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Vitamin D 3 Deficiency and Bone Resorption – A Review.

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ABSTRACT

Vitamin D deficiency (serum 25 hydroxyvitamin D (25 (OH) D) causes osteomalacia and rickets but there is good proof that lesser degrees of hypovitaminosis D have deleterious effects on bone and other organs. Evidence of impaired mineralization has been found in bone biopsies. Suggestive of vitamin D insufficiency. The increased bone resorption of vitamin D insufficiency is important. Increased bone resorption may lead to osteoporosis and increased bone loss and, increased turnover appear to increase fracture risk in its own. Serum 25 (OH) D levels should be maintained at 50 nmol/L or greater in the elderly to minimize the occurrence of fractures

Keywords: Vitamin D, bone resorption, Vitamin D deficiency.

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INTRODUCTION

Vitamin D plays a major role in physiological processes. Which includes bone and calcium metabolism, immunity, cellular growth and differentiation and cardiovascular function [12] Vitamin D is a secosteroid which is synthesized from 7-dehydrocholesterol, is derived from diet [3]. vitamin D is considered chiefly as a cure for rickets. Rickets occurs in infancy prior to fusion of the epiphyses. When the epiphyses fail to mineralized because of insufficient vitamin D, they become irregular and thickened, and growth is retarded. By 1940 researchers had found both forms of the vitamin (vitamin D2 and vitamin D3), had unraveled much of the mechanism by which it is altered into its active form, and understood its potent result in rickets. [4].

Vitamin D

Vitamin D is a fat-soluble vitamin produced by both plants and animals, it is a hormone that influences the activity of a variety of tissue and organs in response to changes in the amount of metabolic byproducts in the blood. vitamin D interacts with vitamin D receptors (VDRs) on the surface of cells to stimulate the intracellular production of definite proteins that carry out specific vitamin-D–determined effects [5,6]. The most active form of Vitamin D is calciferols The term "vitamin D" is used collectively to identify two molecules: vitamin D2 (ergocalciferol), which is derived from plants and used to fortify foods; and vitamin D3 (cholecalciferol), which is found in fish oils, eggs, cod liver oil, and animal fats. Another important source of vitamin D3 is the skin, where it is formed from provitamin D3 (7-dehydrocholesterol) in the plasma membrane of keratinocytes. Exposure towards ultraviolet radiation (UV-B; wavelength: 290-315 nm) [5,6] Provitamin D3 undergoes photolysis and is transformed into previtamin D3. The temperature of the skin, then triggers the transformation of previtamin D3 to vitamin D3.

Bone Remodeling

Remodeling in response to rapid changes in mechanical stress and serum calcium levels is mostly carried out by osteoblasts and osteoclasts primarily in the endosteum, and to a lesser degree, in the periosteum. Osteoblasts synthesize and secrete osteoid, the organic matrix of bone that undergoes rapid mineralization to form a new, functional bone. Osteoclasts are multinucleated cells that contribute in bone resorption. It is critical for bone resorption and deposition to occur at more or less the same rate to prevent a loss of bone strength. Both rates decline with age, a incident that is most evident initiation in midlife, but may begin during early adulthood. Resorption usually begins when osteocytes spot the damaged or deformed bones, then send signals to regulate the amount of remodeling appropriate for the change in load or pressure. We expect that assists in the damaged tissue undergo apoptosis, which triggers the release of biochemical and chemotactic signals that are detected by osteoclasts, which actually remove the damaged tissue. Osteoclastogenesis is mediated by vascular growth factors, osteoblast precursors, macrophages, and activated T cells. Osteoclasts are formed from precursors that are released into the bloodstream as monocytes, fuse to form multinucleated cells, and aggregate at bone resorption sites.

Metabolism of Vitamin D

Vitamin D is transported in the bloodstream mainly by a vitamin D-Binding Protein (DBP) which is synthesized in the liver, and to a much lesser extent by albumin. Vitamin D is transformed into its physiologically active form—1,25 dihydroxyvitamin D (1,25[OH] D) — through 2 hydroxylation reactions [3]. The first takes place in the liver, where vitamin D undergoes 25-hydroxylation, a reaction that is catalyzed by cytochrome P450-like enzymes in the hepatic mitochondria and microsomes [6]. This reaction produces the vitamin D metabolite 25-hydroxyvitamin D (25 [OH]D), the main form of vitamin D circulating in the blood and stored in Body tissues. The half-life for this metabolite is relatively long – approximately 2 to 3 weeks in healthy adults – and this hydroxylation step is relatively unregulated. Thus, serum 25 (OH) D levels closely reflects substrate availability, making it the metabolite of choice for evaluating
Vitamin D status [7,8].

The second hydroxylation reaction takes place in the kidney proximal tubule cells, where 25 (OH) D is transformed into the purely active molecule, 1,25 (OH) 2D in a reaction catalyzed by 25 (OH) D-1-alpha-hydroxylase, a mixed-function microsomal oxidase [7-9]. The metabolites of this reaction are secreted into bile and are reabsorbed through the hepatic circulation.. The calcium absorption is improved by vitamin D and by parathyroid hormone (PTH), which increases calcium levels in the blood by promoting its release from bone [5, 8].

Mechanism of Action

The primary bone-related function of vitamin D is to maintain calcium homeostasis. Vitamin D activity begins when 1,25 (OH) 2D binds with a vitamin D receptor (VDR) [6].

This receptor mediates the regulation of gene expression they form a complex with DNA sequences that express proteins which control gene expression [5]. The VDR/DNA complex induce the expression of proteins that participate in bone formation, calbindin *9K* an intestinal calcium-binding protein that is facilitating the active transport of calcium the bone matrix proteins osteocalcin and osteopontin, which are secreted by osteoblasts and help calcium bind to the bone matrix during the bone mineralization process and type I collagen, which is also secreted by osteoblasts to form the primary component of the bone matrix and undergo calcification to form mature bone. VDR also suppresses the transcription of genes that express parathyroid hormone (PTH), and since PTH promotes the mobilization of calcium from bone, VDR thus inhibits resorption. However, VDR can also induce up-regulation of the RANK ligand, which promotes the differentiation and activity of osteoclasts, which participate in resorption. By balancing the expression of gene products that favor bone production with those favoring bone resorption, vitamin D allows bone to adapt rapidly to changes in load and tension while maintaining bone strength [6, 8, 9].

Vitamin D deficiency

Severe vitamin D deficiency causes rickets in children and osteomalacia in adults, is associated with hypocalcemia, impaired mineralization of bone, muscle weakness and deformity, and produces the characteristic radiographic findings of flaring of the epiphyses

in children, Looser's zones (fissure fractures) and ill-defined trabeculae [10]. Bone biopsies show increased amounts of unmineralized bone matrix (osteoid) and decreased mineralization time. These changes are related to serum 25 hydroxyvitamin D levels below 12.5 nmol/L [11]. sunlight generated vitamin D from 7 dehydrocholesterol in the skin, now it appears that significant bone disease occurs with 25(OH)D levels above 12.5 nmol/L and inside the previous reference interval of about 40–160 nmol/L.

Vitamin D and bone resorption

Vitamin D deficiency (osteomalacia) causes an increase in bone resorption (rise in PTH caused by hypocalcemia) and a rise in serum ALP is considered an important feature of the syndrome. However, bone markers are also raised in patients with vitamin D insufficiency [12]. There was an inverse relationship between serum 25 (OH) D and serum alkaline phosphatase (ALP). Sahota et al. Reported that UK women with vitamin D insufficiency had higher serum bone specific alkaline phosphatase and osteocalcin and higher urine hydroxyproline and deoxypyridinoline than patients with normal 25 (OH) D levels [13]. Lips et al. Reported in an international study of 7546 osteoporotic women that serum ALP was higher in those with lower 25(OH) levels [14] .

CONCLUSION

Vitamin D3 plays a major role in preventing bone resorption,rickets and osteomalacia. The $1,25(OH)_2D_3$-VDR system plays a role in calcium homeostasis and its dysfunction may lead to bone resorption and oral disease.

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