LINKS BETWEEN OBESITY, SELENIUM SUPPLEMENTATION, AND TITRE OF THYROID PEROXIDASE ANTIBODIES

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Keywords: *obesity, thyroid peroxidase antibodies, selenium, autoimmune thyroiditis*

Abstract: *Introduction: Evaluation of the influence of administration of selenium supplements over a period of 6 months on the evolution of titers of anti-thyroid peroxidase antibodies in patients with chronic autoimmune thyroiditis. Materials and methods: We monitored data collected from the archive of Endocrinology Ambulatory in Târnăveni city, for a group of 109 female patients with newly diagnosed chronic autoimmune thyroiditis, with or without impairment of thyroid hormone status. Results: Our study confirms that selenium supplementation at a dose of 200 micrograms per day over a 6-month period resulted in a significant decrease in serum levels of anti-thyroid peroxidase antibodies. The titer of anti-thyroid peroxidase antibodies at 6 months of selenium supplementation, decreased to 85.3% of the investigated patients, with 26.31% of the initial value. Conclusions: Selenium has proven effective in chronic autoimmune thyroiditis in order to maintain a balance of autoimmune thyroid disease.*

INTRODUCTION

Obesity has become an epidemic reality that must be controlled by all means, given the dramatic consequences on individual and public health. Normal weight is controlled by highly complex homeostasis mechanisms, depending both on external factors and on internal factors. External factors are represented by the environmental factors on which industrialization has left its mark, leading to global climate change, including climate change, habitat pollution to food pollution. On the other hand, socio-cultural factors have evolved under the influence of globalization, of multi-ethnic cultures, with a major change in food habits, with important changes in the diet. Stress is an important risk factor in obesity. Sedentarism is interdependent with spontaneous motility and basal muscular tone, disturbing the mechanisms of energy balance regulation. Foods have become increasingly industrialized, more refined, with higher caloric densities, sometimes polluted with food additives that act as endocrine disruptors, stimulating adipocyte proliferation and obesity. Internal factors of weight regulation are complex, being both genetic and epigenetic, interacting strongly with external factors, food, and eating behaviours.(1-3)

Chronic autoimmune thyroiditis is considered the most common endocrine disorder (4,5) and is the most common cause of hypothyroidism in areas with sufficient iodine intake.(6) It affects approximately 3% of the adult population, predominantly female, with a gender ratio of approximately 10: 1, but it also occurs in children or adolescents. It was first described in 1912 by Japanese physician Hakaru Hashimoto.(7)

Chronic autoimmune thyroiditis is considered to be a multifactorial disease arising from the interaction between genetic factors responsible for the susceptibility to this disease and epigenetic factors.(8) Histologically, thyroid in TCH shows a massive lymphocyte infiltration (both T lymphocytes and B lymphocytes) and plasmacytosis that destroys normal follicular architecture. Several antibodies and antigen-specific T cells directed against thyroid antigens have been described in chronic autoimmune thyroiditis. The main antigens are thyroglobulin (Tg), thyroid peroxidase (TPO) and thyroid stimulating hormone receptor (TSH receptor). Most patients with autoimmune chronic thyroiditis have an elevated titer of anti-TG antibodies in the early stages, then they may disappear, but anti-TPO antibodies are present from the onset and persist for many years. They may have a direct cytotoxic effect on thyrocytes, but their importance is reduced compared to LT-induced cytotoxicity. In TCH, the Th1 CD4 + LT helper is predominant, which by the secretion of interleukin-2 (IL-2), gamma interferon and TNF-β (tumour necrosis factor-beta) predominate the apoptotic destruction of thyroid cells.(9,10) Infection, stress, sex steroids, pregnancy, iodine intake, and radiation exposure are the known possible precipitating factors for Hashimoto's thyroiditis.(11)

Selenium is a microelement essential to human health.(12,13) It strengthens the immune system by activating T lymphocytes (which recognize viruses, bacteria by adding specific antibodies) and macrophages.(14) The need for selenium is estimated to be between 50-200ug/day.(15) Selenium is not found in sufficient quantities in the soil of Europe and Romania, with insufficient food intake.(16)

Selenium may be available both in inorganic compounds (selenomethionine and selenocysteine) and in organic compounds (selenite and selenate).(17) An organic form has better absorption, and it seems to be the preferred formulation for supplementation or treatment.(18) In its organic state, it forms the active center of 25 enzymes (selenoprotein-enzymes) encoded by the human genome.(19) These selenoproteins have a strong anti-inflammatory role, for example, glutathione peroxidases (GPXs): it stops the propagation of reactive oxygen species by reducing lipid hydroperoxidation; metabolizes the intermediate hydroperoxides that are born in the synthesis of eicosanoids catalyzed by cyclooxygenases and lipoxygenases, preventing the production of pro-inflammatory leukotrienes and prostaglandins; in

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Article received on 29.04.2019 and accepted for publication on 30.05.2019
ACTA MEDICA TRANSILVANICA June 2019;24(2):12-15

particular P-selenoproteins have the ability to inactivate ROS/RNS peroxynitrites with a high destructive potential, resulting from the action of nitric oxide superoxide and which depolymerizes hyaluronic acid and destroys proteoglycans.(20)

Controlled randomized trials have found that selenium supplementation lowers Hashimoto's thyroid-specific antibody levels. The level of selenium in plasma depends directly on selenium intake and correlates well with the organic availability of this nutrient. Several papers have argued that there is no evidence of the effects of supplementation with Se, while other research has suggested that there is beneficial evidence for selenium supplements, including lower titers of thyroid peroxidase antibodies, improving thyroid hormone secretion.(21)

PURPOSE

The present study aims to establish the links between the effects of selenium and obesity on levels of anti-thyroid-peroxidase antibodies in a group of Romanian patients with Hashimoto chronic thyroiditis.

MATERIALS AND METHODS

The present study is a prospective one, carried out within the ambulatory endocrinology cabinet of "Dr. Gheorghe Marinescu" hospital of Târnăveni city, between November 2017 and January 2018. During this period, 109 newly diagnosed patients with chronic autoimmune thyroiditis were investigated. Inclusion criteria: age ≥ 18 years, serum anti-thyroid peroxidase antibody ≥ 35 IU/mL. Exclusion criteria: history of hyperthyroidism, radioactive iodine treatment, thyroid surgery; immunomodulators or other drugs that affect; planned pregnancy or breastfeeding; allergy to any ingredient in the organic selenium supplement; previous supplements with selenium; non-compliant patients.

The study samples were divided into two: the sample at the time of diagnosis (baseline), the 6-month sample of selenium supplementation. Each patient was examined by monitoring changes in laboratory parameters (thyroid stimulating hormone (TSH), free thyroxine (FT4), thyroid peroxidase antibody (TPOAb) and calculating the body mass index. These assessments were made at the time of diagnosis and at 6 months of selenium supplementation. In this study, patients have received selenium-selenium-methionine treatment at 200 micrograms daily.

RESULTS

In our study, we enrolled 109 patients, ranging between 18 to 87 years of age (one third of them under 50 years old), and 91 of whom were women (83.48%); 66.97% had overweight or obesity (BMI ≥ 24.9 kg/m^2), 74% of whom were affected by hypothyroidism (TSH <5); 85% of all had hypothyroidism (subclinical or manifest) at the time of diagnosis, and 15% had thyroid parameters within the baseline. Also, there is a statistically significant association between the high level of anti-thyroid peroxidase antibodies and presence of hypothyroidism (subclinical or manifest), in those with hypothyroidism, the median of the TPOAb at the initial time was higher than the value associated with those without hypothyroidism (figure no. 1).

The titer of TPOAb at 6 months of selenium supplementation, decreased to 85.3% of the investigated patients, with 26.31% of the initial value. 14.7% of patients did not experience a statistically significant decrease in thyroid peroxidase autoantibody titer. It was noted that there was a statistically significant difference (p <0.0001) in the decrease of a titer of thyroid peroxidase autoantibody after 6 months of selenium supplementation (figure no. 2), demonstrating the efficacy of this micronutrient in Hashimoto's thyroid management.

Figure no. 1. Distribution of TPOAb blood level and hypothyroidism/euthyroid

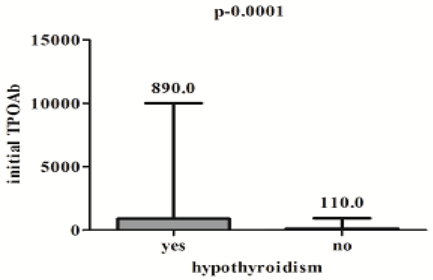
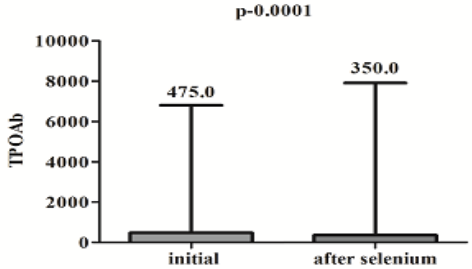
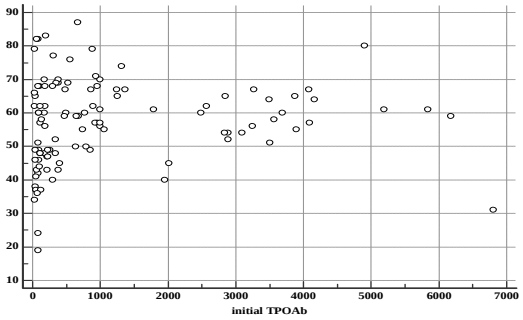


Figure no. 2. Statistical analysis - TPOAb levels initially and after selenium supplementation



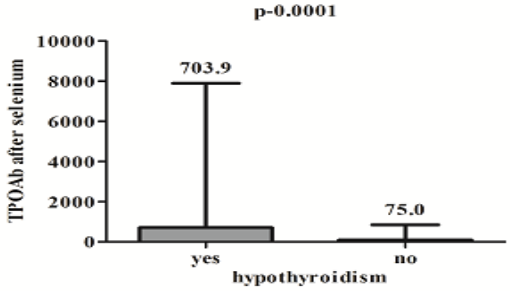
The age of patients correlates positively (rho = 0.24) and statistically significant (p = 0.012) with the titer of TPOAb, higher values of anti-thyroid peroxidase antibodies occur at older ages (figure no. 3).

Figure no. 3. Age correlates with the titer of TPOAb



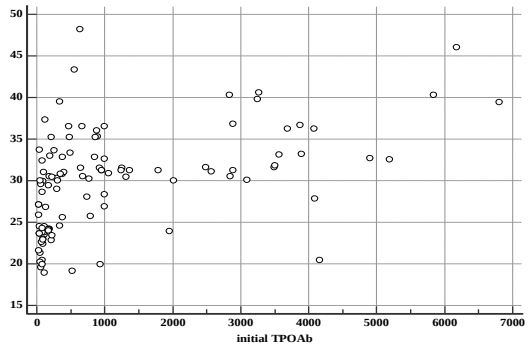
In our sample, a titer of TPOAb is recovered in a higher percentage in those with reduced thyroid hormone secretion (subclinical or manifest hypothyroidism) (figure no. 4).

Figure no. 4. Statistical analysis - hypothyroidism, and TPOAb after selenium



Also, there are statistically significant correlations between the body mass index and the titer of the TPOAb (figure no. 5).

Figure no. 5. Correlation between body mass indexes and initial TPOAb



DISCUSSIONS

Chronic autoimmune thyroiditis is the most common human organ-specific autoimmune disease, characterized by the aggression of the body by its own immune system. Thus, the thyroid gland cannot produce enough hormones and hypothyroidism is set up. For this reason, it is considered that thyroid dysfunction is the cause of a wide variety of symptomatic accusations that negatively affect the quality of life. The thyroid is the organ with the highest selenium concentrations per gram of all tissues. Selenium, an essential nutrient for humans, is a micronutrient element composed of more than two dozen selenoproteins that play a critical role in the metabolism of thyroid hormones, reproduction, DNA synthesis and in protecting the body from oxidative stress and infection. Modern research has reported that selenium is important for antioxidant defense, and selenium adjunctive supplements may be beneficial to patients with chronic autoimmune thyroiditis in immune responses. The plasma level of selenium interferes with immunoregulation, which is essential for preventing responses that can lead to chronic inflammation and autoimmunity. Selenium contributes to T cell proliferation and selenium deficiency is associated with Th2 markers.(22)

Many clinical studies have reported the importance of selenium supplementation in decreasing levels of anti-thyroid peroxidase antibodies after 6 months (23) of selenium supplementation and after 12 months of selenium.(24) Our study found selenium supplementation for 6 months significantly reduced the titer of TPOAb. No side effects have been reported during selenium administration. Thus, the results obtained by us in this paper are consistent with some meta-analyses supporting selenium supplementation.

Several clinical trials have studied a possible link between thyroid function and obesity, reporting that elevation of TSH would be a consequence of thyroid reset in response to weight gain, meaning TSH increased in an obese person does not signify true hypothyroidism.(25,26)

Several studies have reported positive correlations between obesity and TSH or between TSH and body mass index, by a direct action of TSH on adipogenesis by leptin intervention, or by stimulation of preadipocyte differentiation.(27,28) In our study, 73 participants had overweight or obesity and 78 patients had hypothyroidism, with higher titers of thyroid peroxidase than patients who had a normal thyroid status and a body mass index of <24.9 kg/m^2. An important role in the relationship between obesity and chronic autoimmune thyroiditis is attributed to leptin, by this hormone obesity is involved in increasing the risk of thyroid autoimmunity.(29)

Lifestyle has changed, stress has increased, especially emotionally, and sedentary lifestyle has become a defining feature of modern society, all of which have led to weight gain. The imbalance in the fragile mechanism of weight-bearing homeostasis leads to global health perturbations, endocrine disorders, and psycho-behavioural disorders. Adipose tissue has self-regulation properties and controls through the hypothalamus, the amount of food ingested, and metabolism. Hormones and inflammatory compounds secreted by adipocytes pass from fatty tissue into the bloodstream, being transported throughout the body, producing adverse effects on the brain, liver, cardiovascular system, musculoskeletal system. The higher the fat mass, the more it secretes larger amounts of leptin, which is involved in the autoimmune thyroid process, with the increase in titer peroxidase antibody titer. Leptin encoded by the ob gene is a protein synthesized and secreted in both the white adipose and the brown adipose. Small amounts are also secreted in the skeletal muscle, the gastric and placental glands. It acts as a satiety hormone by regulating appetite by controlling again the receptors located at the level of the hypothalamus neurons, lowering food intake and increasing energy consumption. Leptin increases in overeating (in the obese) and decreases in fasting, in parallel with insulin. Overweight and obese people do not experience the feeling of satiety and stop eating, thus leading to leptin resistance. It is higher in women than in men. There are complex interactions between leptin and insulin, and in obesity, it is involved in the induction of insulin resistance. In addition to its role in regulating the energy balance, leptin is also involved in differentiating hematopoietic cells, regulating immune function, initiating puberty development, maintaining reproductive function, regulating the growth process.(30-31)

CONCLUSIONS

We have noticed in our survey the efficacy of administering selenium supplements at a dose of 200 micrograms per day for 6 months in patients with chronic autoimmune thyroiditis in both levothyroxine substitution and those with euthyroidism, and the importance of obesity in inducing thyroid autoimmunity, emphasizing the importance of screening, along with personalized treatment and diet, for patients with autoimmune thyroiditis.

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