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The Effect of Selenium Replacement Therapy on Children and Adolescents with Autoimmune Thyroiditis

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Abstract

Back ground: Autoimmune diseases are increasing in prevalence due to the penetration of negative environmental conditions and endocrine disruptors into daily life. With the development of etiological factors there is also an uprise in childhood autoimmune thyroid diseases. Selenium (Se) is an essential element to the human body that helps regulate anti-inflammatory, immune-regulatory, antioxidant and endocrine functions both as a structural component and as a cofactor. It joins the molecular formation of the enzyme glutathione peroxidase which plays an active role in thyroid metabolism.

Aim: To investigate the role of selenium deficiency in the etiology of autoimmune thy-roiditis and the effect of selenium replacement therapy especially in early stage diseases.

Study design: Case control study

Materials and Method: The studies included were 54 subclinical hypothyroidism cases. After the detailed history of the all cases, anthropometric measurements, physical examination, biochemistry, hormonal (thyroid hormone, antibodies, spot iodine in urine, serum selenium levels…) bone age and thyroid ultrasonography were performed. Subclinical hypothyroidism diagnoses were made for cases with elevated TSH levels, normal sT4 levels (prepubertal TSH: 0.6-5.5 mIU/L, sT4: 0.8-2.2 ng/mL; pubertal TSH: 0.5-4.8 mIU/L, ST4: 0.8-2.3 ng/mL). After determining the etiology of subclinical hypothyroidism cases were categorized into two groups; as the first group autoimmune thyroiditis (n: 28) and second group without autoimmune thyroiditis (n: 26). Thyroid function tests were analyzed chemiluminescence immunoassay, Se levels was analyzed atomic absorption spectrophotometer method. Cases with Se deficiency were given oral selenium replacement therapy (50 mcg/day).

Results: All of the cases, %61.1 were girls and %38.9 was boys; %53.1 was prepubertal and %46.9 was pubertal. A total of %18.5 cases were obese, %9.25 was overweight, and %18.5 cases were malnourished. Mean selenium level was 64.4±14.19 g/dl in Group I and 100.7±20.1 g/dl in Group II, there was a remarkably significant difference between the two groups. Group I had notably low Se levels in contrast to high TSH, anti-TG and anti-TPO levels. There was a negative correlation between Se deficiency and elevated anti-TPO levels. Group II showed positive correlation between serum Se and fT4. Statistically significant regression was observed in anti-TG (p: 0.006) and anti-TPO (p: 0.00) levels 3 months after oral selenium replacement therapy.

Conclusion: Our study suggests that after oral Se treatment, progression of autoimmunity were diminished. Hence that selenium replacement might be useful in childhood and adolescents especially (with low titer antibody elevation) early stages autoimmune thyroiditis.

Introduction

Selenium (Se) is an essential element vital for human life [1]. It contributes to the formation of many enzymes as a cofactor and plays a major role in various biological path-ways such as thyroid hormone mechanisms, antioxidant enzyme defense, and immune system regulation [2, 3].

Proteins carrying Se in their active zones are defined as selenoproteins and are dependent on Se to function properly. The human body possesses approximately 100 selenopro-teins and 30 of them have been defined [4]. The most prominent of these are the enzymes glutathione peroxidase (Gpx), Thioredoxin reductase (TRS), and iodothyronine deiodinase (ID) [5]. Many selenoproteins contribute to specific biochemical reactions other than antioxidant defense such as iodothyronine deiodinase (DIOs) which has a major role in thyroid hormone synthesis, glutathione peroxidase-4 (Gpx4) which contributes to spermatogenesis and selenophosphate synthetase 2 (SPS2) which plays a part in selenoprotein synthesis. Selenoprotein P (SelP) and glutathione peroxidase-3 (Gpx3) activity can also be used as an indicator for plasma Se levels [6].

Selenium's crucial role in thyroid gland functions was first brought to the agenda with the definition of myxedematous endemic cretinism in the Democratic Republic of the Congo; a medical condition characterized by iodine deficiency, hypothyroidism, myxedema, developmental delay, and cognitive impairment [7-8].

Iodothyronine deiodinase ±-1, which carries Se, has been shown as the primarily responsible enzyme for peripheral T4-T3 transformation [5]. Some studies have interestingly detected ID-1 inhibition in rats that were given diets lacking Se [9]. Thyroid gland cells are protected from the oxidative stress of H202, which is essential for iodination during

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hormone synthesis, by the antioxidant effects of the selenoprotein-carrying enzyme Gpx [10]. Selenium deficiency has been shown to cause a decrease in T4-T3 transformation, thus leading to an increased T4/T3 ratio in tissues with ID-1 and ID-2 [9]. Selenium deficiency prevents thyroid peroxidase (TPO) and Gpx from functioning normally, causing inefficient protection against free radicals, cell injury, and the eventual autoimmune destruction of the gland itself [11]. Selenium may suppress the secretion of cytokines and increase CD4+/CD25 FOXP3 and regulatory T cell activity via various selenoproteins and prevent apoptosis and thyroiditis. Selenium replacement therapy may improve the level of inflammation for patients suffering from autoimmune thyroiditis [12].

Selenium deficiency is not common among childhood and adolescents that consume a regular diet because meat, seafood, food grain, and dairy products contain Se. Clinical findings such as darkened hair colour, white nails, and cardiac dysfunction can be signs of Se deficiency [13]. While Se toxicity (selenosis) may be acute or chronic it is not a common medical presentation among humans. Selenosis symptoms may be as follows: nausea, emesis, abdominal pain, diarrhea, brittle nails, and peripheral neuropathy [10]. Selenium can be found in food obtained from animal (selenocysteine) or plant (selenomethionine) sources. Dietary Se is primarily selenomethionine (50%) [14]. Up to half of Se is lost when food is cooked however this can be reduced by cooking at low pH [15]. Scientific data recommends Se replacement therapy for pediatric patients whose Se levels are below 4g/dL [16]. The minimum uptake required to prevent deficiency-related symptoms is 10 μg/day; the tolerable maximum uptake is 400 μg/day [17].

Materials and Method

Study design and protocol

After getting approval from the ethics committee of Ufuk University (research file number: 12024861-48), the study started. For the patients included in the study, consent forms were obtained from the parents for the 2-8 year-olds, and for the 8-18 year-olds consent forms were obtained from the child and a parent.

The study population consisted of 54 pediatric cases who applied to the pediatric endocrinology department for various medical conditions and were diagnosed with subclinical hypothyroidism. Findings obtained from detailed medical histories, anthropometric evaluations, physical examinations, and thyroid examinations (WHO UNICEF) were analyzed. Thyroid function tests, thyroid autoantibodies (anti-TG, anti-TPO), spot iodine in urine, serum Se levels, and thyroid USG were evaluated. Thyroid function tests and thyroid autoantibody levels were analyzed in IU/mL via chemiluminescence immunoassay (CLIA) whereas serum Se levels were analyzed in mcg/L via atomic absorption spectrophotometer. Thyroid USG was performed with the use of high-resolution 7.5 MHz probes.

Subclinical hypothyroidism diagnoses were made for cases with elevated TSH levels and normal sT4 levels (prepubertal TSH: 0.6-5.5 mIU/L, sT4: 0.8-2.2 ng/mL; pubertal TSH: 0.5-4.8 mIU/L, ST4: 0.8-2.3 ng/mL) (28). Autoimmune thyroid disease (AITD) diagnoses were made with ultrasonographic findings of heterogenous echotexture accompanied by elevated titers of thyroid antibodies Anti-TPO (N: 0-5.61 IU/mL) and Anti-TG (N:0-4.11 IU/mL). The patient group included 28 cases that had thyroid dysfunction and were diagnosed with AITD (Group 1), while the control group included 26 cases that had thyroid dysfunction but were not diagnosed with AITD (Group 2). Selenium deficiency was determined according to serum Se levels by age for the Turkish pediatric population [18]. The normal serum selenium levels by age for the Turkish pediatric population [18]. All cases with Se deficiency were given 50 mcg/day of Se oral replacement therapy before follow-up. Patients included in the study showed normal ranged complete blood count, folate, vitamin B12, ferritin, and vitamin D results. Patients with dyslipidemia, malignancies, other Endocrinologica problems, and chronic diseases were excluded.

Statistical analyses

All statistical analyses were performed using the SPSS software for Windows V16.0. All data are expressed as mean ± standard deviation of 95% C.I. For each continuous variable, normality was evaluated using the Shapiro-Wilk test. The Mann-Whitney U test was performed for non-normally distributed data and Student's t-test was performed for normally distributed data. The patients' thyroid function test results before and after selenium replacement treatment were analyzed using the paired t-test or Wilcoxon test. A p-value below 0.05 was considered statistically significant.

Results

A total of 54 cases, 33 girls (61.1%) and 21 boys (38.9%), aged 2-17 years of age (Total mean: 9.87±4.1 yr, Group I mean: 10.53±3.45 yr, Group II mean: 9.52±4.6 yr) were included in the study. 28 cases were (Group I) determined to have Se deficiency and elevated thyroid autoantibody levels. the number of cases for groups I and II.)

In all of the cases, 26 (53.1%) were prepubertal and 23 (46.9%) were pubertal. The patient group (Group I) consisted of 18 girls (64.3%) and 10 boys (35.7%); 10 were prepubertal (41.7%) and 14 were pubertal (58.3%). The control group (Group II) consisted of 15 girls (57.7%) and 11 boys (42.3%); 16 cases were prepubertal (64%) and 9 (36%) were pubertal. There was no significant difference between sex and puberty parameters according to the Chi-square test. The gender, chronological age, bone age, and anthropometric features (Tanner stages, BMI P...) of all cases.

Patients were grouped according to their body mass index (BMI) as normal (5-85 percentile), obese (>95 percentile), overweight (85-95 percentile), and malnourished (<5 percentile). A total of 10 cases (18.5%) were obese, 5 cases (9.25%) were overweight, and 10 cases were malnourished (18.5%). In the patient group, 8 children (28.57%) were obese, 2 children (7.1%) were overweight and 5 children were malnourished (17.85%). In the control group 2 children (7.6%) were obese, 3 children (11.5%) were overweight and 5 children (19.23%) were malnourished.

Selenium deficiency was accompanied by elevated anti-TG and anti-TPO levels in group I (51.8%). Selenium levels were normal by age for 26 patients in group II (48.2%) with negative thyroid antibodies. the mean levels of fT4, TSH, anti-TG, anti-TPO, spot iodine in urine, and serum Se levels. the group's selenium level distribution. The Mann-Whitney U test showed a remarkably significant difference between the two groups for Se levels (p: <0.001), anti-TG (p: <0.009), anti-TPO (p: <0.001), and TSH levels (p: <0.012). Group I, had notably low Se levels in contrast to high TSH, anti-TG, and anti-TPO levels. The Spearmen's correlation showed a negative correlation (-0.762 p: 0.010) between Se deficiency and elevated anti-TPO levels. The control group showed a positive correlation (0.455 p: 0.044) between serum Se and fT4. Statistically, significant regression was observed in anti-TG (p: 0.006) and anti-TPO (p: 0.00) levels 3 months after oral selenium replacement therapy (50 mcg/day). The thyroid function test results of Group I

before and after selenium replacement therapy.

Discussion

Studies regarding the impact Se has on autoimmunity have prevailed over the past years. Selenium initially drew attention with its anti-carcinogenic effects. Scientific literature re-views show an increase in the number of Se studies with the pediatric population but data is not yet sufficient. Selenium is an essential element to the human body that helps regulate anti-inflammatory, immune-regulatory, antioxidant, and endocrine functions both as a structural component and as a cofactor. Se deficiency has been proven to lead to thyroid destruction in experimental studies.

Zagrodzki et al. compared the Se and iodine levels of children aged 7-16 years old from Poland's southeastern endemic iodine-deficient region with their peers from other regions and found that serum Se levels and plasma GPx activity were much lower in the study group than the control group. There was a significant statistical difference between male and female cases of the study group for Se deficiency and sT4 and TSH, indicating that Se and iodine deficiencies were affected by sex [19]. There was no significant statistical difference based on sex between the two groups in our study.

In a study conducted by Çelik et al. with children aged 6-12 years old from our country's endemic iodine-deficient region analyzed whether or not iodine deficiency was accompanied by Se, zinc, copper, or molybdenum deficiency via urine samples. Selenium and iodine deficiency was shown to be in correlation with iodine deficiency. It was emphasized that Se and zinc deficiencies should be taken into consideration for cases of iodine deficiencies in regions where endemic goiter is prevalent [20]. We believe that patients from non-endemic goiter regions who visit pediatric endocrinology outpatient clinics should also be specially screened for parameters such as urine iodine, serum Se and zinc levels, and bone age.

Recent studies have tried to elucidate the role Se replacement therapy has in the physiology of Hashimoto's thyroiditis and the formation of thyroid gland enzymes [21]. GPx, which protects the thyroid gland from oxidative stress; thyroid peroxidase, which is critical for thyroid hormone synthesis; and ID, which is necessary for T3 synthesis, are all enzymes that are defined as selenoproteins. It is assumed that Se replacement therapy may be beneficial for cases with both Hashimoto's thyroiditis and Se deficiency by lowering antibody levels and the required dosage of levothyroxine therapy. [22] Biological studies have shown a possible connection between iodine deficiency-related hypothyroidism and Se deficiency [23]. Studies, where urine iodine and serum Se levels were analyzed, have shown that women and men with goiters suffer from Se deficiency much more than those who do not have goiters [24]. A study by Keshteli et al. with 2331 Iranian schools did not show a correlation between urine iodine concentration and Se levels. However, goiter was still highly prevalent among these patients. Girls and boys with goiters showed lower Se levels as opposed to their peers who did not. In addition, the need for studies on the deficiency of micronutrients and the role of goitrogens was emphasized [25]. In our study, we could not determine a significant correlation between urine iodine levels and serum Se levels. New studies with greater pediatric populations are required.

A study carried out by Etani et al. in Japan with children receiving parenteral or enteral nutritional support stated that patients followed up due to severe intestinal dysfunction, potential bowel malabsorption, emesis or diarrhea may need to be screened for Se deficiency caused by the intestinal loss of Se. It was recommended that patients receiving parenteral or enteral nutrition support be analyzed for serum Se levels every 2-3 months. It was stated that these patients, who are unable to follow an ordinary diet, showed clinical recovery after receiving a 12-month diet consisting of supplements for Se and trace elements or rice and fish soup. A selenium supplement dosage of 150-175 g/week for children and 350 g/week for adolescents was considered to enough elevate Se levels efficiently [13]. Currently, there are no studies from our country that analyze the effects of Se-rich food supplementation on children with Se deficiency. Kyrgios et al. studied the effects of high-dose organic Se (200 ug l-selenomethionine) on thyroid antibody titers among AITD-diagnosed children and adolescents. The study con-clouded that the Se group showed a much more statistical significance in lowering anti-TG levels in comparison to the placebo group [26]. In our study, a significant improvement was found in thyroid autoantibody levels after 50 mcg/day of oral selenium replacement therapy in the case group.

The data from our study points out that Se replacement may have positive effects, espe-cially in the early stages of AITD (with low titer antibody elevation). This study shows the necessity for Se analysis among pediatric AITD cases. Therefore we believe that Se levels should be screened after oral replacement therapy. Both our studies and scientific literature reviews show the impact of Se deficiency on AITD and other autoimmune diseases [27]. We believe it is essential to study and elucidate the effects that Se and other trace elements may have on pediatric AITD cases.

Pediatric Se levels must be evaluated according to the age-based reference range set down by the respective country the study was conducted in. Patients diagnosed with selenium deficiency should receive supplement therapy suitable for their age and benefit from Se's anti-inflammatory effects on stopping the progression of autoimmune diseases in their early stages. There is currently not enough scientific data to support the safety of the long-term and high-dose use of oral Se supplement therapy. Therefore monitoring serum Se levels is crucial for preventing toxicity.

Data sharing statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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References

1. Tajaddini MH, Keikha M, Razzazzadeh A, Kelishadi R (2015) A systematic review on the association of serum selenium and metabolic syndrome. J Res Med Sci 20: 782-789.
2. Iglesias P, Selgas R, Romero S, Díez JJ (2013) Selenium and kidney disease. J Nephrol 26: 266-272.
3. Roman M, Jitaru P, Barbante C (2014) Selenium biochemistry and its role for human health. Metallomics 6: 25-54.
4. Brown KM, Arthur JR (2001) Selenium, selenoproteins and human health: a review. Public Health Nutr 4: 593-599.
5. Beckett GJ, Arthur JR (2005) Selenium and endocrine systems . J Endocrinol 184: 455-465.
6. Goyens P, Golstein J, Nsombola B, Vis H, Dumont JE (1987) Selenium deficiency as a possible factor in the pathogenesis of myxoedematous endemic cretinism. Acta Endocrinol (Copenh) 114: 497-502.
7. Rayman MP (2008) Food-chain selenium and human health: emphasis on intake. Br J Nutr 100: 254-268.

8. Muntau AC, Streiter M, Kappler M (2002) Age-related reference values for serum selenium concentrations in infants and children. Clin Chem 48: 555-560.
9. Xia Y, Hill KE, Li P (2010) Optimization of selenoprotein P and other plasma selenium biomarkers for the assessment of the selenium nutritional requirement: a placebo-controlled, double-blind study of selenomethionine supplementation in selenium-deficient Chinese subjects. Am J Clin Nutr 92: 525-531.
10. Ventura M, Melo M, Carrilho F (2017) Selenium and Thyroid Disease: From Pathophysiology to Treatment. Int J Endocrinol 2017:1297658.
11. Mueller AS, Mueller K, Wolf NM, Pallauf J (2009) Selenium and diabetes: an enigma. Free Radic Res 43: 1029-1059.
12. Capalbo D, Alfano S, Polizzi M (2020) Cognitive Function in Children with Idiopathic Subclinical Hypothyroidism: Effects of 2 Years of Levothyroxine Therapy. J Clin Endocrinol Metab 105: 46.
13. Duntas LH, Benvenga S (2015) Selenium: an element for life. Endocrine 48: 756-775.
14. Giammanco M, Leto G (2019) Selenium and Autoimmune Thyroiditis. EC Nutrition 5: 449-450.
15. Turker O, Kumanlioglu K, Karapolat I, Dogan I (2006) Selenium treatment in autoimmune thyroiditis: 9-month follow-up with variable doses. J Endocrinol 190: 151-156.
16. Etani Y, Nishimoto Y, Kawamoto K(2014) Selenium deficiency in children and adolescents nourished by parenteral nutrition and/or selenium-deficient enteral formula. J Trace Elem Med Biol 28: 409-413.
17. Boosalis MG (2008) The role of selenium in chronic disease. Nutr Clin Pract 23: 152-160.
18. Hincal F, Yetgin S, Ataçeri N (1989) Selenium status in Turkey. I. Serum selenium levels in infants and children in Ankara. Biol Trace Elem Res 20: 161-167.
19. Zagrodzki P, Szmigiel H, Ratajczak R, Szybinski Z, Zachwieja Z(2000) The role of selenium in iodine metabolism in children with goiter. Environ Health Perspect 108: 67-71.
20. Çelik T, Savaş N, Kurtoğlu S(2014) Iodine, copper, zinc, selenium and molybdenum levels in children aged between 6 and 12 years in the rural area with iodine deficiency and in the city center without iodine deficiency in Hatay. Turk Pediatri Ars 49: 111-116.
21. Toulis KA, Anastasilakis AD, Tzellos TG, Goulis DG, Kouvelas D(2010) Selenium supplementation in the treatment of Hashimoto's thyroiditis: a systematic review and a meta-analysis. Thyroid 20: 1163-1173.
22. Van Zuuren EJ, Albusta AY, Fedorowicz Z, Carter B, Pijl H (2014) Selenium Supplementation for Hashimoto's Thyroiditis: Summary of a Cochrane Systematic Review. Eur Thyroid J 3: 25-31.
23. Kandhro GA, Kazi TG, Sirajuddin (2011) Effects of selenium supplementation on iodine and thyroid hormone status in a selected population with goitre in Pakistan. Clin Lab 57: 575-585.
24. Thomson CD, Campbell JM, Miller J, Skeaff SA, Livingstone V (2009) Selenium and iodine supplementation: effect on thyroid function of older New Zealanders. Am J Clin Nutr 90: 1038-1046.
25. Keshteli AH, Hashemipour M, Siavash M, Amini M(2009) Selenium deficiency as a possible contributor of goiter in schoolchildren of Isfahan, Iran. Biol Trace Elem Res 129: 70-77.
26. Kyrgios I, Giza S, Kotanidou EP (2019) l-selenomethionine supplementation in children and adolescents with autoimmune thyroiditis: A randomized double-blind placebo-controlled clinical trial. J Clin Pharm Ther 44: 102-108.
27. Hurst R, Armah CN, Dainty JR (2010) Establishing optimal selenium status: results of a randomized, double-blind, placebo-controlled trial. Am J Clin Nutr 91: 923-931.