Nutritional Treatment Strategies of Thyroiditis of Hashimoto

Subjects: Endocrinology & Metabolism

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Since the thyroid gland is one of the organs most affected by autoimmune processes, many patients with thyroiditis of Hashimoto (TH) seek medical advice on lifestyle variance and dietary modifications to improve and maintain their hyroid function. For most TH patients, the hormone-replacement therapy with levothyroxine is indispensable. Nevertheless, an appropriate dietary regimen and ecological lifestyle can complement the standard treatment and favor remission of TH by improving the function of the thyroid gland, as well as by regulating the levels of thyroid-stimulating hormone (TSH), free triiodothyronine (T3), thyroxine (T4), antibodies to thyroid peroxidase (Ab-TPO) and thyroglobulin (Ab-Tg). Other less significant parameters may be a repercussion of healthier body reactions and improvement of life quality, such as better sleep and alertness. Compliance with nutritional guidelines with a focus on the prevailing anti-inflammatory diet and controlled vitamin D dosing may help individual TH patients to reduce the need for medicines, slow down the course of the disease, and avoid relapses.

thyroiditis of Hashimoto Nutrients Inflammatory

1. Introduction

The thyroid gland is the organ most affected by autoimmune processes [1]. Between 20% and 40% of American Caucasians and British citizens show lymphocytic infiltration in post-mortem specimens, while the highest percentage is typical for white females [2]. The intra-thyroidal lymphocytic infiltration induces chronic inflammation and autoimmune conditions, which most often results in autoimmune hypothyroidism or thyroiditis of Hashimoto (TH) [3]. TH development leads to scarring and destruction of the thyroid gland and is manifested by by a decrease of plasma free triiodothyronine (T3) and thyroxine (T4), elevated plasma levels of thyroid-stimulating hormone (TSH) and by the presence of antibodies to thyroid peroxidase (Ab-TPO) and thyroglobulin (Ab-Tg) [4]. It is generally accepted that the pathogenesis of TH, like other autoimmune diseases, represents the combination of environmental (i.e., lighting regimen, pollution, micronutrients, variety of physical and social factors), existential (lifestyle, hormonal status, diet, gut microbiota), as well as genetic factors that provoke immunological dysfunction and support the autoimmune destruction of the gland [4].

To treat the condition in the long term, patients with TH-associated hypothyroidism often require lifetime hormone replacement therapy with levothyroxine [5][6]. There is growing evidence of the existence of a thyroid–gut axis that controls many autoimmune disorders, and patients frequently report changes in their quality of life and thyroid function as a result of dietary modifications.

Genetic factors contribute to 70–80% of autoimmune thyroid diseases [7]. The major histocompatibility complex genes (HLA class I and II), thyroid-related genes, genes associated with thyroid peroxidase antibody synthesis (BACH2, TPO), and genes regulating immune response (CD40, CTLA4, PD1) are the common genetic factors [7][8].

From the environmental factors, a vast variety of nutrients play an important role in the onset and development of TH. High iodine intake, deficiencies of selenium and iron, inadequate intake of proteins, unsaturated fatty acids, and dietary fibers could favor TH [1][9][10]. Proinflammatory foods may induce dysbiosis and oxidative stress [11] that can cause intestinal inflammation and spread it towards different organs, including the thyroid gland [4][12][13]. The reduction and replacement of commensal microbiota caused by dietary supplementation significantly change the immune function and epithelial metabolism of the intestinal mucosa and the absorption of nutrients [11][14]. Drugs such as pembrolizumab, interferon-α, anti-retroviral therapy, and estrogens used for oral contraception or hormone replacement therapy are also crucial for TH [7][8]. Smoking and moderate alcohol consumption protect against TH, but quitting smoking may provoke this disease [8]. Immunomodulatory therapies and infections such as rubella, hepatitis C, and Epstein-Barr virus could also be responsible for the development of TH [8].

Cyanotoxins such as cylindrospermopsin (CYN) and microcystins, in addition to their general toxicity, increase the permeability of epithelial and model pseudo-epithelial layers of human intestines. They even possess the ability to affect the function of the gastrointestinal epithelium and other cell types, and thus induce “leaky gut” syndrome, inflammation, oxidative stress, and apoptosis [15]. Furthermore, microcystins dose-dependently reduce thyroid hormone levels, and influence deiodinase activity and transcription of genes related to thyroid hormones’ synthesis and metabolism [1]. Direct harmful effects of acute and chronic exposure to cyanotoxins on the hypothalamic–pituitary–thyroid (HPT) axis may lead to hypothyroidism [16][17].

Individual characteristics such as age, lifestyle, gender, pregnancy, and certain diseases, such as allergic rhinitis, prolactinoma, and subacute thyroiditis, may serve as an important predisposition or triggers for TH [7][8]. Current treatment of TH in hypothyroid subjects includes replacement monotherapy with levothyroxine, which greatly reduces relapses of the disease and slows down the progression of thyroid damage. However, a proportion of the patients continue to experience various symptoms and deteriorating overall quality of life. Unfortunately, there are limited data on any effective concomitant treatment other than levothyroxine, which by itself does not target the autoimmune processes related to disease severity. It is already known that the diet and lifestyle of patients with TH can play a key role in the management of disease episodes, which necessitates an in-depth study of complex external and internal factors. Intensive research shows that many dietary supplements have the potential to positively affect TH symptomatology due to their anti-inflammatory and antidepressant activity, thus improving the overall sense of well-being. Among the most attractive candidates which may be able to influence the severity of clinical symptoms and improve thyroid function are vitamins from the groups A, B, C, and D, fatty acids, antioxidants, phytochemicals, but also the indole-amine melatonin [4][10].

The interest in dietary vitamin D and melatonin is based on research findings of their physiological role as regulators of the production of inflammatory cytokines and prostaglandins. The controlled dietary supplementation of vitamin D and melatonin might represent an essential strategy for treating TH via their molecular mechanisms on

the cellular level. Data suggest that appropriate nutritional protocols may help to decrease the chronic inflammation in the thyroid gland, other tissues, and organs, as well as to suppress or stop the thyroid gland degradation and thus improve patients' quality of life [4][11].

2. Anti-Inflammatory Nutrients

An exponentially growing number of papers are focused on anti-inflammatory foods and their impact on health. Anti-inflammatory nutrients are those nutrients that can alter the expression of the inflammatory genes. Therefore, they are employed in different nutritional regimens to reduce inflammation and re-establish hormonal balance [18].

Furthermore, implementing these nutrients in the diet can help to maintain good nutrition while silencing inflammation. Therefore, they are considered as a novel molecular cutting-edge approach.

3. Adaptive Responses Involved in the Control of Immune Reactions

Melatonin has been investigated in the therapy of several autoimmune diseases, including systemic lupus erythematosus, MS, type 1 diabetes mellitus, rheumatoid arthritis, and inflammatory bowel disease, with controversial results. However, its impact in autoimmune thyroid diseases (AITD), including Graves' disease (GD) and TH, has been examined in rare cases. For example, a recent study investigated the possible associations of single-nucleotide polymorphisms (SNPs) of melatonin receptor type 1A (MTNR1A) and 1B (MTNR1B) with AITD in an ethnic Chinese population.

Melatonin was shown to regulate mucosal immunity and protect against gut inflammation, at least in ulcerative colitis, a chronic inflammatory disease of the colon. Nevertheless, its role in response to LPS remains controversial [19]. The rise in LPS levels expressed by the gut microbiota increases the blood LPS through gut inflammation. LPS is recognized by LPS-binding protein (LBP) in the serum, which brings the LPS to the surface of various cells such as macrophages and endothelial cells to form a complex with CD14, a receptor molecule for LPS [20]. Providing a comprehensive research of environmental and existential factors with an impact on MS, the researchers use a mechanistic approach to propose a new pathway leading to neuroinflammation and MS by including different factors such as latitude, sunlight, vitamin D, melanopsin, intestinal calcium, pineal gland, gut stasis, gut endotoxins (LPS), and CD14/TLR4 [19]. They proposed a leading role of LPS produced by gut microbiota for the etiopathogenesis of MS by generating neuroinflammation and deterioration of melatonin synthesis [19]. If such a pathway can be applicable to TH and other autoimmune disorders remains to be explored.

4. Beneficial Effects of Vitamin D and Melatonin as Antioxidants

Melatonin has several biological functions, including control of circadian and seasonal rhythms, ROS scavenging, influence on puberty, etc. However, the relationship between melatonin and the HPT axis remains controversial [21]. For example, one animal study showed that TSH was higher in the melatonin-treated group than the control group. At the same time, there was no significant difference in peripheral thyroid function. In contrast, another study demonstrated that melatonin could inhibit TSH secretion and directly inhibit the secretion of T4 [21].

In regard to thyroid gland function, research has focused mostly on a specific feature of melatonin—its potent antioxidant activity. Antioxidants remove potentially damaging reactive oxygen species (ROS) generated in the cells during their life. ROS are essential and trigger the so-called oxidative reactions, which when in excess can cause damage to macromolecules, thus violating their proper functioning [22]. In the thyroid gland, ROS are necessary for completing the synthesis of thyroid hormones. Some research showed that parafollicular cells of the thyroid gland which secrete calcitonin are capable of serotonin and melatonin production, and that this is influenced locally by TSH. It seems that melatonin and TSH balance themselves out, but there is no convincing evidence showing this. It is generally accepted that alterations in the circadian pattern of melatonin secretion are indicative of health problems and distress. Melatonin may block thyroid cell proliferation and thyroid hormone synthesis [21], and its use as a dietary supplement has to be controlled in regard to thyroid function to prevent compromised disease management.

Melatonin is widely accessible over the counter as a sleep aid. According to the National Institutes of Health, short-term use of melatonin supplements appears safe. Still, very little research exists on the long-term effects. A study from 2001 looked at the impact of melatonin on females with hypothyroidism, 36 of whom were perimenopausal, and 18 were postmenopausal [23]. The study revealed that the group taking melatonin at bed time showed significantly higher thyroid hormone levels than the placebo group after 3–6 months, and the participants experienced improvement of mood and overall alertness. Low melatonin levels due to aging may be connected with low levels of thyroid hormones, explaining why taking a melatonin supplement also improved TSH levels [23]. Unfortunately, large-scale trials to confirm that melatonin is safe and effective for people with hypothyroidism are still lacking.

5. Diets Aimed at Liver Detoxication and Cleansing

The nutritional management of TH includes liver detoxification and heavy metal cleansing. Promising studies report the detoxification effect of diets, often combined with an exercise plan, that additionally lead to weight loss and improved health [4]. Detoxification or detoxication is the physiological removal of toxic substances from the human body, which is carried out mainly by the liver, kidneys, intestines, lungs, lymphatic system, and the skin. However, when organs and systems are compromised, toxins and other impurities are not properly excreted, and the body is adversely affected by inflammation and the autoimmune response. The accumulation of heavy metals in the human body leads to severe injury to various organs, specifically the nervous, respiratory, endocrine, gastrointestinal, and reproductive systems [10][24]. Many foods were found to protect the human body via anti-inflammatory, antioxidative, anti-cancer, antibacterial, and other properties due to their detoxicating and cleansing effects on the liver, kidney, blood, gut, and other organs and tissues.

6. Ecological Dietary Regimen for TH

Malnutrition risk in TH patients has not been adequately explored, and no precise conclusions may be drawn [25]. Currently, there is no convincing evidence for an effective clinical indication of dietary supplementation with vitamin D and melatonin as a complementary treatment against TH symptomatology. It is important to note that melatonin modulates the immune system by suppressing proinflammatory molecules in a dose-dependent fashion due to its physiological circadian pattern. The differences in its function can come from the dose when taken as a medication, 10 or 100 times higher than the levels produced generally in the healthy body [26]. The timing of assessment and dose–response dynamics may be essential aspects to consider when investigating the effects of vitamin D on mood and sleep due to potential vitamin D-induced moderations in serotonin and melatonin synthesis.

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