

Vitamin D: A Molecule of Universal Interest and Its Measurement

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Introduction

Vitamin D deficiency is a worldwide health problem that affects not only musculoskeletal health, but also a wide range of acute and chronic diseases. Vitamin D deficiency is the most common nutritional deficiency and likely the most common medical condition in the world. The major cause of vitamin D deficiency has been the lack of appreciation that the body requires 5 to 10 fold higher intakes than is currently recommended by health agencies [1]. There is now overwhelming and compelling scientific and epidemiologic data suggesting that the human body requires a blood level of 25(OH)D above 30 ng/mL for maximum health. There is an epidemic of vitamin D deficiency sweeping across our modern world, and it is an epidemic of such magnitude and seriousness that is not only alarmingly widespread, but a root cause of many serious diseases, such as rickets, MS, cancer, diabetes, osteoporosis, tuberculosis and heart disease. Public interest in vitamin D is rising because there is intense and growing activity in the research community on the functions and benefits of vitamin D. Vitamin D receptor has created new interest into the research circles, as it is present in most of the cells and tissues of human body. People living near the equator who are exposed to sunlight without sun protection have robust levels of 25-hydroxyvitamin D—above 30 ng/ml [2,3]. However, even in the sunny counties like United Arab Emirates where the sun shines is all round the year, vitamin D deficiency is common. Studies from Saudi Arabia, the United Arab Emirates, Australia, Turkey, India and Lebanon, 30 to 50% of children and adults had 25-hydroxyvitamin D levels under 20 ng/ml [4-7]. As the results of new studies become public, people who have been quietly and desperately suffering with health issues are finding vitamin D to be a remarkable solution for them. Vitamin D is actually a steroidal hormone like estrogen or testosterone. It stands alone as the only 'vitamin' the body can produce on its own. Vitamin D is needed by the body to properly use other substances like calcium, magnesium, zinc and boron to build and maintain healthy tissue, skin, bone, teeth and nerves. Vitamin D is called the "Sunshine Vitamin" because the body naturally produces it through exposure of your skin to the sun. Sun is the key source of vitamin D3 as 90% of total vitamin D3 comes from the sun. Lanolin, which is full of cholesterol and fatty acids is often used as a raw material from the skin of furry animals like sheep to extract vitamin D3. A healthy young light-skinned person can generate up to 12,000 IU of vitamin D, with just 20 minutes of sufficient bare skin exposure to a strong noon day sun under good conditions.

Vitamin D (which includes both D2 and D3) carries out essential biologic functions through both an endocrine mechanism and an autocrine/paracrine mechanism. Vitamin D3 is derived from a cholesterol precursor in the skin, 7-dehydrocholesterol(7-DHC). When the skin absorbs UV-B radiation, the precursor is converted to previtamin D3, which undergoes thermally induced transformation to vitamin D3 (cholecalciferol). Vitamin D2 (ergocalciferol) is a synthetic product produced by irradiation of plant sterols asclepius, mushrooms, etc. Asclepius is a plant grown wildy over the mountains of Colorado, USA, and believed as God of medicine and healing in ancient Greek religion.

Metabolism

Vitamin D, whether from the diet or the skin, is metabolized in the liver to 25(OH)D by 25-hydroxylase enzyme. Since 25(OH)D is the most plentiful and stable metabolite of vitamin D in the human bloodstream, it has been accepted as the functional indicator of vitamin D status. 25(OH)D is a prohormone that serves as an immediate precursor to the active form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)2D; calcitriol). A single enzyme, 25(OH)D-1- α -hydroxylase (encoded by CYP27B1), is responsible for production of 1,25(OH)2D, in the kidneys which serves as a high-affinity ligand for the vitamin D receptor (VDR). In its endocrine action, 25(OH)D is converted by hydroxylation in the kidney to its active form i.e. 1,25(OH)2D, which circulates in the blood as a hormone to regulate mineral and skeletal homeostasis. The primary target of 1,25(OH)2D is the intestinal mucosa, in which it directs the calcium transport system to adapt to varying calcium intakes. Extra skeletal role of vitamin D is dependent on the fact that VDR is present in most of the cells and tissues of the human body. Most of the vitamin D research during the last two decades is concentrated on these non classical or autocrine/paracrine pathways.

Measurement of Vitamin D Levels

Status of 25(OH)D is routinely measured at Sheikh Khalifa Medical City with a Waters HPLC 2695 separation module with UV detection using Chromsystems kits (Chromsystems Instruments & Chemicals GmbH, Heimbürgerstrasse, Munich, Germany), by using a modified high-performance liquid chromatography (HPLC) method. This method was used in 2006 for vitamin D testing and successfully modified and applied to measure both the forms of vitamin D (D2 and D3) in the same run [8-10]. The last decade has witnessed a dramatic increase in both clinical and public awareness of the health implications associated with vitamin D status [1]. HPLC method is simple, has high throughput, and is sensitive, accurate and precise for the analysis of serum 25(OH)D2 and 25(OH)D3. Consequently, clinical laboratories are receiving an increasing number of requests to measure vitamin D levels, which has led to the need for highly automated assays. The Roche Diagnostics Vitamin D total assay is a competitive electrochemiluminescence protein binding assay intended for the quantitative determination of total 25-OH vitamin D in human serum and plasma. The assay employs a vitamin D binding protein (VDBP) as capture protein, which binds to both 25(OH)D3 and 25(OH)D2 (Roche Diagnostics, Mannheim, Germany) [4]. The majority of the study population had the D3 form

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of the vitamin (cholecalciferol Roche Diagnostics—Vitamin D total electrochemiluminescence protein binding assay, in a population where the majority have the D2 form of the vitamin D (ergocalciferol) is becoming popular among laboratory workers. The advantages are many over other conventional methods and Roche Diagnostic assay is a fully automated system where vitamin D can be measured on a large number of blood samples at the same time. Several reference laboratories have now switching to Roche-vitamin D total assay and LC-MS/MS, which measure both 25(OH)D₃ plus 25(OH)D₂, quantitatively. The total 25(OH)D, i.e. 25(OH) D₂ plus 25(OH) D₃, is what physicians need to be aware of their patients. A level of 30 ng/mL (75 nmol/L) is now considered to be the preferred healthful level that all children and adults should maintain throughout the year [11-14].

Conclusion

The endocrine pathway of vitamin D has been most useful for understanding its contribution to maintaining plasma calcium and phosphate homeostasis. But the new paradigm now provides a plausible explanation for the observational data that optimal health outcomes are associated with higher levels of serum 25(OH)D than previously considered. Further, basic research in this area will likely to continue elucidating about this most fascinating and universally interested molecule. Research during the last two decades in the field of vitamin D suggests that vitamin D is much more than a nutrient needed for bone health; it is an essential hormone required for regulation of a large number of physiologic functions. All studies, in virtually all nations, irrespective of latitude, sun shine, and/or seasonal variation show that the majority of the world's population has inadequate vitamin D status. It is clear that sufficient levels of serum 25(OH)D are essential for optimizing human health. There is a growing consensus that the optimal range for 25(OH)D values lies above 30 to 32 ng/mL (75-80 nmol/L) for getting maximum benefits of vitamin D.

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