BONE MINERAL DENSITY CHANGE IN RELATION TO THE PHYSIOLOGICAL VALUES OF THYROID HORMONES

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Abstract: *Physiological concentrations of thyroid hormones are necessary for skeletal development, the clinical trials indicating that euthyroid status is essential for a normal bone turnover, for a normal mineralization and for maintaining the optimal bone strength. The aim of the study was to observe the influence of the physiological values of FT4 on bone mineral density. We studied a total number of 650 patients, with and without thyroid pathology, divided into three groups and three age groups, in whom we dosed the thyroid hormones; bone mineral density was measured by the DEXA method. We analyzed the influence of FT4 on bone mineral density, we followed if there is a correlation between its physiological values and the T score independent of TSH. According to our study results and of the existing data in the literature, the idea that there is a direct relation between FT4 and the degree of bone demineralization can not be supported.*

Cuvinte cheie: *hormoni tiroidieni, tiroidectomie, densitate minerală osoasă*

Rezumat: *Concentraţiile fiziologice ale hormonilor tiroidieni sunt necesare pentru dezvoltarea scheletului, studii clinice indicând faptul că statutul de eutiroidian este esenţial pentru un turnover osos normal, pentru o mineralizare normală, precum şi pentru menţinerea rezistenţei osoase optime. Scopul studiului a fost de a urmări influenţa valorilor fiziologice a FT4 asupra densităţii minerale osoase. Am luat în studiu un număr de 650 de paciente, cu şi fără patologie tiroidiană, împărţite în trei loturi şi pe trei grupe de vârstă, la care s-au dozat hormonii tiroidieni, s-a determinat densitatea minerală osoasă prin metoda DXA. Am analizat influenţa FT4 asupra densităţii minerale osoase, am urmărit dacă există o corelaţie semnificativă statistic între valorile fiziologice ale acestuia şi scorul T independent de TSH. Conform rezultatelor studiului nostru şi a datelor existente în literatura de specialitate nu se poate susţine ideea că există o relaţie directă între FT4 şi gradul de demineralizare osoasă.*

INTRODUCTION

The thyroid hormones, important homeostatic regulators are lipophilic hormones, poorly soluble in water, and in blood flow, at a rate of over 95%, are bound to transport proteins: thyroglobulin, transteritina and other lipoproteins

Thyroid hormone receptors are part of many nuclear hormone receptors and function as transcription factors, together with co-regulator proteins.

The last two decades research has shown that thyroid hormones, through receptors affect the bone remodelling process through direct effects on osteoblasts, the increase of osteoclasts activity is most likely the consequence of coupling the bone turnover.

The two types of thyroid receptors TRα and TRβ, with their subclasses have different actions: TRα mediates the long-term effects of chronic changes in thyroid hormones and TRβ mediates the acute effects produced by the transient changes in the levels of thyroid hormones.(8)

PURPOSE

The purpose of this study was to identify the relation between the changes in FT4 values in the euthyroid interval and the changes in bone mineral density in the patients with thyroid pathology.

METHODS

The study included 650 patients, aged between 50-70 years old, with and without thyroid pathology, divided into three groups: with total or partial thyroidectomy, with thyroid pathology, under hormone replacement therapy and the control group.

The data were collected between 2008 and 2012; the patients were selected based on inclusion and exclusion criteria and were within the Ambulatory Endocrinology and Recovery I Clinic of the Clinical County Emergency Hospital of Sibiu.

The patients were evaluated clinically (anamnesis), by ultrasound and biologically (hormonal dosage); bone mineral density was performed at the level of the lumbar spine using the energy x-ray absorbmetry method – DEXA.

The measurement of bone mineral density was assessed in accordance with osteoporosis screening guidelines. The results obtained following DEXA were classified in the three groups according to the WHO staging: T score < -1 or osteopenia; T score < -2,5 or osteoporosis.

The biological assessment has been made by FT4 and TSH dosage through the chemiluminescence technique with IMMULITE device; the normal values range between 0,89-1,79 ng/dl for FT4 and 0,4 -4 μUI/ml for TSH.

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RESULTS

The study is a retrospective one and analyzes a sample of 131 patients with total and subtotal thyroidectomy, a group of 257 patients with thyroid pathology and a control group of 262 patients without thyroid pathology, but with changes in bone mineral density (osteoporosis and osteopenia). All three groups were divided into three age groups: 50-59 years old, 60-64 years old, 65-70 years old.

The origin environment is preponderantly urban - 80%, compared to those coming from the rural areas 20%, the distribution on the three age groups (50-59 years old, 60-64 years old, 65-70 years old) being similar proportionally; the average age of the analysed population being of 58.47 ± 5.53 years old.

The patients were analyzed taken into account the study groups and the age groups, according to the value of FT4 hormone, which normally ranged from 0.89 to 1.79 ng/dl and which was divided into two subintervals: one to the lower limit of the normal values 0,89 to 1.1 ng/dl, the other to the upper limit of the normal values 1.1 to 1,79 ng/dl. We have also studied the relation between FT4 values and bone mineral density measured by the DEXA method.

The distribution of FT4 with normal values per study groups and age groups was as follows: in the age group of 50-59 years old, the proportion of patients with normal FT4 was of 89,5% (340 cases out of a total of 380), distributed as follows: 20% in the operated group, 45.6% in the unoperated group and 34.4% in the control group.

In the age group of 60-64 years old, 91.8% of the cases (145 of 158) were within the euthyroid FT4. Their distribution was as follows: 11% in the group of the operated patients, 29.7% corresponding to the unoperated group pof patients and 59.35 in the control group.

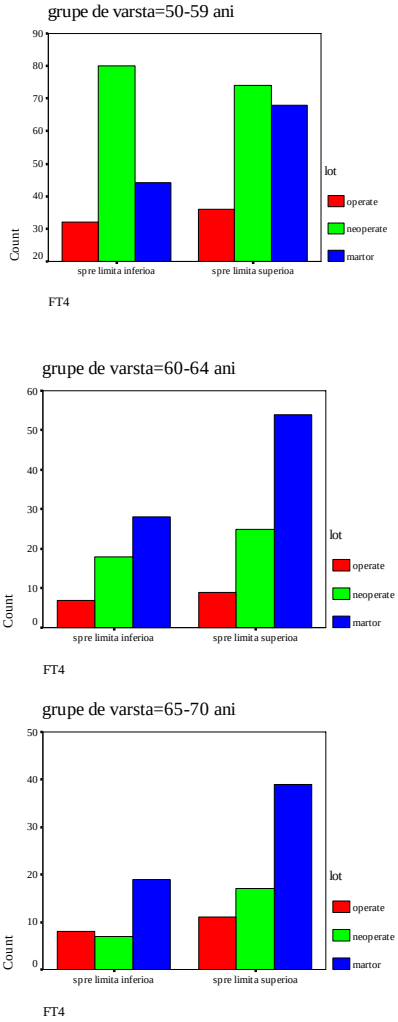
For the age group of 65-70 years old, the incidence of cases with FT4 normal was of 91,8% (101 of 110), their distribution being as follows: 18,8% in the operated group, 23,8% in the unoperated group of patients and 57,4% in the control group. Towards the lower limit of the normal interval of FT4, within the group of operated patients, we had 32 cases (20,5%), 80 cases (51,3%) in the group of unoperated patients and 44 cases (28,2%) in the control group, all of them in the age group of 50-59 years old.

For the age group of 60-64 years old, the patients' repartition was as follows: 7 cases (13,2%) in the operated group, 18 cases (34%) in the unoperated group of patients and 28 cases (58,8%) in the control group. In the age group of 65-70 years old, the repartition was as follows: 8 cases (23,5%) in the operated group, 7 cases (20,6%) in the unoperated group and 19 cases (55,9%) in the control group.

Regarding the upper limit of the FT4 euthyroid, in the age group of 50-59 years old, we had 36 patients (20,2%) of the operated group, 74 patients (41,6%) in the unoperated group and 68 patients (38,2%) in the control group.

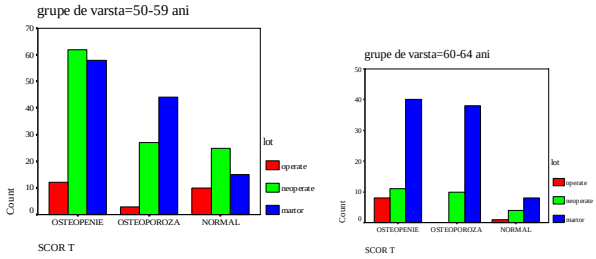
The age group of 60-64 years old includes: 9 patients (10,2%) in the operated group, 25 patients (28,4%) in the unoperated group and 54 patients (61,4%) in the control group. The age group of 65-70 years old includes: 11 patients (16,4%) in the operated group, 17 patients (25,4%) in the unoperated group and 39 patients (58,2%) in the control group.

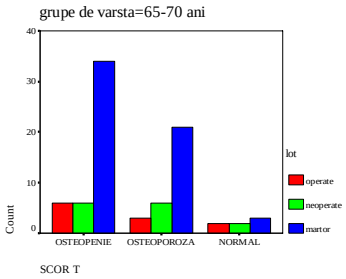
Figure no. 1. Distribution of normal FT4 per age groups



We also analyzed the situations where the FT4 was above the upper limit (> 1.79 ng/dL) and below the lower limit (<0.89 ng/dl) of the normal values. 2 patients had elevated FT4 within the operated group, 14 patients in the unoperated group. In the case of low FT4, 26 patients are in the operated group and 20 patients in the unoperated group. We noticed whether bone mineral density measured by the DEXA method and expressed by the T-score was influenced under euthyroid conditions (normal FT4, TSH normal). In the age group of 50-59 years old, 51.6% of patients had osteopenia, the majority belonging to the unoperated group (54.4%); corresponding to the age group of 60-64 years old, 49.2% were still with osteopenia and in the age group of 65-70 years old, 55.1% were in the same situation (p = 0.004).

Figure no. 2. Distribution of normal FT4 and TSH on goups of patients and age groups

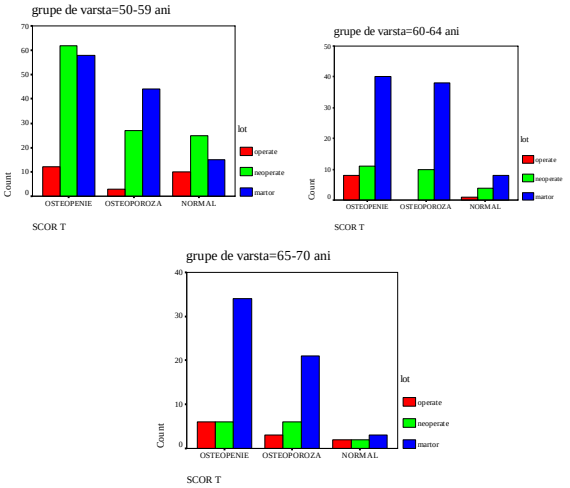




If the value of FT4 is at the lower limit, we talk about osteopenia in the age group of 50-59 years old, 55.9% of the study patients, in the age group of 60-64 years old, 52.4% and in the age group of 65-70 years old, 55.6%, the increased weight occurring in each age group of the unoperated group (p = 0.047).

If FT4 value is at upper limit, we also talk about osteopenia in all groups and in all age groups, within the group of unoperated patients, it also is more expressed compared to the control group of patients and those operated and, in the age group of 50-59 years old (p = 0.004).

Figure no. 3. Distribution of FT4 towards the upper limit per groups of patients and age groups



We analyzed the situation when FT4 is at the lower limit of the normal values and TSH is increased, the results were as follows: 74.3% of the patients of the age group of 50-59 years old had osteopenia, with a share of 77.8% in the unoperated and 70,6% in the operated group. Regarding the patients of the age group of 60-64 years old, a total of 63.6% had a T score corresponding to osteopenia, 75% in the operated group and 57.1% in the unperated group. For the age group of 65-70 years old, 50% had osteopenia, of which 66.7% were in the operated group and 33.3% in the unoperated group (p = 0.85).

It was followed the situation when FT4 was at the upper limit of the normal values and TSH is increased, in the age group of 50-59 years old, 34.6% had osteopenia, 23.1% had osteoporosis; in the age group of 60-64 years old, 57.1% cases had osteopenia and in the age group of 65-70 years old, 60% had osteoporosis.

Regarding the association of FT4 at the upper limit and low TSH, osteopenia occurred in 69.2% of patients within the age group of 50-59 years old, in 71.4% of those aged between 60-64 years old and in 66, 7% of those aged between 65-70 years old.

DISCUSSIONS

In the case of FT4 distribution per groups of patients and age groups, there is a similar distribution of FT4 (p = 0.81). The fact that the majority of patients in the three study groups are within the euthyroid range can be interpreted as subclinical disease stage, hypo or hyperthyroidism. In our study, we had predominantly normal FT4 with values at the upper limit of the euthyroid interval in all the three groups and all age groups.

Recent studies have attempted to demonstrate whether FT4 values towards the lower and upper limit of the euthyroid interval influence the bone mineral density. Kim et al., Murphy and colleagues followed this issue but they considered the normal values of TSH those up to 5μUI/ml and from 0.04 μUI/ml.(5.6) In our study, these values associated with normal FT4 correspond to the subclinical hypo and hyperthyroidism. It is known that subclinical hyperthyroidism is associated with an increased risk of fracture, so mineral density is low, according to other studies, it has been developed the idea that hypothyroidism may be associated with an increased risk of fracture, but with increased bone mineral density.(6) There is still debate on the possibility of TSH involvement through its receptor (TSHR) present in bone cells.(7) The operated and unoperated groups of patients were also analyzed in terms of the parameters mentioned in the previous studies, FT4 values taken into consideration those included within the reference euthyroid range. It was noted that when FT4 is associated to high TSH, osteopenia frequency is increased, compared with osteoporosis, mentioning that in the age group of 65-70 years old, for FT4 at the upper limit, we had reserves regarding the soundness of the data because of the limited number of patients who met these criteria.

Based on the results obtained in our study, the patients who had normal FT4 and at the upper limit are numerous than those who had FT4 to the lower limit, both in the study groups and in the age groups. It is possible that the association of FT4 at the upper limit of the euthyroid interval with normal TSH, in the age group of 50-59 years old, to significantly influence the degree of bone demineralization; otherwise, there is nothing to guide us for an influence of the physiological values of FT4 on bone mineral density.

CONCLUSIONS

The present research doe not emphasize significant changes of bone mineral density in case FT4 is at the upper or lower limits of the normal values.

A significant correlation has been observed between the age of the patients and bone mineral density and not between the TSH variations above the normal limits.

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