

Original article

Association of Bone Mineral Density and Vitamin D Levels in Postmenopausal Women in Ankara

(Ankara'da yaşayan postmenopozal ev hanımlarında kemik mineral dansitesi ve D vitamini Arasındaki İlişkinin İncelenmesi)

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ÖZET

Amaç: D vitamini, kemik mineralizasyonu için gerekli olup, eksikliğinde osteoporoz, rikets, osteomalazi ve kemik kırıkları oluşabilmektedir. Postmenopozal kadınlarda, fizyolojik olarak hem östrojen hormonu düzeyinin azalması, hem de yaşa bağlı kemik mineral dansitesinde azalma olmaktadır. Postmenopozal kadınlarda kemik sağlığını etkileyebilecek faktörlerin birden fazla olması nedeniyle, D vitamini düzeyleri ve kemik sağlığı arasındaki ilişkinin belirlenebilmesi zordur. Bu nedenle araştırmamızda Ankara şehir merkezinde yaşayan, ev hanımı, menopoz sonrası kadınlarda D vitamini düzeyini ve D vitamininin kemik mineral dansitesi ile arasındaki ilişkiyi belirlemek istedik.

Materyal ve Metot: 2012 yaz döneminde Ankara'da yaşayan, yaş ortalaması 59,7±9,2 olan, güneş ışığına yeterince maruz kalabilecek şekilde giyinen 223 postmenopozal kadın çalışmaya dahil edildi. Vitamin D, kalsiyum, parathormon, fosfor, kemik taraması ve genel laboratuvar testleri değerlendirildi.

Bulgular D vitamini ortalaması 27,4±21,3 ng/ml olarak saptandı. Osteopenik ve osteoporotik olan gruba göre kıyaslandığında normal kemik dansitometrisi olanlarda D vitamini düzeyleri daha yüksekti (p<0,05). Femur boyun dansitesi ve vertebra dansiteleri D vitamini düzeylerine göre kıyaslandığında anlamlı fark izlenmedi (p>0,05).

Sonuçlar: Sağlıklı kemik mineralizasyonu için, postmenopozal kadınlar mutlaka D vitamini açısından kontrol edilmeli ve eksikliği durumunda gerekli takviye verilmelidir.

Anahtar Kelimeler: D vitamini, kemik mineral yoğunluğu; menapoz; osteoporoz; femur boynu; vertebra

ABSTRACT

Background: It is known that bone mineral density changes with sexual hormone levels and age in postmenopausal women.

Introduction: The association between vitamin D levels and bone mineralization in postmenopausal women is not completely understood. Our study aimed to determine the levels of vitamin D in postmenopausal women and their association with bone mineral density.

Material and Methods: In summer 2012, 223 postmenopausal housewives (mean age 59.7±9.2) living in Ankara and dressing in a manner such that they could be exposed to sufficient sunlight were included in the study. Vitamin D levels, bone density, serum calcium, phosphorus, magnesium, parathyroid hormone (iPTH), alkaline phosphatase, fasting glucose, lipid profile and thyroid function tests were performed and analysed. Systolic and diastolic blood pressure measurements, exercise, daily sunshine exposure, body mass index and duration of menopause were recorded and associations of these parameters to vitamin D were assessed.

Results: The mean level of vitamin D of the cases was found to be 27.4±21.3 ng/ml. The vitamin D level was found to be higher in the group with normal bone densitometry compared to the osteopenic and osteoporotic groups (p<0.05). No difference was found between femur neck density and vertebral density in respect to vitamin D levels (p>0.05).

Conclusions: To ensure bone mineralization, vitamin D levels of postmenopausal women must be analysed routinely and vitamin D must be supplemented.

Key Words: Vitamin D; bone mineral density; menopause; osteoporosis; femur neck; vertebrae

INTRODUCTION

Vitamin D is a hormone which plays an important role in bone metabolism. In humans, 90% of vitamin D is supplied by synthesis in the skin via ultraviolet sunlight; a small portion is obtained from food intake¹. Multi-pigmented skin, inadequate exposure to sunlight, obesity, inadequate intake,

malabsorption and medication are known factors for vitamin D deficiency.

Vitamin D deficiency causes osteomalasia in adults. In senile osteoporosis, decreased vitamin D causes secondary hyperparathyroidism and decreased osteoblast activity with age. After menopause, the sensitivity of bone to parathyroid hormone (PTH) is increased, so a greater amount of calcium is mobilized from bone tissue to circulation.

Secondary to hypercalcemia, vitamin D production is decreased. Post-menopausal osteoporosis is

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characterized by decreased trabecular bone mass and vertebrae-radius fracture. It is known that replacement of vitamin D causes a significant reduction in fractures, but there is no consensus about the vitamin D level in postmenopausal women necessary to protect bone-mass density.

Therefore, the objective of the current report was to study vitamin D levels and its association with bone mineral density in postmenopausal housewives.

MATERIAL and METHODS

The study was conducted between July and August 2011 at Turgut Ozal University Hospital, Ankara, Turkey. Two hundred and twenty-three postmenopausal women under the age of 75 (mean age 59.7 ± 9.2) and living in the city centre were included in this study. Informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the Declaration of Helsinki, as reflected in its prior approval by the institution's human research committee. The local ethics committee also approved the study.

Because some drugs may affect vitamin D values, patients using thyroid hormone preparations, diuretics, oral contraceptives and steroids were excluded. Women with a history of surgical menopause or of using alcohol were also excluded.

Body mass index (BMI), diet, duration of menopause, age, medications, accompanying diseases and exercise habits of patients were evaluated.

The BMI was calculated as weight in kg/height in meters squared, for all participants.

Blood samples were collected from patients and a control group after an overnight fast. 25-hydroxy-vitamin D3 (25-(OH) D3), PTH, calcium (Ca), phosphorus (P) and alkaline phosphatase (ALP) levels were studied.

Patients were divided into four groups according to their vitamin D levels: 1) 25-(OH)D3 level below 10 ng/mL ($n=36$); 2) between 10-20 ng/mL ($n=64$); 3) between 20-30 ng/mL ($n=52$); and 4) vitamin D level above 30 ng/mL ($n=71$). Age distribution was similar for all groups.

25-(OH)D3 vitamin levels were tested using an E-170 device using the electro chemiluminescence method (Roche Ltd, Germany).

Ca, P and ALP levels were studied in the same serum samples using reagents (Integra 800 device, Roche, Germany). Intact PTH was tested using the electrochemiluminescence method with an Immulite 2000 device.

Bone mineral densitometry measurements were performed from the neck of right femur and lumbar vertebrae using a Hologic QDR Explorer device and the X-ray absorptiometry method.

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 14.0 package of programs (SPSS Inc., Chicago, Illinois, USA). Data were presented as mean $\pm$ SD unless otherwise noted. Differences between the groups were analysed using a Mann-Whitney U-test. The Kolmogorov Smirnov test was used to calculate whether or not the distribution is normal. The relationships among the variables were analysed using Spearman's correlation test. A p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 223 postmenopausal women under the age 75 were included in the study. The mean age of the group was 59.7 ± 9.2 years. Patients were divided into four groups according to vitamin D levels: 1) Apparent vitamin D deficiency, 25-(OH)D3 level below 10 ng/mL; 2) Normal vitamin D deficiency, between 10–20 ng/mL; 3) Mild vitamin D deficiency, between 20–30 ng/mL; 4) Normal vitamin D group, vitamin D level above 30 ng/mL. There was no significant relationship between age and vitamin D levels ($p>0.05$).

Vitamin D levels were higher in patients with normal bone mineral density compared to osteopenic and osteoporotic groups ($p<0.05$). Also, vitamin D levels were higher in the osteopenic group than in the osteoporotic group, but the difference was not statistically significant.

There was no significant difference in vitamin D levels between patients with only femur-neck, only vertebrae, and femur neck + vertebrae osteoporosis. Comparisons of vitamin D levels between these groups are shown in Table 1.

Table 1. Vitamin D Values Compared with Bone Mineral Density

	Mean vitamin D levels (ng/ml)	$\pm$ SD	Minimal	Maximal
Normal BMD	35.3	25.5	3.20	118.00
Femur-neck osteoporosis	27.2	26.5	13.00	67.00
Vertebrae osteoporosis	30.2	16.1	8.00	67.00
Femur + vertebrae osteoporosis	30.6	22.6	9.00	77.00
Total	33.0	22.5	3.20	118.00

BMD: Bone mineral densitometry

Table 2. Comparison of Demographic Features of Patient Groups According To Vitamin D Levels

	Apparent vitamin D deficiency	Normal vitamin D deficiency	Mild vitamin D deficiency	Normal vitamin D group	Total
Age (years)	59.5±10.2	58.8±8.2	61.1±8.6	59.6±10.1	59.7±9.2
Exposure to sun (hour per day)	2.3±1.2	3.5±1.7	2.7±1.5	7.5±6.3	3.1±2.9
Age of menopause (years)	48.3±4.1	46.7±4.8	49.5±4.5	48.3±5.1	48.1±4.8
Duration of menopause (years)	7.2±4.7	11.4±6.9	9.1±7.9	8.7±6.9	9.3±7.2
Systolic BP (mmHg)	135.3±23.0	130.6±17.3	132.0±17.5	134.2±17.9	132.7±18.1
Diastolic BP (mmHg)	85.3±14.5	81.5±9.6	83.0±8.8	84.5±9.5	83.3±10.0

BP: Blood pressure

The average duration of exposure to the sun was higher in group 4, but the difference between groups was not statistically significant.

Serum calcium levels were similar between groups with apparent vitamin D deficiency and those with a level above 30 ng/mL. Also, there were no significant relationships between serum magnesium, phosphorus and alkaline phosphatase and vitamin D levels ($p>0.05$). Serum free t4, but not t3 or thyroid-stimulating hormone, levels were relatively lower in the patients with <10 ng/mL vitamin D level ($p<0.05$).

The mean of PTH levels was 75.8 pg/mL. Also, PTH levels were not significantly related to vitamin D levels ($p>0.05$), and blood glucose and lipid profile were also not associated with vitamin D levels.

The mean BMI of group 1 patients was significantly lower compared to group 2 patients, but there was no significant difference between the BMI values of normal, osteopenic and osteoporotic groups ($p>0.05$). Comparisons of the demographic features of patients grouped according to vitamin D levels are given in Table 2.

DISCUSSION

Vitamin D is essential to maintaining skeletal calcium balance by promoting calcium absorption in the intestines, promoting bone resorption by increasing osteoclast number, maintaining calcium and phosphate levels for bone formation, and allowing proper functioning of parathyroid hormones to maintain serum calcium levels.

In our study, we have observed that bone mineral density is lower in patients with vitamin D deficiency. These results are similar with to the populations examined in previous studies^{2,3}.

There are also some studies that found no relationship between bone density and vitamin D levels⁴, so the differences among these studies may depend on the demographic features of the study population.

The mean vitamin D level was 22.3±10.9 ng/mL in osteoporotic patients. In another study, the mean value of this hormone was measured as 17.8 ng/mL, but the mean age of patients ($n=53$) in that study was 82, which is older than the current study, and the number of patients was also lower than in the current study⁵.

A higher mean vitamin D level was also measured in another study. Lips et al.⁶ conducted a study in five countries with 7,654 postmenopausal women. All of the subjects were osteoporotic and had at least 2 lumbar osteoporotic fractures. The mean vitamin D level was 28.36 ng/mL in this patient group. Only 28% of patients had vitamin D levels below 29 ng/mL, whereas 44.7 % of our patient group had this level. The population of this study had a more severe osteoporotic state compared to our patients. These results show that a vitamin D level above 20 ng/mL is not sufficient to protect bone mineral density. Higher levels must therefore be targeted for patients. The vitamin D level required to protect bone integrity is not well-documented yet.

The mean vitamin D level was 21.9 ng/mL and most osteoporotic patients had 25(OH)-D3 vitamin levels above 25 ng/mL in a study conducted in Belgium. This study also supported the view that a vitamin D level of about 25 ng/mL is not sufficient to protect bone integrity in postmenopausal women⁷.

The vitamin D level was lower in patients with femur-neck osteoporosis when compared to vertebra-osteoporotic subjects (27.2 vs 30.2) in our study. Vitamin D is more effective on cortical bone than trabecular bone tissue. This difference was not statistically significant, but this may be related to the small study population. However, it has been proven in another study that parathyroid hormone level can be decreased to normal values when vitamin D level is maintained above 20 ng/mL and normal femur-neck bone density can be achieved when vitamin D is increased to 28 ng/mL⁸.

In our study, 16% of patients had 10 ng/mL vitamin-D and 44.7% of them had vitamin D levels below 20 ng/mL. It has previously been found that 40-100% of people living in USA and Europe have vitamin D deficiency⁹. In a study performed in Australia (n= 1,098), its prevalence is estimated about 26%¹⁰. Also, 700 postmenopausal women were assessed in Italy for vitamin D deficiency and the mean of this hormone level was about 10.6 ng/mL¹¹. Differences between the reports may be related to genetic and environmental factors.

Calcium absorption from intestine increases by 45-60% when the vitamin D level is elevated to 20-32 ng/mL¹². Vitamin D deficiency causes hypocalcaemia, leading to calcium resorption from the bone and increased alkaline phosphatase. In our report, calcium, phosphorus and ALP levels were not associated with vitamin D. It is proven in some reports that only severe vitamin D deficiency (≤ 10 ng/mL) can cause significant changes in ALP, Ca and phosphorus levels¹³. These reports are compatible with our study results.

Synthesis of vitamin D depends on various factors, such as geographical features, seasons, the melanin concentration of the skin, clothing style and age of skin. Our study was performed in the summer time in a sunny city. The mean vitamin D level was 27.4 ± 21.3 ng/mL in our women population. A study conducted in the United States evaluated vitamin D levels in the late summer and in the late winter and found levels of 49 ng/mL and 30 ng/mL, respectively. No change in calcium levels were observed in the same study¹⁴.

Age, BMI, hypertriglyceridemia and hyperglycaemia are inversely proportional to vitamin D levels. In our study, age was not significantly associated with the vitamin D level. In patients with apparent vitamin D deficiency, the mean BMI was 33.9, whereas in patients with normal vitamin D deficiency the average BMI was 28.7 ($p < 0.05$). The reason for this is the accumulation of vitamin D in adipose tissue in obese patients.

Vitamin D can increase insulin synthesis¹⁵; and vitamin D deficiency may cause insulin resistance and risk of diabetes¹². We did not find any significant relationship between blood glucose and vitamin D levels. The reason for this may be the exclusion of diabetic patients from our study.

Vitamin D also increases the amplitude of myocardial contraction. In a previous study, patients were exposed to the sun for three months. A three-times increase in vitamin D levels was observed alongside a 6 mmHg decrease in systolic blood pressure¹². We did not find any relationship between vitamin D and blood pressure levels.

CONCLUSIONS

In conclusion, bone mineral density is affected by vitamin D levels. If severe vitamin D deficiency exists, calcium, phosphorus and parathyroid hormone levels can also change due to bone resorption. Our study sheds light on the determination of intended vitamin D levels in postmenopausal women.

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REFERENCES

1. Heath DA, Shaw NJ. Calcium and bone metabolism. Ed: Brook CGD, Hindmarsh PC, Clinical Pediatric Endocrinology. Oxford. Blackwell Science Press 2001;pp:377-89, Oxford, ABD.
2. Mezquita-Raya P, Munoz-Torres M, Luna JD, et al. Relation between vitamin D insufficiency, bone density, and bone metabolism in healthy postmenopausal women. *J Bone Miner Res* 2001;16:1408-15.
3. Malavolta N, Pratelli L, Frigato M, Mule R, Mascia ML, Gnudi S. The relationship of vitamin D status to bone mineral density in an Italian population of postmenopausal women. *Osteoporos Int* 2005;16:1691-7.
4. Garnero P, Munoz F, Sornay-Rendu E, Delmas PD. Associations of vitamin D status with bone mineral density, bone turnover, bone loss and fracture risk in healthy postmenopausal women. The OFELY study. *Bone* 2007;40:716-22.
5. Sakuma M, Endo N, Oinuma T, et al. Vitamin D and intact PTH status in patients with hip fracture. *Osteoporos Int* 2006;17:1608-14.
6. Lips P, Duong T, Oleksik A, et al. A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial. *J Clin Endocrinol Metab* 2001;86:1212-21.
7. Neuprez A, Bruyere O, Collette J, Reginster JY. Vitamin D inadequacy in Belgian postmenopausal osteoporotic women. *BMC Public Health* 2007;7:64.
8. Nakamura K, Tsugawa N, Saito T, et al. Vitamin D status, bone mass, and bone metabolism in home-dwelling postmenopausal Japanese women: Yokogoshi Study. *Bone* 2008;42:271-7.
9. Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence? *Br J Nutr* 2003;89:552-72.
10. Kudlacek S, Schneider B, Peterlik M, et al. Assessment of vitamin D and calcium status in healthy adult Austrians. *Eur J Clin Invest* 2003;33:323-31.
11. Isaia G, Giorgino R, Rini GB, Bevilacqua M, Maugeri D, Adami S. Prevalence of hypovitaminosis D in elderly women in Italy: clinical consequences and risk factors. *Osteoporos Int* 2003;14:577-82.
12. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007;357:266-81.
13. Hashemipour S, Larijani B, Adibi H, et al. The status of biochemical parameters in varying degrees of vitamin D deficiency. *J Bone Miner Metab* 2006;24:213-8.
14. Francisco B, Luiz G, Patricia D, Catia E, Cristina F. Vitamin D deficiency: A global perspective. *Arq Bras Endoc Metab* 2006;50:640-6.
15. van der Wielen RP, Lowik MR, van den Berg H, de Groot LC, Haller J, Moreiras O, et al. Serum vitamin D concentrations among elderly people in Europe. *Lancet* 1995;346:207-10.