Rev Clin Esp. 2014;214(7):396–402

Revista Clínica Española

www.elsevier.es/rce

CLINICAL UP-DATE

Vitamin D: Present and future☆

M. Varsavsky[a], G. Alonso[b,*], A. García-Martín[c]

[a] Unidad de Endocrinología, Hospital Sant Pau i Santa Tecla, Tarragona, Spain
[b] Departamento de Endocrinología. Humane Especialidades Médicas, Río Cuarto, Argentina
[c] Servicio de Endocrinología y Nutrición, Hospital Universitario San Cecilio, Granada, Spain

Received 17 February 2014; accepted 14 April 2014
Available online 11 June 2014

KEYWORDS
Vitamin D;
Vitamin D deficiency;
Fractures, Stress;
Osteoporotic fractures;
Osteoporosis

Abstract In recent years there has been a growing interest in vitamin D, not only for its important role in the bone mineral metabolism, but also for the extra-osseous effects. Most of the scientific societies consider that deposits are sufficient if the serum concentration of 25-OH vitamin D is above 30 ng/ml and are considered deficient if levels are below 20 ng/ml. The majority of studies found that supplements of calcium plus vitamin D have a positive effect in reducing the risk of fracture and the risk of falls in the elderly, although several specifies that doses should be 700–1000 IU daily. The treatment of the deficit can be performed with vitamin D2, D3 as well as calcidiol or the active metabolite calcitriol. In certain pathologies also selective vitamin D receptor activators can be used.

PALABRAS CLAVE
Vitamina D;
Deficiencia de vitamina D;
Fracturas de estrés;
Fracturas osteoporóticas;
Osteoporosis

Vitamina D: presente y futuro

Resumen En los últimos años se ha producido un creciente interés por la vitamina D, no solo por su importante papel en el metabolismo mineral óseo, sino también por sus efectos extraóseos. La mayoría de las sociedades científicas consideran que los depósitos son suficientes si la concentración plasmática de 25-OH vitamina D está por encima de 30 ng/ml y deficientes si están por debajo de 20 ng/ml. La mayoría de los estudios encuentran que los suplementos de calcio más vitamina D tienen un efecto positivo en la reducción del riesgo de fractura en un 20% aproximadamente y del riesgo de caída en los ancianos, y las dosis deberían ser de 700–1.000 UI diarias. El tratamiento del déficit se puede realizar con vitamina D2, D3 o sus metabolitos activos como el calcidiol o el calcitriol. En ciertas patologías también puede utilizarse los activadores selectivos del receptor de la vitamina D.

☆ Please cite this article as: Varsavsky M, Alonso G, García-Martín A. Vitamina D: presente y futuro. Rev Clin Esp. 2014;214:396–402.
* Corresponding author.
E-mail address: galonso.humane@gmail.com (G. Alonso).

Clinical case

This case concerns a 78-year-old woman with a history of type 2 diabetes mellitus, arterial hypertension, dyslipidemia and osteoporosis who was on treatment with alendronate (70 mg/week), metformin (1700 mg/day) and enalapril (20 mg/day). The patient presented the following serum concentrations: parathyroid hormone (PTH), 130 pg/mL (normal values [NV], 14–72); calcemia, 9 mg/dL (NV, 8.5–10.5); phosphatemia, 3.4 mg/dL (NV, 2.4–4.1); 25-hydroxy vitamin D, 9 ng/mL (NV, >30); and creatinine, 0.9 mg/dL (NV, 0.60–1.2). After analyzing the laboratory results, we arrived at the first diagnostic option that our patient presented hyperparathyroidism secondary to vitamin D deficiency. We then considered the following questions:

- What are the possible causes of the patient's vitamin D deficiency?
- Is there an indication for treatment with vitamin D supplements?
- What vitamin D levels should we establish as an objective for this patient?
- What benefits would our patient receive by normalizing her vitamin D levels?
- Which vitamin D supplements should we use?
- What dosage should we use to normalize her levels?
- What adverse effects could the patient experience from vitamin D supplements?

Vitamins are essential substances that the body cannot synthesize in sufficient concentrations and that therefore must be obtained through dietary intake. In this regard, vitamin D would be better defined as a prohormone, given that it is mostly produced in the epidermis after exposure to sunlight. Subsequently, successive processes of hydroxylation generate vitamin D's active metabolite. To maintain appropriate vitamin D levels, a healthy individual with sufficient sun exposure does not need to eat food with vitamin D. The most important and studied action of vitamin D is related to bone mineral metabolism. Sustained vitamin D deficiency causes rickets in children and osteomalacia in adults.[1] There has been a growing interest in vitamin D in recent years, not only because of its significant role in bone mineral metabolism, but also because of its increasingly known extraskeletal effects. Various diseases such as cancer, multiple sclerosis, type 2 diabetes mellitus, inflammatory bowel disease, other autoimmune diseases, arterial hypertension and various cardiovascular diseases could be related to low serum vitamin D concentrations.[2] A high prevalence of vitamin D deficiency or insufficiency has been observed in various populations, both healthy and sick. Vitamin D deficiency can have an extrinsic (lack of solar exposure or supply) or intrinsic (absorption or metabolism disorders) origin (Table 1).[3]

Table 1 Pathogenic mechanisms involved and causes of vitamin D deficiency.

Extrinsic
- Inadequate dietary intake
- Little exposure to the sun
- Use of creams with ultraviolet radiation filters (sun protection factor >8)
- Skin hyperpigmentation

Intrinsic
- Advanced age (reduced cutaneous vitamin D synthesis)
- Malabsorption
  - Gastrectomy (total, partial, gastric bypass)
  - Celiac disease
  - Primary biliary cirrhosis
  - Crohn's disease
  - Pancreatic insufficiency (e.g., cystic fibrosis)
  - Treatment with cholestyramine
  - Chronic cholestasis
- Increased vitamin D catabolism
  - Anticonvulsants
  - HIV antiretroviral agents
  - Tuberculostatics agents
  - Hyperparathyroidism
  - Paget's disease of bone
- 25-hydroxy hepatic deficiency
  - Severe chronic liver disease
- Renal 1α-hydroxylation deficiency
  - Chronic renal failure
  - Vitamin D-dependent rickets – type I
- Renal loss of 25-hydroxy vitamin D
  - Nephrotic syndrome
- 1.25-OH-vitamin D receptor abnormalities
  - Vitamin D-dependent rickets – type II

Assessment of vitamin D levels in the body

The best method for determining the body state of vitamin D deposits consists of measuring the serum concentration of 25-hydroxy-vitamin D. The hepatic production of 25-hydroxy-vitamin D is substrate-dependent, is not hormonally regulated and has a long half-life (2–3 weeks).

A fundamental problem in determining 25-hydroxy-vitamin D levels lies in the precision and reproducibility of available biochemical methods. Until fairly recently, the measurement of 25-hydroxy-vitamin D was restricted to research institutions, which employed methods based on protein competition or high-performance liquid chromatography (HPLC). Other methods were later validated for healthcare use, such as radioimmunoassay, immunoenzyme methods and chemiluminescence. The dissemination of HPLC technology in tandem with mass spectrometry (LC–MS/MS) has improved the performance of 25-hydroxy-vitamin D measurements and is enabling the standardization of results with conventional techniques. However, the coefficients of variation among the various laboratories that use HPLC and mass spectrometry are still high (20%), due to the lack of standardized procedures for the analysis of vitamin D. Given the variety of applied methods, a number of authors suggest conducting a follow-up of every individual patient using the same methodology for all cases.[4]