DOI: 10.5455/msm.2019.31.115-118
Received: April 19 2019; Accepted: June 11, 2019

ORIGINAL PAPER Mater Sociomed. 2019 Jun; 31(2): 115-118

Evaluation of Thyroid Hormone Status and Bone Density Ratio in Euthyroid Postmenopausal Women in Early and Late Stage of Bone Loss

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ABSTRACT

Introduction: Osteoporosis is a consequence of reduction in bone mass and disorders of bone structure, which makes the bones prone to fractures . Physiological variations of thyroid-stimulating hormone (TSH) may be an early indicator of the predisposing basis of the emergence of osteoporosis. Aim: To evaluate the thyroid hormone status and bone density ratio in euthyroid postmenopausal women in early and late stage of bone loss. Methods: The research is an observational, intersected, controlled study involving postmenopausal women admitted to the Clinic for Nuclear medicine and endocrinology of the Clinical Center University of Sarajevo (CCUS). The study included a total of 120 postmenopausal subjects divided into two groups. First group included 60 postmenopausal patients with osteoporosis, 30 of them were at the early stage of postmenopause, and 30 were in the late postmenopausal phase. The second group consisted of 60 postmenopausal patients with preserved bone mass, 30 of which were in the early stage of postmenopause and 30 in the late postmenopausal phase. For all patients included in the study follicle-stimulating hormone (FSH), TSH, free thyroxine (FT4), free triiodothyronine (FT3) were analyzed. Results: The mean duration of the postmenopausal period was statistically significantly higher in the group of women with osteoporosis (11.4 ± 1.1 years). The mean values of FSH were statistically significantly higher in the group of women with osteoporosis (54.0 ± 2.6 IU / L). The mean level of TSH and FT3 did not statistically significantly differ in the group of women with osteoporosis compared to the control group of women. The mean FT4 level in women with osteoporosis was statistically significantly lower (14.7 ± 0.29 pmol / L) compared to the control group of women (15.95 ± 0.3 pmol / L) (p = 0.004). Conclusion: In our examined group, the FT4 patient (mean) was significantly lower in the serum of women with osteoporosis compared to subjects with preserved bone mass. It would be most effective to recognize risk factors in order to influence them on time, and to alleviate and slow down the consequences of osteoporosis. One of these possible factors is the hormonal status of the thyroid gland, that is, TSH whose physiological variations may be an early indicator of the predisposing basis for the emergence of osteoporosis. The frequency and prevalence of these medical problems require additional research, and it is also a great challenge to understand the effects of thyroid hormone on bone tissue.

Keywords: thyroid gland, thyroid hormones, osteoporosis.

1. INTRODUCTION

Osteoporosis is a consequence of reduction in bone mass and disorders of bone structure, which makes the bones prone to fractures (1). This is a systemic skeletal disease which occurs when the amount of bone decomposed in the unit of time is greater than the amount of newly born bone (1). The incidence of osteoporosis is constantly increasing. It is estimated that about 30% of women in menopause are affected by osteoporosis in the United States, and about 162,000 women are affected in Bosnia and

Herzegovina (2). The disease is more present because of the modern way of life, but also due to prolonged life (3, 4). The effect of pituitary gland hormones is vital in achieving and maintaining bone mass, since each of the hormones directly or indirectly affect the bone mass. The most important role of gonadotrophic hormones, and the loss of estrogen at a later generative age and menopause leads to bone resorption disorders caused by increased secretion of osteoclastogenic cytokines and consequent rapid loss of bone mass.

Osteoporosis and thyroid disorders are common diseases in the elderly, and it is known that increased thyroid function may be the cause of osteoporosis (5). It is thought that about 10% of women over 50 years have a thyroid gland disorder and 30% have osteoporosis. For now, the relation of thyroid hormone status and osteoporosis, or osteoporosis and the replacement hormone therapy in the conditions of its reduced function, have not been sufficiently investigated. (1, 5) The frequency and prevalence of these medical problems require additional research. It would be most effective to recognize risk factors in order to influence them on time, and to alleviate and slow down the consequences of osteoporosis. Physiological variations of thyroid-stimulating hormone (TSH) may be an early indicator of the predisposing basis of the emergence of osteoporosis. (6)

2. AIM

Aim of article was to evaluate the thyroid hormone status and bone density ratio in euthyroid postmenopausal women in early and late stage of bone loss

3. METHODS

The research is an observational, cross-sectional, controlled study involving postmenopausal women admitted to the Clinic for Nuclear medicine and endocrinology of the Clinical Center University of Sarajevo (CCUS). The research was approved by the Ethics Committee CCUS and patients gave informed consent.

The study included a total of 120 postmenopausal subjects divided into two groups. First group included 60 postmenopausal patients with osteoporosis, 30 of them were at the early stage of postmenopause, and 30 were in the late postmenopausal phase. The second group consisted of 60 postmenopausal patients with preserved bone mass, 30 of which were in the early stage of postmenopause and 30 in the late postmenopausal phase. In our study, an early stage of bone loss (early postmenopausal phase) includes a period of up to five years after the last menstrual bleeding, while the late bone loss phase (late postmenopausal phase) includes a period of five years after the last menstrual bleeding.

All patients included in the study were sent to the Clinic for Nuclear medicine and endocrinology with suspected osteoporosis. The study excluded all patients with diseases and conditions that can lead to increased bone tissue degradation like endocrine disorders, rheumatoid arthritis and long-term immobilization. For all patients included in the study follicle-stimulating hormone (FSH), TSH, free thyroxine (FT4), free triiodothyronine (FT3) were analyzed. Blood samples for laboratory analysis were taken from the cubital vein into the gel tubes according to the standard procedure, in the morning. The results obtained were analyzed by a t-test or corresponding nonparametric tests (Mann-Whitney test), if irregular distribution of variables was found. The correlation degree was tested using the Pearson or Spearman correlation coefficient. The values of $p < 0.05$ were considered statistically significant.

4. RESULTS

The average age of postmenopausal women included in the study was 58.2 ± 0.7 years. The average duration of menopause was 9.8 ± 0.72 years, while the average duration of the reproductive period was 33.39 ± 0.45 years. The mean values of FSH in women included in the study were 48.2 ± 1.87 IU / L.

Analysis of the general characteristics of women with osteoporosis in relation to women with preserved bone mass (control group) in postmenopause, no significant difference was found between the average age, the average period of the last menstrual period, or the duration of the reproductive period between the group with osteoporosis compared to the control group (Table 1).

	Osteoporosis group (N=60) (mean + SD)	Control group (N=60) (mean + SD)	p value
Age	58,70±1,0	57,76±1,0	NS
Body weight (kg)	72,4±1,3	81,8±1,3	<0,001
Body height (cm)	164,2±0,74	165,4±0,72	NS

Table 1. General characteristics of postmenopausal women in relation to the presence of osteoporosis. NS–non significant value

The mean duration of the postmenopausal period was statistically significantly higher in the group of women with osteoporosis (11.4 ± 1.1 years) compared to the group of women in the control group (8.5 ± 0.9 years) ($p = 0.043$). The mean values of FSH were statistically significantly higher in the group of women with osteoporosis (54.0 ± 2.6 IU / L) compared to the group of women in the control group (43.2 ± 2.5 IU / L) ($p = 0.004$). The mean level of TSH and FT3 did not statistically significantly differ in the group of women with osteoporosis compared to the control group of women (Table 2). However, the mean FT4 level in women with osteoporosis was statistically significantly lower (14.7 ± 0.29 pmol / L) compared to the control group of women (15.95 ± 0.3 pmol / L) ($p = 0.004$) (Table 2).

The mean level of TSH and FT3 did not statistically significantly differ in the group of women at an early age compared to the group of women in the late menopause (Table 3). However, the mean level of FT4 in the serum of

	Osteoporosis group (N=60) (mean + SD)	Control group (N=60) (mean + SD)	p value
TSH (mU/L)	3,8±0,55	3,02±0,3	NS
FT4 (pmol/L)	14,7±0,29	15,95±0,3	0,004
FT3 (pmol/L)	5,26±0,43	5,1±0,09	NS

Table 2. Thyroid hormone levels in postmenopausal women in relation to the presence of osteoporosis. NS–non significant value

women at the early stage of the postmenopausal period was statistically significantly lower (15.1 ± 0.28 pmol / L) relative to the group of women during late postmenopausal

	Osteoporosis group (N=60) (mean + SD)	Control group (N=60) (mean + SD)	p value
TSH (mU/L)	2,6±0,21	2,37±0,19	NS
FT4 (pmol/L)	15,1±0,28	16,0±0,3	0,029
FT3 (pmol/L)	5,0±0,1	5,5±0,43	NS

Table 3. Thyroid hormone levels in postmenopausal women in relation to postmenopausal period duration. NS–non significant value

(16.0 ± 0.3 pmol / L) (p = 0.028) (Table 3).

5. DISCUSSION

Osteoporosis is an age-old illness characterized by reduced bone mass and loss of bone microarchitecture with a significantly increased risk of fractures and disabilities, which, given the demographic trends in developed countries, is a very important public health problem. It is a "silent epidemic" because the number of patients is constantly increasing and most patients do not have symptoms until the onset of the first bone fracture (1). The costs of reviewing and treating women with postmenopausal osteoporosis are increasing worldwide.

Because of all of the above, in the world, many studies have been under way to identify a link between factors that would indicate in advance the existence of a predisposition to the emergence of osteoporosis or to the disease itself while it is still not clinically manifested, which could be preventive. It would be most effective to recognize risk factors in order to influence them on time, and to alleviate and slow down the disease and prevent the consequences of osteoporosis (5.6). The issue of clinical research is whether substitution treatment of thyroid hormones in the conditions of its reduced function (hypothyroidism) leads to undesirable effects on mineral bone density (7). The links between thyroid gland hormones, which are within physiological limits, and bone density are controversial, and existing studies are controversial, which is thought to be the consequence of a small number of patients and scant information. Kim et al. have proven that lower, but also normal TSH values are associated with low mineral bone density in healthy euthyroid women (8). The general characteristics of women in menopause in our study (mean age, duration of menopause, average BMI, average FSH) were in line with the general characteristics of women in postmenopausal other researchers (9). In our study, the average levels of TSH and FT3 did not differ significantly in the patient group with osteoporosis and the group of patients with preserved bone mass whereas the mean level of FT4 was statistically significantly lower in serum women with osteoporosis compared to women in the control group. Also, the average levels of TSH and FT3 did not significantly differ in the group of women at an early age compared to the late postmenopausal phase, while FT4 in the group of women who were in the early postmenopausal phase was statistically significantly lower than those who were in the late postmenopausal phase. Unlike our results, Garton et al. in their study stated that FT3 can regulate bone resorption (10). Williams et al. came to similar result and claimed that FT3 has a direct impact on bone remodeling and mineral bone density (11), which corresponds to results of Murphy et al. (12). In the group of patients with osteoporosis compared to the control group no statistically significant correlation was observed between thyroid hormone levels and bone mineral density (BMD), which is in line with the research carried out by Pater and et al. and they did not find the evidence that variations in TSH values in euthyroid postmenopausal women have an impact on BMD and risk for fractures (13). The results of the study conducted by Marwah et al. showed that TSH has no effect on mineral bone density in euthyroid women (14).

6. CONCLUSION

The practical application of the results obtained in clinical practice is to set the cut-off value of hormone status of the thyroid gland, i.e. thyroid hormone (FT4, FT3), and especially serum TSH, which is a risk factor for bone loss. In our examined group, the FT4 patient (mean) was significantly lower in the serum of women with osteoporosis compared to subjects with preserved bone mass. It would be most effective to recognize risk factors in order to influence them on time, and to alleviate and slow down the consequences of osteoporosis. One of these possible factors is the hormonal status of the thyroid gland, that is, TSH whose physiological variations may be an early indicator of the predisposing basis for the emergence of osteoporosis. The frequency and prevalence of these medical problems require additional research, and it is also a great challenge to understand the effects of thyroid hormone on bone tissue.

- Author's Contribution: A.B. and A.A.H. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. A.B. had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Conflicts of interest: There are no conflicts of interest
- Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
- Financial support and sponsorship: Nil.

REFERENCE

1. Akkawi I, Zmerly H. Osteoporosis: Current Concepts. Joints. 2018;6(2):122–127.
2. Avdić D., Buljugić E. Kako spriječiti, kako liječiti osteoporozu. „Off-Set" d.o.o. Tuzla, Tuzla 2008. 35-60.
3. Fukumoto S, Matsumoto T. Recent advances in the management of osteoporosis. F1000 Res. 2017;6:625.
4. Ensrud K E, Crandall C J. Osteoporosis. Ann Intern Med. 2017;167(03):ITC17–ITC32.
5. Lee J, Lee S, Jang S, Ryu OH. Age-Related Changes in the Prevalence of Osteoporosis according to Gender and Skeletal Site: The Korea National Health and Nutrition Examination Survey 2008-2010. Endocrinol Metab (Seoul). 2013;28(3):180–191.
6. Williams GR, Bassett JHD. Thyroid diseases and bone health. J Endocrinol Invest. 2018;41(1):99–109.
7. Greenspan SL, Greenspan FS. The effect of thyroid hormone on skeletal integrity. Ann Intern Med 1999;130(9):750-8.

8. Kim DJ, Khang YH, Koh JM, Shong YK, Kim GS. Low normal TSH levels are associated with low bone mineral density in healthy postmenopausal women. Clin Endocrinol (Oxf). 2006;64(1):86-90.
9. Deniz CH, Keskin LH, Secen IE, Yegin FG, Akcay Y, Ustuner I, et al. Thyroid Dysfunction Does Not Affect the Bone Mineral Density in Postmenopausal Women. J Clin Anal Med. 2014; 5 (1): 25-8.
10. Garton M, Martin J, New S, Lee S, Loveridge N, Milne J, et al. Bone mass and metabolism in women aged 45-55. Clin Endocrinol (Oxf). 1996;44(5):563-70.
11. Williams AJ, Barnard JC, Bassett JHD, Williams GR. Thyroid hormones stimulate osteoblast differentiation but inhibit mineralization of bone nodules in vitro. Endocrine Abstracts. 2006; 11 OC55.
12. Murphy E, Williams GR. T3 rather than TSH mediates the effects of altered thyroid status on bone turnover in man. Endocrine Abstracts. 2007; 13:P328.
13. Pater A, Nowacki W, Sypniewska G. Thyroid-Stimulating Hormone Within Normal Range Does Not Affect Bone Turnover in Euthyroid Postmenopausal Women with Osteoporotic Fracture–A Preliminary Report. EJIFCC. 2011;22(4):113–117.
14. Marwaha RK, Garg MK, Tandon N, et al. Thyroid function and bone mineral density among Indian subjects. Indian J Endocrinol Metab. 2012;16(4):575–579.