

Sosa Henríquez M^{1,2}, Gómez de Tejada Romero MJ¹

1 Universidad de Las Palmas de Gran Canaria - Instituto Universitario de Investigaciones Biomédicas y Sanitarias - Grupo de Investigación en Osteoporosis y Metabolismo Mineral - Las Palmas de Gran Canaria (España)

2 Hospital Universitario Insular - Unidad Metabólica Ósea - Las Palmas de Gran Canaria (España)

3 Universidad de Sevilla - Departamento de Medicina - Sevilla (España)

Vitamin D in the 21st century. Beyond osteoporosis

DOI: <http://dx.doi.org/10.4321/S1889-836X2017000200001>

Correspondence: Manuel Sosa Henríquez - Universidad de Las Palmas de Gran Canaria - Grupo de Investigación en Osteoporosis y Metabolismo Mineral - C/Espronceda, 2 - 35005 Las Palmas de Gran Canaria (Spain)
e-mail: manuel.sosa@ulpgc.es

Introduction

Interest in vitamin D has increased dramatically in recent years. As shown in figure 1, the number of journal articles published and indexed in the PubMed database has multiplied almost by 4 from 2000 to 2016.

Vitamin D, which maintains its name by habit or history related to its discovery, is actually a complex hormonal system¹, its structure being very similar to that of steroid hormones.

Hormone D, as it should actually be termed², began to be studied and related to bone mineral metabolism. It is well known that its deficiency produces a skeletal disease in children referred to as rickets and osteomalacia in adults³. Subsequently and already in the 20th century, it was verified that practically all the cells of the organism have receptors for this hormone. Thus our knowledge was expanding into other pathophysiological and clinical aspects, including osteoporosis³⁻⁵ as in other bone diseases. The relationship of vitamin D to these processes has been termed "extra-bone effects of vitamin D"^{3,6-9}.

Nowadays we have a better understanding of vitamin D's relation with muscle and falls¹, with diabetes mellitus, both type 1 and 2¹⁰, with arterial hypertension and ischemic heart disease¹¹, immune system and autoimmune diseases¹², respiratory infections¹³, Bronchial asthma¹⁴ or cancer^{3,7,8,15}, to name some of the relationships on which an increasing number of articles have been published.

Vitamin D has a complex, delicate and well-known regulatory system, according to whether its cutaneous synthesis or its ingestion produces vitamin D₃ or cholecalciferol, which is transported to the liver where it is hydroxylated in 25-hydroxyvi-

tamin D or calcifediol, this being the metabolite that best measures the organic reserve of vitamin D. Subsequently, in the kidney, a new hydroxylation takes place that leads to the formation of the active metabolite of the hormone that is 1,25 dihydroxycalciferol or calcitriol^{1,16-19}.

These differences should be taken into account, as there is no established bioequivalence between the different metabolites, nor are vitamin D₃ or cholecalciferol, 25-hydroxyvitamin D or calcifediol²⁰ nor the final metabolite, 1,25 hydroxyalcalciferol, which by their potency and therapeutic limitations, its pharmacological presentation would require an inspection stamp for its prescription.

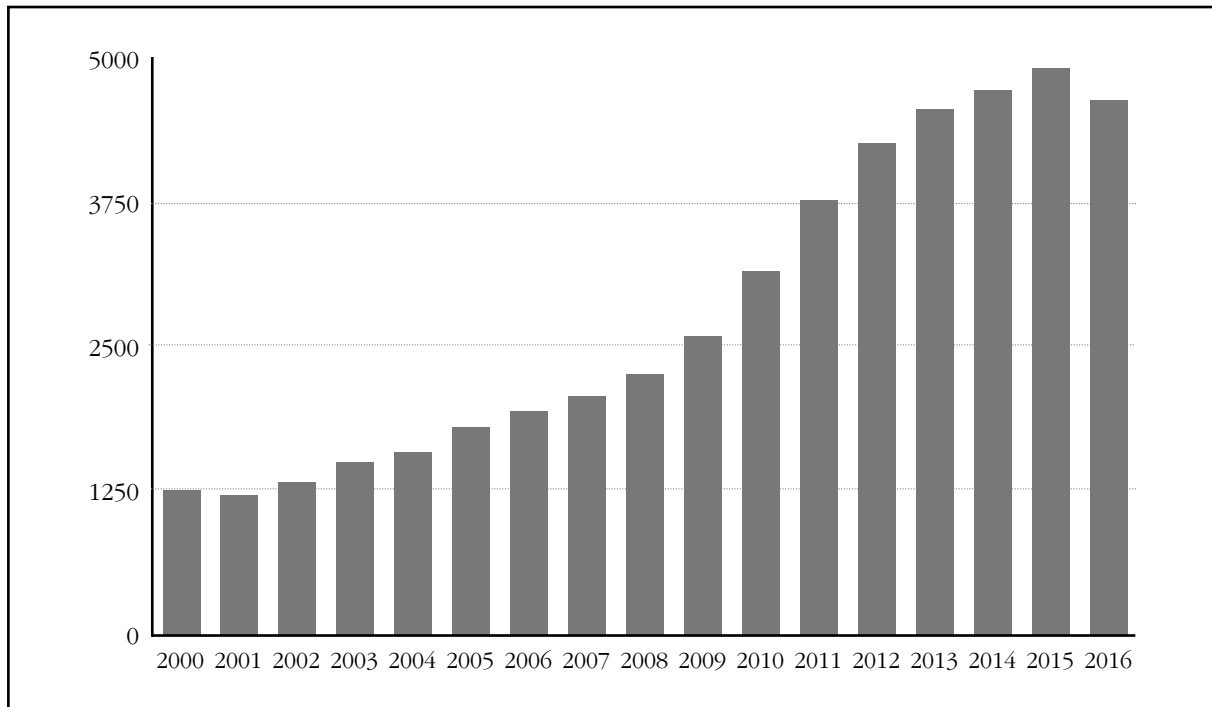
In this paper, we intend to make an update on some of the aspects that have seemed most interesting about vitamin D, such as the prevalence of vitamin D deficiency in our country, something that from a theoretical point of view would be difficult to accept in our "sunny Spain", to other less well-known aspects like vitamin D deficiency in children, as well as a different view of vitamin D in women.

We complete the paper with an update on vitamin D and its use in the prevention and treatment of osteoporosis and fractures due to fragility, and other aspects such as endocrine and rheumatic diseases.

The collaborators are all authors of recognized prestige and great experience in the field of bone mineral metabolism. We can only hope that readers find the paper useful for better treatment of patients, which is medicine's *raison d'être*.

Conflict of interest: The authors declare they have no conflict of interest regarding this work.

Figure 1. Publications in PubMed including only the term "vitamin D" from January 1, 2000 to December 31, 2016



Bibliography

1. Bischoff-Ferrari H. Vitamin D - from essentiality to functionality. *Int J Vitam Nutr Res.* 2012;82(5):321-6.
2. Norman AW. From vitamin D to hormone D - fundamentals of the vitamin D system. *Am J Clin Nutr.* 2008;88(suppl):491s-9s.
3. Holick M. Vitamin D deficiency. *N Engl J Med.* 2007; 357(3):266-81.
4. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc.* 2006;81(3):353-73.
5. Holick MF. Resurrection of vitamin D and rickets. *J Clin Invest.* 2006;116(8):2062-72.
6. Lips P, Duong TU, Oleksik A, Black D, Cummings S, Cox D, 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(3):1212-21.
7. Bikle DD. Extra-skeletal actions of vitamin D. *Ann New York Acad Sci.* 2016;1376:29-52.
8. Holick MF, Chen TC. Vitamin D deficiency: a worldwide health problem. *Am J Clin Nutr.* 2008;87:1080-6.
9. Holick MF. Vitamin D status: measurement, interpretation and clinical application. *Ann Epidemiol.* 2009;19(2):73-8.
10. Al-Timimi DJ, Ali AF. Serum 25(OH) D in diabetes mellitus type 2: relation to glycaemic control. *J Clin Diagnostic Res.* 2013;7(12):2686-8.
11. Alkhatatbeh MJ, Abdul-Razzak KK, Khasawneh LQ, Saadeh NA. High prevalence of vitamin D deficiency and correlation of serum vitamin d with cardiovascular risk in patients with metabolic syndrome. *Metab Syndr Relat Disord.* 2017 Mar 27. [Epub ahead of print].
12. Broder AR, Tobin JN, Putterman C. Disease-specific definitions of vitamin D deficiency need to be established in autoimmune and non-autoimmune chronic diseases: a retrospective comparison of three chronic diseases. *Arthritis Res Ther.* 2010;12(5):1-8.
13. Martineau A, Jolliffe D, Hooper R, Greenberg L, Aloia J, Bergman P, et al. S102 Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of individual participant data. *Thorax.* 2016;71(Suppl 3):A60-1.
14. Kim Y-R, Seo S-C, Yoo Y, Choung JT. Are children with asthma in south korea also associated with vitamin D deficiency? *Environ Health Toxicol.* 2017;1-7.
15. Acevedo F, Pérez V, Pérez-Sepúlveda A, Florenzano P, Artigas R, Medina L, et al. High prevalence of vitamin D deficiency in women with breast cancer: the first Chilean study. *The Breast.* 2016;29:39-43.
16. Binkley N, Krueger D, Cowgill CS, Plum L, Lake E, Hansen KE, et al. Assay variation confounds the diagnosis of hypovitaminosis D: A call for standardization. *J Clin Endocrinol Metab.* 2004;89(7):3152-7.
17. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int.* 2005;16(7):713-6.
18. Glendenning P. Measuring vitamin D. *Aust Prescr.* 2015;38(1):12-5.
19. Glendenning P, Inderjeeth CA. Vitamin D: methods of 25 hydroxyvitamin D analysis, targeting at risk populations and selecting thresholds of treatment. *Clin Biochem.* 2012;45(12):901-6.
20. Navarro-Valverde C, Sosa-Henríquez M, Alhambra-Expósito MR, Quesada-Gómez JM. Vitamin D₃ and calcidiol are not equipotent. *J Steroid Biochem Mol Biol.* 2016;164:205-8.