Doses not exceeding 200 mg per day (equivalent to two vitamin B_6 tablets twice daily) are considered safe, whereas many cases of sensory neuropathy associated with the administration of larger doses have been reported [24].

Vitamin D

Discoveries made during the last few years have greatly increased our understanding of the role of vitamin D. Its influence is not limited to organs involved in calcium homeostasis (such as the gut, bones, kidneys and parathyroid glands). Vitamin D receptors have been found in more than 35 tissues and it has been demonstrated to participate in immune processes, insulin secretion, the regulation of the cardiovascular system and the development of the central nervous system [25]. Data on the metabolism of vitamin D in hyperthyroidism is not consistent. Differences result from factors including patient selection, dietary vitamin D intake, sunlight exposure and seasonal variability of vitamin D concentration. Both normal [26–28] and decreased [29–31] concentrations of 25-OH-cholecalciferol have been found in hyperthyroid patients before treatment. A study from Japan including 200 euthyrotic patients with Graves' disease found vitamin D deficiency in 40% of women and around 20% of men [32]

It has been demonstrated that hyperthyroidism leads to reversible loss of bone mass and temporarily increases the risk of femoral neck fracture [33]. This risk returns to baseline after approximately a year, whereas bone mineral density does not return to baseline until one to four years after treatment of hyperthyroidism is started [33].

In view of the above, the usefulness of vitamin D_3 supplementation in patients treated for hyperthyroidism should be considered, as its possible deficiency could negatively influence bone healing.

Vitamin B_{12}

Vitamin B_{12} deficiency may result in a number of neurologic, psychiatric, hematologic, gastrointestinal and metabolic disturbances (Table I). The commonest etiology of decreased absorption of vitamin B_{12} is atrophic gastritis which also increases the risk of developing gastric cancer, hyperplasia of enterochromaffin-like cells and gastric carcinoid. There is compelling evidence for the increased prevalence of vitamin B_{12} deficiency in the population of patients with thyroid disease.

Centanni et al. examined 62 patients with autoimmune thyroid disease (AITD). Patients with increased serum gastrin underwent endoscopic, pathologic and immunologic testing. Atrophic gastritis was confirmed in 22 cases (35%) [34]. Ness-Abramof et al. found decreased concentrations of vitamin B_{12} in 32 out of 115 (28%) patients with AITD. The authors recommended routine measurements of vitamin B_{12} every 3-5 years in these patients. In those with decreased vitamin B_{12} concentrations, further management should depend on the level of gastrin, as the presence of hypergastrinemia is highly suggestive of concomitant atrophic

Table I. *Clinical sequelae of vitamin B_{12} deficiency*
Tabela I. *Kliniczne następstwa niedoboru witaminy B_{12}*

Neurological symptoms	Non-neurological symptoms
Peripheral neuropathy	Glossitis
Subacute combined degeneration of spinal cord	Gastrointestinal disturbances Weight loss
Focal demyelination of white matter in the brain	Anemia
Optic nerve inflammation/atrophy	Impaired fertility
Psychiatric symptoms (depression, cognitive deficit, psychosis)	Hyperhomocysteinemia

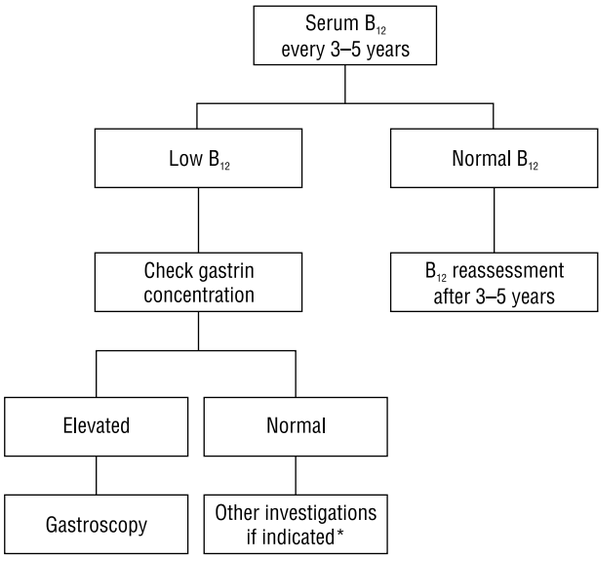

Figure 1. *Evaluation of vitamin B_{12} deficiency in patients with autoimmune thyroid disorder (as proposed by Ness-Abramof et al.) *Schilling test, anti-transglutaminase antibodies, serum homocysteine, serum methylmalonic acid*

Rycina 1. *Ocena występowania niedoboru witaminy B_{12} u pacjentów z autoimmunologiczną chorobą tarczycy wg Ness-Abramoff i wsp. *test Schillinga, przeciwciała przeciwko transglutaminazie, stężenie homocyteiny, kwasu metylomalonowego w surowicy*

gastritis [35]. The suggested management algorithm is summarized in Figure 1.

Orzechowska-Pawilojc et al. found that both the hypothyroid [36] and hyperthyroid [37] state in women is associated with lower concentration of vitamin B_{12} when compared to a healthy control group. However, the authors did not report the higher prevalence of vitamin B_{12} deficiency in the study groups [36, 37].

Summary

It seems that the only indisputable conclusion of the current literature regarding the role of vitamins in patients with thyroid disorders is that this issue requires further study. With that in mind, a physician caring for patients with thyroid disorders should realize that supplementation of antioxidant vitamins probably does not prevent thyroid malignancies, but can decrease symptoms in patients with hyperthyroidism. It is also possible that supplementation of vitamin D in these patients accelerates bone healing. There is no scientific data justifying supplementation of vitamin B_6 in these patients. Atrophic gastritis often coexists with autoimmune thyroid disease and periodic evaluation of vitamin B_{12} levels seems justified in this patient population. When counselling patients about the use of vitamin supplements, it should be remembered that several studies have demonstrated adverse consequences of their action.

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