



ASSESSMENT OF VITAMIN D STATUS AND CALCIUM-PHOSPHORUS METABOLISM IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS.

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SUMMARY:

This study aims to assess vitamin D levels in women with postmenopausal osteoporosis and healthy women in menopause. Two groups of women over 50 years of age took part in the study – 41 women with osteoporosis and 22 without osteoporosis. The levels of vitamin D, parathormone, alkaline phosphatase, calcium and phosphorus were examined.

16 women with osteoporosis (39%) were with normal levels of vitamin D, 14 (34,1%) were with insufficiency, and 11 (26,9%) with deficiency of vitamin D. Within the control group, 8 women (36,4%) were with normal levels of vitamin D, 12 (54,5%) were with vitamin D insufficiency and 2 (9,1%) with deficiency.

The patients with vitamin D deficiency were significantly older both in the osteoporosis group and the control group ($r = -0.32$, $p < 0.05$). A negative correlation with the increase of parathormone levels among the patients with osteoporosis and vit D deficiency was found ($r = -0.46$, $p < 0.01$). There is a significant statistical difference in the average values of BMI in both groups. The average value of BMI in the patients with osteoporosis is 24.2 while in the patients of the control group, it's 29.5 ($p < 0.0001$). The same trend is seen in the patients with vitamin D deficiency both in the women with and the women without osteoporosis (24.4 to 28.2, respectively, $p < 0.05$). The results show an overall bad status of vitamin D. 61% of the patients with osteoporosis and 63,6 % of the healthy controls have levels of vitamin D, showing either insufficiency or deficiency.

Keywords: postmenopausal osteoporosis, insufficiency and deficiency of vitamin D,

INTRODUCTION:

Osteoporosis is the most frequent systemic disease of the skeleton, characterized by bone mass loss and damaged micro architectonic of the bones. The first definition of osteoporosis was elaborated during the consensus conference of the World Health Organization WHO back in 1993: It's a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tis-

sue, with a consequent increase in bone fragility and risk of fractures [1]. The course of osteoporosis is either asymptomatic or oligosymptomatic, most often without characteristic symptoms until a spontaneous fracture of a bone or a vertebra occurs. Osteoporotic fractures result in serious deterioration of the affected patients' quality of life, serious disability and risk of life-threatening complications and death.

Osteoporosis is an illness, which poses an increasing demand for countries' health protection systems due to ageing population and increased life expectancy. The social significance of the illness and the serious expenses for the treatment of its complications suggest that we must concentrate our efforts on early diagnosis of patients suffering from osteoporosis and their timely and continuous treatment before fractures and disability occur. 20% of patients with hip fractures die about a year after the incident. In Bulgaria, the new osteoporotic fractures are more than 38 000 a year, and the cost for their treatment is 1,6% of the common health care expenses.

European countries share troubling data, showing that only 15-20% of women with osteoporosis get the necessary treatment. In comparison, according to experts there are about 426 000 women with osteoporosis in Bulgaria and the percentage of women under treatment in our country is even lower – 3-4% due to the low level of reimbursement for the cost of osteoporosis medicine. This means more efforts are needed for the improvement of the existing data for osteoporosis in Bulgaria.

Postmenopausal osteoporosis occurs in women between 45 and 65 years of age and is due to the decline of their ovarian function. It's characterized by progressive loss of bone mass and subsequent fractures. The vertebral bodies are most frequently affected. The major pathogenetic factors are the hormonally determined increase of bone resorption and the increased loss of bone mass during the first 5-10 years after the menopause as a result of estrogen deficiency. According to WHO standards, the diagnosis is based on the results of measuring bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA).

The role of vitamin D. Vitamin D is a hormone and a

fat-soluble vitamin. Its plays a major role is in calcium-phosphorus exchange and bone metabolism. Vitamin D deficiency is a risk factor for the development of osteoporosis.

Calcium, phosphorus and parathormone (PTH) are the regulators of vitamin D synthesis. PTH increases the production of 1.25(OH)2D in kidneys and thus influences the resorption of calcium in the small intestine and its reabsorption in the tubules of the kidneys. Vitamin D levels are closely linked to the stimulation or the suppression of PTH secretion through the levels of calcium. Vitamin D stimulates osteoid mineralization and modulates the activity of osteoblasts and osteoclasts by providing the organism with calcium as well as with some of its other direct effects. The consequences of vitamin D deficiency are hypocalcemia, secondary hyperparathyroidism, bone destruction, leading to osteoporosis and fractures as well as mineralization defects, which can cause osteomalacia in the long-term and muscle fatigue leading to falls and fractures.

Vit D also influences muscle tone. It stimulates the synthesis of proteins in muscle cells and the calcium influx required for muscle contraction. Vitamin D deficiency is expressed by muscle fatigue and soreness, which can be a reason for frequent falls and fractures [2].

The serum level of 25(OH)D is defined by the committee of the Institute of Medicine (IOM) in 1997 as the best functional indicator for the vitamin D status, as it reflects the sum of the vitamin synthesis by the skin as well as its oral intake. [3].

According to vitamin D levels consensus in Bulgaria serum levels changes of PTH at different levels of vitamin D serve as a criterion for sufficiency:

- Severe deficiency of vitamin D - below 25 nmol/l.
- Insufficiency of vitamin D - 25 - 49.99 nmol/l.
- Normal level of vitamin D - above 50 nmol/l [4].

MATERIALS AND METHODS:

Two groups of women in menopause were examined.

Experimental group – 41 women in menopause aged over 50 with newly diagnosed osteoporosis who hadn't been under treatment. They were diagnosed by DXA of the spine – T score above -2,5.

Table 2.

Patients with OP	Levels of vitamin D		
	Normal - above 50 to 120 nmol/l	Insufficiency 25-50 nmol/l	Deficiency - below 25 nmol/l
Number of women	16 (39%)	14 (34,1%)	11(26,9%)
Average age	63.3 ± 8.3	64.2 ± 7.5	72.0 ± 7.0
BMI	23.7 ± 3.8	24.5 ± 5.7	24.4 ± 2.8
Vitamin D	73.0 ± 17.0	40.8 ± 6.4	18.0 ± 5.6
PTH	50.0 ± 24.2	62.2 ± 21.7	103.1 ± 67.6
AP	81.13 ± 18.6	92.0 ± 20.1	89.1 ± 34.3
Calcium	2.43 ± 0,12	2.40 ± 0.1	2.40 ± 0.2
Phosphorus	1.27 ± 0,2	1.20 ± 0.2	1.20 ± 0.2

Control group – 22 women in menopause over the age of 50 without osteoporosis and with normal bone density found during DXA.

Both groups underwent anthropometric and BMI measurements.

Biochemical and immunological tests on venous blood of participants of both groups were made to measure their levels of parathormone, vitamin D, alkaline phosphatase, calcium and phosphorus. The data was collected during the autumn-winter period.

The biochemical tests for calcium and phosphorus were made by the biochemical analyzer Cobas E 411, Roche Diagnostic kits. The immunological tests for parathormone, vitamin D (Vitamin D total) and alkaline phosphatase were made via electro-chemiluminescent immunoassay by the immunological analyzer Cobas E 411, Roche diagnostic kits. The referent values of the kits used are shown in Table 1:

Table 1.

Index	Reference values
PTH	15-65 pg/ml
Vitamin D / Vitamin D total/	≤ 25 nmol/l deficiency 25-50 nmol/l insufficiency ≥ 50 nmol/l norm
Alkaline phosphatase	≤ 128 U/l
Calcium	2,15 – 2,55 mmol/l
Phosphorus	0,87 – 1,45 mmol/l

The women were divided into 3 groups – with normal levels of vitamin D, with insufficiency of vitamin D and with deficiency of vitamin D.

The statistical processing of our data was made by SPSS v.19.0, Microsoft Office Excel 2003. p < 0,05 was used as a significance level that rejects the null hypothesis.

RESULTS:

The vitamin D levels in the patients with osteoporosis are shown in Table 2:

The vitamin D levels in the healthy controls are presented in Table 3:

Table 3

Healthy controls	Levels of vitamin D		
	Normal - above 50 to 120 nmol/l	Insufficiency 25-50 nmol/l	Deficiency - below 25 nmol/l
Number of women	8 (36,4%)	12 (54,5%)	2 (9,1%)
Average age	61.4 ± 3.3	64.3 ± 8.8	74.5 ± 6.4
BMI	28.6 ± 4.7	30.3 ± 6.3	28.2 ± 1.3
Vitamin D	65.8 ± 14.4	36.0 ± 7.7	14.2 ± 0.7
PTH	43.2 ± 11.0	76.2 ± 26.5	66.7 ± 7.4
AP	69.9 ± 23.8	73.0 ± 12.9	84.5 ± 6.4
Calcium	2.40 ± 0.1	2.43 ± 0.1	2.45 ± 0.1
Phosphorus	1.20 ± 0.1	1.24 ± 0.1	1.11 ± 0

The levels of serum calcium, phosphorus and alkaline phosphatase were within the referent values both in the patients with OP and in the healthy controls. A difference in the average values of AP was discovered between the patients with osteoporosis and the healthy controls: OP patients had higher AP values compared to the healthy controls (86.9 to 72.9, $p < 0.01$).

16 of the women with osteoporosis (39%) were with normal vitamin D values (73.0 ± 17.0 nmol/l), 14 of them (34,1%) were with vitamin D insufficiency (40.8 ± 6.4 nmol/l) and 11 (26,9%) – with vitamin D deficiency (18.0 ± 5.6 nmol/l). 8 of the healthy controls (36,4%) had normal vitamin D values (65.8 ± 14.4 nmol/l), 12 of them (54,5%) were with vitamin D insufficiency (36.0 ± 7.7 nmol/l) and only 2 of them (9,1%) were with vitamin D deficiency (14.2 ± 0.7 nmol/l).

There was no statistically significant difference in the average age between patients with normal values and those with vitamin D deficiency in both groups. However, there were statistically significant differences in the age of patients with vitamin D deficiency in both groups. The patients with vitamin D deficiency were significantly older in both the group with osteoporosis and the control group. ($r = -0.32$, $p < 0.05$). In the group of osteoporosis patients with Vitamin D deficiency, a negative correlation was found with the increase of parathormone values ($r = -0.46$, $p < 0.01$). Significant differences in the average values of BMI were observed in both groups. In patients with osteoporosis, the average BMI was 24,2 compared to 29,5 in the healthy controls ($p < 0.0001$). There was a similar tendency in patients with vitamin D deficiency both in the women with osteoporosis and the healthy controls (24.4 compared to 28.2, respectively, $p < 0.05$).

DISCUSSION:

There is sufficient information in international scientific literature confirming the fact that vitamin D deficiency is relatively frequent. There is data showing low values of vitamin D in patients with osteoporosis. Lots of clinical investigations of patients with fractura colli femo-

ris demonstrate low vitamin D values [5]. There are also materials showing how the normal levels of vitamin D preserve and even increase bone mineral density in menopausal women and could most likely prevent the risk of fractures [6]. That's why vitamin D is used for primary and secondary prophylaxis of osteoporosis as well as for its treatment.

At the present moment, there are officially published results from several multicenter studies about the levels of vitamin D in several populations of healthy people. Epidemiological data about the status of vitamin D in the Bulgarian population demonstrate a deficiency in 21,3%, insufficiency in 54,5% and normal levels in 24,2 % [7,8]. Generally, 75,8% of the people examined show a level of 25 (OH) D below the desired value ≥ 50 nmol/l. This means that the bigger part of the Bulgarian population is in a state of deficiency or insufficiency of vitamin D. The status of vitamin D in our country is rather poor, and this problem has been overlooked so far [8].

We found during our study that in the group of patients with osteoporosis, 16 were with a severe form of the illness based on the DXA results and the information about previous fractures (8 of them informed us about vertebral fractures and the other 8 informed us about nonvertebral fractures). 8 women from the healthy controls informed us about previous nonvertebral fractures. The results of the investigation of the vitamin D levels show that 61% of the patients with osteoporosis and 63,6% of the healthy controls have levels of vitamin D speaking of either insufficiency or deficiency. The average age of women with vitamin D deficiency is statistically significantly higher in patients from both groups. Most likely, many factors contribute to this situation. It could be due to decreased skin production of vitamin D, low intake of food that includes this vitamin, insufficient physical activity, insufficient time spent outdoors and coexisting illnesses that limit the usual physical activity of elderly people.

The negative correlation with the increase of parathormone in patients with vitamin D deficiency was expected. The deficiency of vitamin D through the low lev-

els of calcium is connected to the development of secondary hyperparathyroidism, a risk factor for the development of osteoporosis and consequent fractures.

The low body mass index increases the risk of fractures. BMI 20 kg/m increases the risk of fractures 2 times while BMI 16 kg/m increases this risk 4 times.[2].

The results of our study show significant differences in the average values of BMI for both groups. The average BMI of patients with osteoporosis was 24.2 compared to 29.5 in the healthy controls ($p < 0.0001$). There is a similar tendency seen in women with osteoporosis and healthy controls (24,4 to 28,2, respectively, $p < 0.05$). The higher BMI is considered a protective factor that prevents the development of osteoporosis in women.

CONCLUSION:

The results of vitamin D levels tests show that 61% of the patients with osteoporosis and 63,6% of the healthy controls have vitamin D insufficiency and vitamin D deficiency. The results of our study are consistent with the data about insufficiency and deficiency of vitamin D collected during studies of vitamin D levels in healthy people. The poor vitamin D status in patients with osteoporosis suggests the need for more efforts for early discovery of women at risk of developing osteoporosis and for taking preventive measures before fractures, complications and disability occur.

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