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LETTERS TO THE EDITOR

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 demineralization 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

1. Bendik I, Friedel A, Roos FF, Weber P, Eggersdorfer M. Vitamin D: a critical and essential micronutrient for human health. *Front Physiol.* 2014;5:248.
2. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96:1911–30.
3. Diab DL, Watts NB. Secondary osteoporosis: differential diagnosis and workup. *Clin Obstet Gynecol.* 2013;56:686–93.
4. Aspray TJ, Bowring C, Fraser W, Gittoes N, Javaid MK, Macdonald H, et al. National osteoporosis society vitamin D guideline summary. *Age Ageing.* 2014;43:592–5.
5. Garg MK, Brar KS, Kharb S. Rapid improvement in the bone mineral density with vitamin D supplementation in postmenopausal woman with vitamin D deficiency. *Indian J Endocrinol Metab.* 2012;16:859–60.
6. Aaron JE, Gallagher JC, Anderson J, Stasiak L, Longton EB, Nordin BE, et al. Frequency of osteomalacia and osteoporosis in fractures of the proximal femur. *Lancet.* 1974;1:229–33.
7. Bhan A, Rao AD, Rao DS. Osteomalacia as a result of vitamin D deficiency. *Endocrinol Metab Clin North Am.* 2010;39:321–31.
8. Bedogni A, Saia G, Bettini G, Tronchet A, Totola A, Bedogni G, et al. Osteomalacia: the missing link in the pathogenesis of bisphosphonate-related osteonecrosis of the jaws? *Oncologist.* 2012;17:1114–9.
9. Saghafi M, Azarian A, Hashemzadeh K, Sahebari M, Rezaieyazdi Z. Bone densitometry in patients with osteomalacia: is it valuable? *Clin Cases Miner Bone Metab.* 2013;10:180–2.
10. Unger MD, Cuppari L, Titan SM, Magalhães MC, Sassaki AL, dos Reis LM, et al. Vitamin D status in a sunny country: where has the sun gone? *Clin Nutr.* 2010;29:784–8.
11. Roux C, Binkley N, Boonen S, Kiel DP, Ralston SH, Reginster JY, et al. Vitamin D status and bone mineral density changes during alendronate treatment in postmenopausal osteoporosis. *Calcif Tissue Int.* 2014;94:153–7.

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The need of travelling to another city to be attended in a Hospital Clinic for obesity. Does it affect to the adequacy of referrals from Primary Care?



¿Afecta la necesidad de desplazamiento a otra ciudad para ser valorado en una consulta hospitalaria de obesidad en la adecuación de las derivaciones desde atención primaria?

Dear Editor,

Obesity is one of the main problems for our Public Health System today. The prevalence of obesity and overweight in adults in Spain is 22.9% and 39.4% respectively.¹ Obesity causes 1 of every 13 deaths in Europe and it is the second cause of evitable mortality behind smoking.² The treatment of obesity always includes hypocaloric diets, exercise, changes in one's way of life and regular medical visits.³ If the results after the previous treatments are not good, the pharmacological treatments are limited in Europe,⁴ so

that, patients with body mass index (BMI) ≥ 35 kg/m² may be referred to a Hospital Clinic. In these patients, we can consider a very-low calorie diet and bariatric surgery.⁵

It is known that referrals to a Hospital Clinic from Primary Care are not homogeneous and, one important factor of this is the need to travel to another city to be attended.⁶ The aim of our study was to know if the need to travel to another city to be attended in a Hospital Clinic for obesity may affect to the adequacy of referrals from Primary Care.

52 213 inhabitants located in the southeast of Castilla-La Mancha are attended in our hospital. 25 024 inhabitants live in the same city where the hospital is located, but 27 389 live in other cities and these people need to travel between 50 and 60 km to be attended in our Hospital. The study was based on a retrospective design and the following variables were collected: age (years), BMI (kg/m²), type of obesity, adequacy of referrals (BMI ≥ 35 kg/m²), and need to travel to be attended (a patient who lives in the same city where the Hospital is located or in a different city) for each of the patients referred because of their obesity or overweight from Primary Care to our Hospital Clinic in first visit in 2014.

Qualitative variables were expressed as absolute and relative frequency. Quantitative variables were expressed as mean, standard deviation, and range. The T-Student test