Original Article

Low Vitamin D Levels in Outpatient Postmenopausal Women from a Rheumatology Clinic in Madrid, Spain: Their Relationship with Bone Mineral Density

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Abstract. To evaluate a possible relationship between vitamin D levels and bone mineral density (BMD) and the prevalence of hypovitaminosis in a population of postmenopausal women from a rheumatologic outpatient clinic in Madrid, Spain, 171 postmenopausal women (aged 47–66 years) divided into two groups (osteoporotic and nonosteoporotic, according to WHO criteria) were studied between November and June. Liver and kidney function were normal in all subjects. Serum parathyroid hormone (PTH) and calcidiol levels were determined and bone densitometry carried out at the lumbar spine and hip level. PTH and calcidiol serum levels did not show any correlation. Serum PTH was inversely related to BMD at both hip and lumbar spine in the total group, and at the hip with calcidiol levels lower than 37 nmol/l. Calcidiol was directly related to hip BMD only when levels were lower than 37 nmol/l. Results of a stepwise multiple regression analysis showed that the single factor which affected BMD at the hip was calcidiol in the subgroup with serum calcidiol levels below 37 nmol/l, while in the subgroup with serum calcidiol levels above 37 nmol/l, the main factor affecting hip BMD was serum PTH. The prevalence of vitamin D deficiency at a cutoff of 37 nmol/l was 64%. In summary, calcidiol serum levels below 37 nmol/l seem to affect bone mass, regardless of the effect of PTH. Vitamin D deficiency is a frequent finding in the postmenopausal women who attend a rheumatology outpatient clinic in Madrid. Vitamin D supplementation should therefore be considered in this population during the winter season.

Keywords: Bone mineral density; Calcidiol; Osteoporosis; Postmenopausal women; PTH; Vitamin D

Introduction

Vitamin D is essential for maintaining a healthy skeleton throughout life. Severe deficiency leads to skeleton mineralization defects that result in rickets or osteomalacia, characterized by biochemical abnormalities such as low serum calcium and phosphate, with high alkaline phosphatase. Bone histology shows increased osteoid volume and decreased bone formation. However, it is also well known that vitamin D insufficiency is a risk factor for osteopenia and bone fractures [1–6] and may precede the clinical symptoms of osteomalacia by many years.

Vitamin D status is most commonly assessed by measuring the level of 25(OH)D (calcidiol), the major circulating vitamin D metabolite. In patients with osteomalacia, serum calcidiol levels are usually below 12.5 nmol/l, and are often undetectable. There is growing evidence supporting the hypothesis that low levels of vitamin D can lead to bone loss [2–4]. Hypovitaminosis D evaluated by a low serum 25(OH)D concentration is associated with physiologic, pathologic, and clinical evidence of vitamin D deficiency, including increased parathyroid hormone (PTH)
secretion, increased bone turnover, osteoporosis and mild osteomalacia, and an increased risk of hip and other fractures [7].

Vitamin supplements can modify bone mineral density (BMD) [8] and serum PTH levels [9] in postmenopausal women.

Different approaches to defining vitamin D insufficiency have been proposed. Many of them are based on the threshold for the appearance of secondary hyperparathyroidism. This threshold, which is based on PTH stimulation, ranges between 25 and 37 nmol/l of serum calcidiol [10,11], 50 nmol/l [12] or even 95 nmol/l [9]. However, there is little evidence on the threshold levels of vitamin D that may affect BMD [2]. The ability of the skin to produce vitamin D decreases with age, resulting in lower vitamin D levels in adults compared with younger subjects [13]. Vitamin D insufficiency in adults and elderly people is a common problem in Europe [14]. Except for some Scandinavian countries, food in our continent is not usually supplemented with vitamin D. During the winter time skin synthesis of vitamin D cannot compensate for a low nutritional intake because Europe is located at a high latitude, even the countries considered to be cherished by the sun such as Italy, Spain and Greece. This factor can lead to the higher prevalence of vitamin D insufficiency described in the Mediterranean area compared with Northern Europe in even elderly people [15].

Although several studies from the Mediterranean area [16,17] and from our own area [18] have calculated the prevalence of vitamin D insufficiency in the elderly, there are few studies on vitamin D status in peri- or postmenopausal women in the Mediterranean area of Europe [19,20]. The aim of this study was to evaluate the prevalence of vitamin D insufficiency and its relationship with BMD in postmenopausal women from a rheumatology outpatient clinic in the Madrid area of Spain.

**Patients and Methods**

**Patients**

A total of 171 postmenopausal women with a mean age ± standard deviation of 56 ± 5 years, range 47–66 years, and a gynecologic diagnosis of natural menopause of at least 2 years (7.9 ± 2 years) were studied. We found 96 women diagnosed for osteoporosis by a T-score < −2.5 in a densitometric study at the lumbar spine, based on the criteria established by the World Health Organization, and 75 nonosteoporotic women with a T-score > −1 at the lumbar spine.

All women were recruited in a consecutive manner as part of a prospective study in a rheumatology outpatient clinic. Recruitment was done between October and June, since during this period vitamin D levels in the study region (Madrid: latitude 40° N) are more stable. Calcidiol levels from June to October are not stable and vary [21] with the individual’s exposure to sunlight, so study subjects were not recruited during this period. A clinical evaluation was performed to fulfill the inclusion criteria. Exclusion criteria were the presence of systemic diseases such as nephropathy, hepatopathy, thyroid affection, neoplasia, and intestinal malabsorption, or the use of drugs such as diuretics, oral anticoagulants, anticonvulsive therapies, bone resorption inhibitors, or hormone replacement therapy and vitamin D supplementation within the year prior to the study. All postmenopausal women had normal renal function defined as a serum creatinine level below 105 μmol/l, aminotransferases below 0.58 μmol/l and normal serum calcium < 2.6 μmol/l. All women lived in their own homes and had no disabilities. In all cases, informed consent was obtained.

**Bone Densitometry**

BMD was quantified by dual-energy X-ray absorptiometry (DXA; Hologic QDR-1000, Waltham, MA) at the lumbar level (L2–L4) and at the hip level (femoral neck, trochanter, Ward’s triangle, and total). Data were obtained for BMD (g/cm²), T-score (deviation with respect to peak bone mass) and Z-score (deviation with respect to the age-matched normal value).

A self-reported personal history of appendicular fracture was obtained which was validated from radiographs. Lateral view radiographs of the thoracic and lumbar spine were performed to determine the presence of vertebral crushing, vascular calcifications and osteophytes, and the required corrections were applied according to Orwoll’s method, excluding those patients who suffered severe arthrosis. Nonosteoporotic women were those who had normal BMD as well as no radiologic evidence of vertebral fracture or self-reported history of peripheral fracture.

**Analytical Methods**

Fasting serum PTH was determined by immunoradiometric assay (IRMA) (Nichols, San Juan Capistrano, CA). The intra-assay and interassay coefficients of variation were less than 6%. Serum calcidiol and calcitriol were measured by a radioimmunoassay (RIA) (Incstar, Stillwater, MN). The inter-assay and intrassay coefficients of variation for calcidiol and calcitriol were less than 15%. Routine chemistry was measured with a Hitachi multichannel analyzer (Tokyo, Japan).

**Definition of Vitamin D Insufficiency**

In the present study, three different cutoffs for serum calcidiol levels were considered to define vitamin D insufficiency: 50 nmol/l, according Malaban et al.’s study [12], 37 nmol/l, according to published data from