Is vitamin D deficiency being considered in the differential diagnosis of osteoporosis in routine practice?

¿Está considerado el déficit de vitamina D en el diagnóstico diferencial de la osteoporosis en la práctica clínica habitual?

Dear Editor,

Vitamin D is essential for promoting calcium absorption in the intestine, maintaining serum calcium and phosphate concentrations, and allowing proper bone mineralization. Insufficient serum 25 hydroxyvitamin D3 (25OHD) concentrations lead to increased PTH secretion, which in turn accelerates bone resorption, especially of the cortical bone.1 Severe vitamin D deficiency occurs when serum 25OHD drops below 10 ng/ml, which may lead to rickets in children and osteomalacia in adults. In addition, osteomalacia during its mild and early clinical course can be misdiagnosed as osteopenia and osteoporosis.

The objective of this study was to evaluate the request of biochemical determination of 25OHD concentration in routine practice during the differential diagnosis and workup of individuals with osteoporosis. A cross-sectional study was performed with a sample of individuals referred from different care settings (primary care and different specialists) with suspicion of osteoporosis for conducting an axial dual-energy X-ray absorptiometry (DXA) bone mineral density (BMD) test at the densitometric unit of the University Hospital of León in Spain. Individuals between 40 and 90 years of age who had received no previous treatment with antiresorptive medications were included. Blood tests were reviewed to assess whether the attending physician requested the determination of vitamin D concentrations, and if so, its value was collected. The following ranges were used to classify the status of vitamin D in: vitamin D deficiency if 25OHD was <20 ng/ml; vitamin D insufficiency if 25OHD was between 20 and 30 ng/ml; and vitamin D sufficiency if 25OHD was >30 ng/ml.2

A total of 640 individuals were recruited, 95% of whom were females, with a median age of 59.4 (interquartile range [IQR]: 14) years. The concentrations of serum 25OHD were requested in 206 individuals (32.2%). The median concentration of 25OHD was 24.5 ng/ml (IQR: 14), with 68% of the individuals presenting a vitamin D status of insufficiency/deficiency. Serum 25OHD concentrations positively correlated with any of the BMD measurements both in the lumbar spine and the femoral neck [Pearson correlation coefficients (95% confidence interval): 0.32 (0.09–0.51) and 0.29 (0.07–0.46), respectively, p < 0.05].

Despite the important role of vitamin D in the diagnosis and therapeutic approach of osteoporosis, the assessment of its concentrations was requested by clinicians only in 32.2% of the study subjects. This may have important implications in the differential diagnosis of secondary causes of osteoporosis like osteomalacia.3 The recent guidance from the National Osteoporosis Society recommends determining concentrations of serum 25OHD in patients with bone diseases, prior to specific treatment where correcting vitamin D deficiency is appropriate, and in patients with bone diseases that may be improved with vitamin D treatment, like osteoporosis and osteomalacia.4 In patients with very low concentrations of vitamin D (and especially if PTH is high), the need for treatment of osteoporosis should be reassessed after correction of the vitamin D concentration. In these patients with severe vitamin D deficiency, a marked increase can be seen in BMD after treatment with calcium and vitamin D, making the treatment for low BMD unnecessary.5 Osteomalacia may occur with low BMD, and histological studies suggest that it is present in up to 40% of patients with hip fractures.6 Although definitive diagnosis is made by bone biopsy, it should be suspected in individuals with low vitamin D, hypophosphatemia, elevated alkaline phosphatase, and calcium in the lower limit of normality.7 If osteomalacia is misdiagnosed as osteoporosis and is treated with bisphosphonates, bone mineralization and risk of osteonecrosis of the jaw may increase.8 In addition, it has been suggested that middle-aged patients with inexplicable low BMD should be treated with high doses of vitamin D and calcium in order to rule out a possible mild or recent onset osteomalacia, and thereafter repeat the BMD test.9 Also, the prevalence of vitamin D deficiency in the study individuals was high. This is consistent with previous studies that have shown that even in countries with many hours of sunshine, the prevalence of vitamin D deficiency is elevated.10 Moreover, the state of vitamin D plays an important role in the success rate
of antiresorptive therapy, especially when bisphosphonates are administered. Studies with alendronate show an inverse correlation between BMD gain and vitamin D status.11

In conclusion, vitamin D deficiency is often not considered during the work-up of osteoporosis, despite its high prevalence. As part of a correct evaluation of possible secondary causes of low bone mass, we recommend the assessment of vitamin D status by measuring the 25OHD concentration in all individuals with suspicion of osteoporosis.

Conflict of interest

All authors declare no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work and no other relationships or activities that could appear to have influenced the submitted work.

References