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Vitamin D and thyroid autoimmunity

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ABSTRACT

Vitamin D deficiency is a global health problem, its role as an immune modulator being recently emphasized. Recent studies are increasingly suggesting that vitamin D plays a significant role in reducing the incidence and progression of autoimmune diseases. Furthermore, it was reported that patients with Hashimoto's thyroiditis, an autoimmune thyroid disease had lower vitamin D levels [1].

We initiated a prospective study, for a period of 6 months with a study group represented by 160 patients admitted to the National Institute of Endocrinology "CI Parhon" in the period 2013 -2014.

Patients were divided into 3 groups: 121 patients without thyroid pathology, 22 patients diagnosed with chronic autoimmune thyroiditis, who received 2000 IU cholecalciferol daily, 17 patients diagnosed with chronic autoimmune thyroiditis, which did not receive cholecalciferol.

We found that patients with chronic thyroiditis have a poor vitamin D status with ATPO values negatively correlating with 25 (OH) vitamin D levels. Treatment

with cholecalciferol not only improves vitamin D status but also lowers antithyroid antibodies titres.

Keywords: vitamin D deficiency, chronic autoimmune thyroiditis

Introduction

Vitamin D deficiency was proved to be more common than thought so far, especially among teenagers, women and elderly representing a real pandemy. Exposure to ultraviolet B light (290–320 nm) is the main source of vitamin D.

The most common causes are limited sun exposure or under UVB and UVA protection (≥ 8 SPF), insufficient consumption of natural foods with high content of vitamin D, lack of fortified food products on the romanian market [2,3]

Although there are some categories of people at risk for vitamin D deficiency, such as: pregnant or breastfeeding women, patients with chronic gastrointestinal complaints, obese patients, patients with hypothyroidism, patients under treatment with antacids, anticoagulants, anticonvulsants, antifungal, antiretroviral, corticosteroids, in fact anyone can have low levels of vitamin D.

Adjacent to well known functions in maintaining

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metabolic and phosphocalcic balance, recent studies emphasize the immunomodulatory role of vitamin D in reducing the risk of autoimmune diseases such as type 1 diabetes, autoimmune thyroiditis, an autoimmune hyperthyroidism, multiple sclerosis, Crohn's disease, lupus erythematosus, rheumatoid arthritis.[4, 5, 6]

The immunomodulatory role of vitamin D has been demonstrated in autoimmune thyroid diseases, low levels of vitamin D being found in patients with Hashimoto's thyroiditis and Graves-Basedow disease. Moreover, there are correlations between vitamin D levels and ATPO and the assumption that vitamin D supplementation ameliorates the evolution of the disease.[8, 9]

In Hashimoto's thyroiditis, the immunologic reaction is triggered when thyrocytes express major histocompatibility complex (MHC) class II surface HLA-DR antigens, a process induced by the production from T helper (Th)1 type lymphocytes, of inflammatory cytokines (especially IFN- γ), which may be inhibited by 1,25[OH]₂D. The genetic polymorphism of the vitamin D receptor (VDR), vitamin D binding protein (DBP) and of 1 α -hydroxylase (CYP1 α) may predispose to the development of chronic autoimmune thyroiditis.[10, 11]

These arguments support the need for extensive studies to determine the effectiveness of vitamin D supplementation in patients with chronic autoimmune thyroiditis, aimed to improve the disease but also establish an optimal protective level of vitamin D.

Objectives

- Identify the prevalence of 25 (OH) vitamin D deficiency among patients without thyroid pathology and its prevalence in patients with chronic autoimmune thyroiditis;

- Highlighting a correlation between the degree of vitamin D deficiency and antithyroid antibody titer;

- Highlighting the inhibitory effects of vitamin

D on an excessive thyroid immune response.

Material and Methods

We initiated a prospective study, for a period of 6 months.

The study group was represented by 160 patients admitted to the National Institute of Endocrinology "CI Parhon" in the period 2013 -2014.

Patients were divided into 3 groups:

- Group of 121 patients without thyroid pathology;

- Group of 22 patients diagnosed with chronic autoimmune thyroiditis, who received 2000 IU cholecalciferol daily;

- Group of 17 patients diagnosed with chronic autoimmune thyroiditis, which did not receive cholecalciferol.

Laboratory variables

Blood samples were collected under fasting conditions (between 8:00 and 10:00 AM). TSH, fT₄, ATPO were measured by direct immunochemiluminiscence assay (Siemens Immulite 2000 System). The lower detection limit was 5IU/ml for ATPO with a reference limit <35IU/ml. 25 (OH) vitamin D, was measured by electrochemiluminiscence (ECLIA, Cobas e601, Roche) with a lower detection limit of 4,2ng/ml. The intra- and interassay variation coefficients in our laboratory were 3,27% and 9,1%, respectively for 25 (OH) vitamin D and 5-6% and 6-8%, respectively for ATPO.

Statistical analysis

For the statistical analysis and interpretation of data we used Microsoft Office Excel vers. 2010.

Results

The 160 enrolled patients had varying ages. Most of them were over 40 years representing 81.87% of the total, with the predominant age groups 50-59 years (36.87%) and 60-69 years at a rate of 25.62% (Fig. 1.).

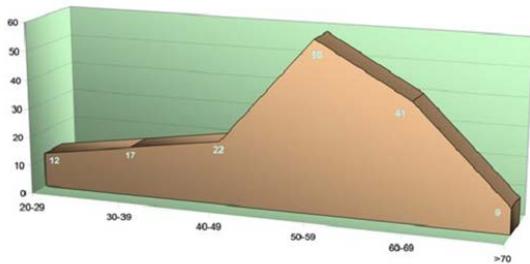


Fig. 1 – Age distribution in studied patients

There were no significant differences in terms of age distribution among patients without chronic thyroiditis and those with chronic thyroiditis. Maximum values were recorded for the age group 50-59 years in both categories of patients representing 36.36% for the group without thyroid pathology and 38.46% for the one with chronic thyroiditis.

Age distribution was also similar in patients with chronic thyroiditis who received or not treatment with vitamin D. The 50-59 years age category prevailed.

Assessment of vitamin D status in all 160 patients provided a surprising aspect, even considering that recent studies have shown increased incidence of over 50% of vitamin D deficiency in the general population. In all age groups the mean values of vitamin D 25HO were found to be below the optimum minimum 20 ng / ml. The lowest values were recorded in patients aged 30-50 years representing 24.37% , patients belonging to active population (Fig. 2).

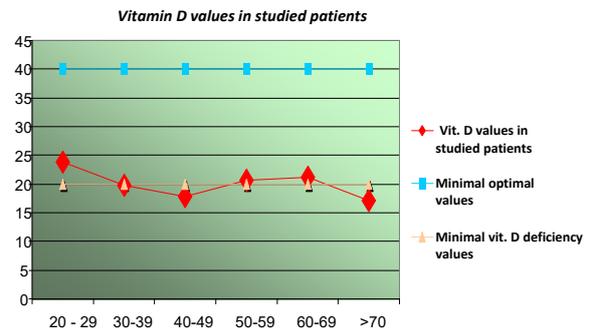


Fig. 2 – Vitamin D values in studied patients

In patients with chronic thyroiditis the age category with the lowest average value of 25 (OH) vitamin D was 40-49 group age (Fig. 3).

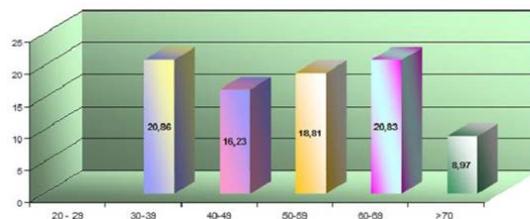


Fig. 3 – Age distribution of thyroiditis patients according to vitamin D levels

Vitamin D showed a similar aspect in patients without chronic thyroiditis, the lowest values belonging to those aged 30-39 and 40-49 with an average level of vitamin D of 19, 22 ng / ml and 18.58 ng / ml, respectively (Fig. 4).

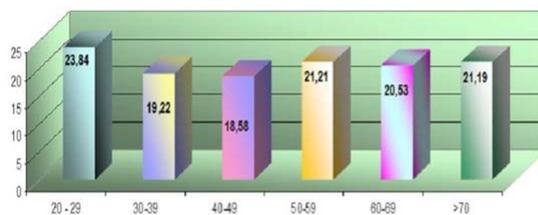


Fig. 4 – Age distribution in patients without thyroiditis according to vitamin D values

The same characteristics were observed in patients diagnosed with chronic autoimmune thyroiditis. In the 40-49 age group the average value of vitamin D was 16, 23 ng / ml and in those above 70 years - 8.97 ng / ml.

By comparing plasma levels of 25 (OH) vitamin D identified in patients with thyroiditis versus patients without thyroiditis, we found significantly lower values in patients with chronic thyroiditis, in all age groups (Fig. 5).

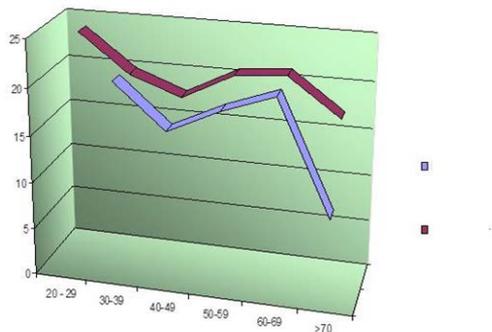


Fig. 5 – Vitamin D status in patients without chronic thyroiditis

In patients diagnosed with thyroiditis, antithyroid antibodies values showed a negative correlation with serum level of 25 (OH) vitamin D (Fig.6).

The negative correlation between 25(OH) vitamin D levels and ATPO values

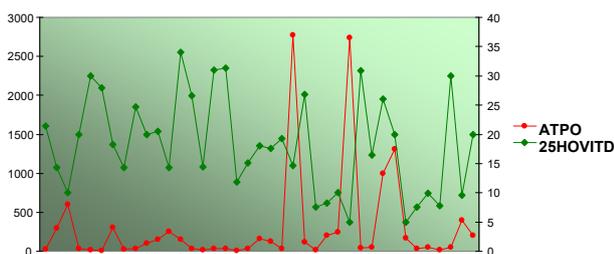


Fig. 6–The negative correlation between 25 (OH) vitamin D levels and ATPO values

After 6 months of treatment with 2000 IU of cholecalciferol daily, antithyroid antibody values have declined significantly. While in patients with chronic thyroiditis without treatment with vitamin D antibody titer increased by 107% in those with

vitamin D therapy titer decreased by 39% and vitamin D status has improved, reaching an average value of 23.44 ng / ml (18% growth). Also in patients with chronic thyroiditis and without supplementation of vitamin D there was a drop in the 25 (OH) vitamin D value by approximately 25%. It is thus demonstrated a negative correlation between 25 (OH) vitamin D values and ATPO (Fig. 7). Antithyroid antibodies values in patients already receiving vitamin D for 12 months fall on the same downward line (data collection in progress).

Evolution of the average values of vitamin D and ATPO in patients with and with treatment at baseline and 6 months

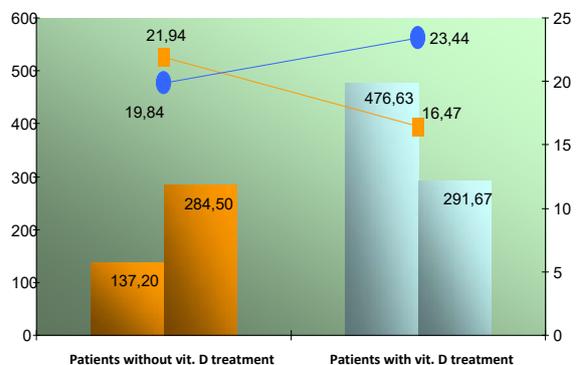


Fig. 7 – Evolution of the average values of vitamin D and ATPO in patients with and without treatment at baseline and 6 months

Discussions

Autoimmune thyroid diseases represent the most common endocrine pathology but also the most common type of autoimmune disease, being reported with a prevalence of 1-2% in men and 7-9% in women. Multiple studies have suggested vitamin D deficiency involvement in the pathogenesis of these diseases, thereby creating premise of a truly effective adjuvant therapy in slowing their evolution [12].

Hashimoto's thyroiditis is a chronic autoimmune disease caused by interactions between

susceptibility genes (CTLA-4, HLA, TSH receptor), environmental factors and hormonal influences, with incompletely understood mechanisms.

The mechanisms by which vitamin D may lower the levels of antibodies which interact with thyroid antigens are intricate and still incompletely understood.

Most effects of vitamin D are mediated through the vitamin D receptor (VDR). The immune modulator properties of vitamin D are assigned to its effect on cells of innate and adaptive systems, including macrophages, dendritic cells (DC) and T and B lymphocytes, all of which possess VDR. Studies have shown that activation of CD4 + T cells which express VDR promotes a Th2 phenotype (production of IL-4 and IL-5) while suppressing Th1 activity (the production of interferon-gamma and IL-2). By such mechanisms Vitamin D is believed to modulate cell-mediated immune responses and to regulate the inflammatory T cell activity. Low vitamin D may increase the degree of autoimmunity and subsequently increase the prevalence of AITDs, which are the most common autoimmune diseases [10, 11, 13].

In addition, 1,25 [OH]₂ D has direct immunomodulatory effects on VDR from T cells. All of these factors combined can lead to protection of thyroid cells in autoimmune diseases, considering that chronic autoimmune thyroiditis is induced by an immunological attack through inflammatory Th1-type cytokine production (especially IFN- γ). The continuous proliferation of B cells can be inhibited and apoptosis may be induced by 1,25 [OH]₂D [14, 15, 16].

Limited exposure to sunlight consequence of extended work schedule, while limiting sport activities are likely some of the causes of vitamin D deficiency in active people.

The same limited sun exposure and other age associated specific causes are definitely involved in low plasma levels of 25 (OH) vitamin D in patients over 70 years.

This study suggests the need for more evidence to establish the safety and effectiveness of vitamin D supplementation in patients with chronic autoimmune thyroiditis as well as to determine the optimal level of vitamin D needed for improving the evolution of this

immunological disorder.

Conclusions

Patients with chronic thyroiditis have a poor vitamin D status (in 64% of the cases) and ATPO values negatively correlate with 25 (OH) vitamin D levels.

Treatment with 2000 IU cholecalciferol daily for 6 months, apart from enhancing levels of vitamin D is associated with significant decrease in antithyroid antibody titers (39%).

The study also points out to the fact that vitamin D deficiency is common in the majority of the evaluated patients, regardless of age.

Given the many beneficial actions of vitamin D, we support the need for a population-based study for an accurate assessment of the problem, premise of efficient measures meant to correct its deficit.

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