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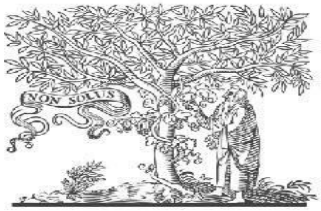

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IMPACT OF VITAMIN-D DEFICIENCY ON MUSCLE ATROPHY

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ABSTRACT
Skeletal muscle weakness and smaller muscle fibre size are also symptoms of vitamin D deficiency, which is prevalent and epidemic. Treatment with vitamin D in humans has been demonstrated to increase skeletal muscular strength, and vitamin D supplementation in animal models has been proven to cure the malfunctioning of skeletal muscles found in vitamin D insufficiency. Adipose tissue contributes greatly to systemic metabolism by acting as a reservoir for energy and a source of adipocytokines. Obesity-related adipose tissue dysfunction is characterised by hypertrophied adipocytes, increased inflammation, hypoxia, and decreased angiogenesis. Obese persons often have insufficient vitamin D levels, despite the fact that adipose tissue is one of the most significant stores of the vitamin. In this review, we show how vitamin D regulates many processes in adipose tissue, the dysregulation of which leads to metabolic disorders. Vitamin D has been found to have direct impacts on the proliferation and differentiation of muscle precursor cells, and its presence has been shown in animal models.

KEYWORDS: Vitamin-D, Muscle Atrophy, muscle weakness

INTRODUCTION

It has been shown that vitamin D is an essential supplement for the prevention of rickets because it aids in the absorption of calcium and phosphate from the diet. Mineral homoeostasis, which is crucial for metabolic activities and bone mineralisation, is maintained in part by vitamin D digestion of calcium and phosphate. Consuming meals rich in calcium is the primary means by which a live organism meets its calcium needs; if this is inadequate, the body will produce calcium from bone and reabsorb calcium via the kidneys. The conventional vitamin D-receptive tissues are the bones, the stomach, the kidneys, and the parathyroid glands; in this instance, vitamin D initiates skeletal repercussions. The prostate, breast, immunological cells, skeletal muscle, cardiac tissue, parathyroid glands, skin, and the brain are just some of the many organs that react to vitamin D. Vitamin D and the protein 1-hydroxylase have further effects on the skeleton, and each of these tissues has a vitamin D receptor (VDR). There are two ways in which vitamin D has an impact on cells: hormone motioning, in which the biologically active structure travels through the circulation to reach target cells, and autocrine/paracrine motioning, in which privately created vitamin D3 influences cells in its immediate vicinity.

VITAMIN D

The regulation of calcium and phosphate balance and bone growth and maintenance is one of vitamin D's primary functions. In physiology, the 1,25-dihydroxyvitamin D [1,25(OH)2D3)] hormone interacts to the vitamin D receptor (VDR), a protein that belongs to the atomic receptor superfamily (2, 3). Again, 1, 25(OH)2D3 interaction to its receptor leads to protein production (4). It's common knowledge that vitamin D aids in the functioning of the digestive tract, kidneys, bones, and parathyroid glands (1). Over the last several decades, vitamin D's importance in a variety of human tissues, particularly skeletal muscle, has become more apparent (2). Clinical investigations of the relationship between vitamin D and muscle function have shown that a deficiency in vitamin D leads to muscle weakness in osteomalacia in adults and hypotonia in babies (5, 6). Deficiency in vitamin D has been associated to myopathy in several studies (7). Low-dose vitamin D supplementation reduced hip fractures and falls among the elderly (8). He found evidence of type II muscle fibre degeneration in eight out of eleven instances using muscle biopsy samples from persons with vitamin D deficiency and proximal myopathy. Vitamin D's direct significance in muscle tissue was further supported by the discovery of the VDR in muscle cells.

Vitamin D3 may potentially stimulate non-genomic activities with a time scale of milliseconds to minutes. This system incorporates the activation of the cAMP-protein kinase-adenylate cyclase signal transduction pathways. There are two signal transduction routes at play here: a and the phospholipase C-diacylglycerol-inositol (1,4,5)-trisphosphate-protein kinase C one. Raf (rapidly accelerated fibrous sarcoma)/MAPK, which are considered second couriers, are of special significance since they may be engaged in cross-talk with the core. Transcaltachia, the fast acceleration of intestinal calcium transport, is one of the earliest and most noteworthy nongenomic activations. It was found that this influence was felt by the keratinocytes of the epidermis and the chondrocytes of the bone development plate. The vitamin D3 receptor was discovered using a VDR architecture that allowed for the discovery of agonists with the potential to induce nongenomic outcomes. This investigation also includes a thorough analysis of the relationship between vitamin D3 and MARRS (a film-related rapid reaction steroid binding protein). The caveolae/lipid pontoons have a layer that houses receptors for kinases, phosphatases, and ion channels.

Vitamin D3 has a significant effect on immunological function (cholecalciferol). Specifically, keratinocytes, which make up the mucocutaneous barrier, upregulate VDR and 1-hydroxylase expression after skin damage to promote immunological responses. The actions of monocytes and macrophages after exposure to Mycobacterium TB or lipopolysaccharides are quite similar. An increase in the production of cathelicidin and -defensin 2 may have antibacterial effects and boost the body's resistance to infection under any conditions. Initiated T and B cells may independently control cytokine and immunoglobulin production and may respond locally to vitamin D3 supplied by monocytes or macrophages. Vitamin D3's many impacts on the immune system are

crucial in the battle against terminal diseases. Vitamin D3 provides natural resistance, which is notably useful against tuberculosis and other viral infections of the upper respiratory tract. Antibacterial effects of vitamin D have been shown, and vitamin D deficiency has been linked to decreased health and longevity. Multiple strategies exist for lowering the likelihood of contracting an infection, such as regulating antimicrobial production, limiting the severity of local immune and inflammatory responses, enhancing the effectiveness of direct attacks on living organisms, and guiding these responses. Therefore, vitamin D offers a minimal preventative and maybe rehabilitative option, either alone or in addition to conventional treatments. Studies in the lab have connected time spent in the sun and the body's ability to produce vitamin D3 to an overall reduction in the incidence of autoimmune diseases such type 1 diabetes, MS, and Crohn's. Several chronic autoimmune diseases, including inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and type 1 diabetes, have recently seen significant increases in their overall prevalence. Blood vitamin D levels seem to be inversely related to corticosteroid use in children with asthma.

Vitamin D: Production, Metabolism And Mechanisms Of Action

Vitamin D is available in two different forms (D2 and D3), which are chemically distinct due to their unique side chains. While the binding to vitamin D binding protein (DBP) and subsequent metabolism are affected by these structural changes, the biological action of the active metabolites is similar. UV light fractures the B ring of 7-dehydrocholesterol to make pre-D3, which the body then converts into vitamin D3. With sustained UV irradiation, pre-D3 isomerizes to tachysterol and lumisterol. D3, which is coupled to DBP, is preferentially taken from the skin. Vitamin D, whether absorbed via the skin or the digestive tract, is metabolised into 25OHD by the liver and other tissues. Numerous enzymes are capable of 25-hydroxylase activity, however CYP2R1 is pivotal. The enzyme CYP27B1 is responsible for the conversion of 25OHD to 1,25(OH)2D, a process that occurs mostly in the kidney but also in other organs such different types of epithelial cells, immune system cells, and the parathyroid gland. The majority of vitamin D's biological effects are caused by 1,25(OH)2D, its primary hormone form. Parathyroid hormone (PTH) stimulates 1,25(OH)2D synthesis in the kidney, whereas calcium, phosphate, and FGF23 suppress it. To a different extent than in keratinocytes and macrophages, cytokines such tumour necrosis factor alpha (TNF) and interferon gamma (IFN) increase 1,25(OH)2D synthesis in the extrarenal tissues (IFNg). Specifically, 1,25(OH)2D induces the 24-hydroxylase, CYP24A1, which catabolizes 1,25(OH)2D. This enzyme hydroxylates 25OHD and 1,25(OH)2D at position 24 to produce 24,25(OH)2D and 1,24,25(OH)3D, respectively. Although 24,25(OH)2D and 1,24,25(OH)3D have their own biological activities, 24-hydroxylation is often the initial step in the catabolism of these active metabolites to the ultimate end product of calcitroic acid. One of the products of CYP24A1's 23-hydroxylase activity is not the same as the

one produced by the enzyme's other hydroxylase activities. The CYP24A1 enzyme has both 23-hydroxylase and 24-hydroxyase activity, however the 24-hydroxyase activity is more prevalent in humans. Expression of CYP24A1 is widespread, similar to that of CYP27B1. This feedback system, in which CYP24A1 is stimulated by 1,25(OH)2D in most tissues, is crucial for preventing vitamin D toxicity. To the contrary of their effects on CYP27B1, PTH inhibits CYP24A1 in the kidney, whereas FGF23, calcium, and phosphate all promote it. Other tissues, however, show no evidence of such control. Due to the lack of or deficiency in CYP24A1 in macrophages, hypercalcemia and hypercalciuria caused by excess 1,25(OH)2D may develop without the counter control by CYP24A1. This is especially true in granulomatous illnesses like sarcoidosis, in which 1,25(OH)2D production is raised in macrophages.

Metabolism

Vitamin D3, once synthesised in the epidermis, has to be further digested before it can be used. Although 25-hydroxylation enzyme activity is most often seen in the liver, it may be present in other tissues as well. The 25-hydroxylase family, as you'll see, is rather enormous. Standard vitamin D is 25-hydroxyvitamin D (25OHD). The vast majority of vitamin D's biological effects are due to 1,25(OH)2D, its most potent metabolite. However, vitamin D metabolites need further hydroxylation at the 1 position by the enzyme CYP27B1 to achieve maximum biological activity. While 25-hydroxylase is present in many different types of cells, 1 hydroxylation is only seen in the kidney. Both 25OHD and 1,25(OH)2D may have all 24 of their hydroxyl groups hydroxylated. The metabolite or analogue may be activated since 1,25(OH)2D and 1,24(OH)2D have similar physiological potency and 1,24,25(OH)3D has activity approximately 1/10 that of 1,25(OH)2D. The 24-hydroxylation of 25OH-containing metabolites, on the other hand, leads to further destruction of these molecules. In the following paragraphs, we'll go into further detail about each answer..

Cutaneous Production of Vitamin D_3

The vitamin D precursor 7-dehydrocholesterol is produced through the Kandutsch-Russell cholesterol pathways (DHC). Many factors, including vitamin D and cholesterol, regulate 7-dehyrocholesterol reductase, the enzyme responsible for converting 7-DHC to cholesterol. This allows for a greater breakdown of 7-DHC and a more efficient conversion to vitamin. The physiologic regulation of this route was not well known until the work of Holick and his colleagues. 7-DHC irradiation resulted in the production of pre-D3 (which subsequently undergoes thermal rearrangement of the triene structure to yield D3), lumisterol, and tachysterol. They discovered that pre-D3 forms fast in the presence of UV or solar irradiation (with maximal effective wavelengths between 290 and 310), and that its concentration may peak within hours. By exposing pre-D3 to ultraviolet light, two compounds are created: lumisterol and tachysterol. The time required to attain this maximum concentration of pre-D3 is correlated with both the degree of pigmentation on the epidermis and the intensity of the exposure, although neither

of these factors really affects the concentration itself. Although pre-D3 levels reach a maximum, the accumulation of inert lumisterol continues. Not only does pre-D3 production occur, but so does tachysterol, however it does not accumulate with time spent in the sun. Reduced amounts of pre-D3 may cause the body to convert lumisterol back into pre-D3. Pre-D3 is converted to D3 at 37oC in the absence of D3. Because of the time required for the skin to undergo the thermal conversion from pre-D3 to D3 and the conversion of lumisterol to pre-D3, even short exposure to sunlight is expected to result in a prolonged synthesis of D3 in the skin. Due to the photoconversion of pre-D3 to lumisterol and D3's own photoconversion to suprasterols I and II and 5,6 transvitamin D3, extended exposure to sunlight would not result in the production of toxic D3.

Transport in Blood

Vitamin D metabolites are mostly transported via DBP (vitamin D binding protein) and albumin (12-15 percent). In contrast to vitamin D metabolites, DBP is only around 2% saturated at normal concentrations of 4-8 M. The vitamin D metabolites 25OHD, 24,25(OH)2D, and 1,25(OH)2D all have a high affinity for DBP, therefore only 0.03 percent of each is free under normal circumstances. Liver disease and nephrotic syndrome both cause decreased DBP and albumin levels, which in turn decreases the total 25OHD and 1,25(OH)2D levels without necessarily affecting the free concentrations. Acute illness also lowers DBP levels, which might make assessing total 25OHD levels difficult. Earlier studies utilising monoclonal antibodies showed that DBP levels were lower among African Americans, but this conclusion was not confirmed using polyvalent antibody-based testing. Hypercalcemia may result from vitamin D intoxication without an increase in 1,25(OH)2D levels.

Most cells are unable to use vitamin D metabolites that are bound to DBP because of this. Therefore, the free hormone hypothesis suggests that the unbound concentration is critical for cellular uptake. DBP acts as a storage location for vitamin D metabolites, but it is the free concentration that enters cells and exerts physiologic action, as shown by studies in mice with the DBP gene deleted or in humans with a mutation. Vitamin D metabolites are likely completely unbound or bioavailable in DBP knockout mice. These mice have extremely low amounts of 25(OH)D and 1,25(OH)2D in their blood, but they do not show signs of vitamin D insufficiency until they are given a vitamin D-deficient diet. 1,25(OH)2D levels and vitamin D action markers, including intestinal TRPV6, calbindin 9k, PMCA1b, and renal TRPV5, are normal in DBP knockout mice. Recently, a family was found to have lost a significant chunk of their DBP gene's coding region (along with the adjacent NPFFR2 gene). After vitamin D therapy, the proband's 25OHD, 24,25(OH)2D, and 1,25(OH)2D levels were low, but his calcium, phosphate, and parathyroid hormone (PTH) were normal (oral or parenteral). Quantities of free 25OHD were within the normal range. When comparing the proband and the normal sibling, the carrier sibling showed higher levels of vitamin D metabolites. Studies in humans and DBP null mice demonstrate

that DBP serves as a circulatory reservoir for vitamin D metabolites. DBP levels, and therefore total 25OHD levels, may be affected by liver sickness, nephrotic syndrome, pregnancy, and inflammatory conditions, thus it is debatable whether the free concentration of 25OHD, for example, is a better marker of vitamin D nutritional status than total 25OHD. The megalin/cubilin complex is present in the kidney, placenta, and parathyroid glands, and it may be responsible for transporting vitamin D metabolites linked to DBP into cells. This may have a function in the supply of vitamin D to the foetus and the regulation of PTH secretion in addition to reducing renal losses. Shorter life span and osteomalacia are seen in megalin/cubilin deficient mice, indicating a role in vitamin D transport into cells engaged in vitamin D signalling.

CONCLUSION

Vitamin D, which was discovered in 1920, quickly became known as a vital nutrient for bone and intestinal calcium homeostasis. A decade and a half later, in 1932, the vitamin D molecule's chemical structure was finally decoded and it was discovered to be a steroid. Though vitamin D has long been known to work as an endocrine gland in the body, it wasn't until the late 1960s that researchers realised that it was also a precursor of a novel steroid hormone,1,25(OH)2-vitamin D3 [1,25(OH)2D3]. vitamin d receptors (VDR) are found in nearly all tissues and cells in the body. In addition, some cells have enzymes that can convert 25-hydroxyvitamin D (the primary form in circulation) into the active form, 1,25-dihydroxyvitamin D (the active form). These findings suggest that vitamin d serves a purpose in the body that extends beyond calcium homeostasis. The vitamin D receptor (VDR) was first found in the gut, bone, kidney, and parathyroid glands, all of which are involved in mineral homeostasis. The VDR has lately been found in a wide range of tissues and cell types, including skin, placenta, skeletal muscle, adipose tissue, pancreas, breast, prostate, colon, and immune cells. There is a wide variety of biological responses to 1,25(OH)2D3 in these non-classic vitamin D target organs.

REFERENCES

[1] Abbas MA: Physiological functions of Vitamin D in adipose tissue. J Steroid Biochem Mol Biol 2017; 165(pt B): 369–381.

[2] Abbas, Manal. (2016). Physiological Functions of Vitamin D in Adipose Tissue. The Journal of Steroid Biochemistry and Molecular Biology. 165. 10.1016/j.jsbmb.2016.08.004.

[3] Adriana S. Dusso, et al (2005) - Vitamin D. Am J Physiol Renal Physiol 289: F8–F28, 2005; doi:10.1152/ajprenal.00336.2004.

[4] Ahmad R, Al-Mass A, Atizado V, Al-Hubail A, Al-Ghimlas F, Al-Arouj M, Bennakhi A, Dermime S, Behbehani K: Elevated expression of the toll like receptors 2 and 4 in obese individuals: its significance for obesity-induced inflammation. J Inflamm (Lond.) 2012; 9: 48.

[5] Ahn J, Yu K, Stolzenberg-Solomon R, Simon KC, McCullough ML, Gallicchio L, et al: Genome-wide association study of circulating

vitamin D levels. Hum Mol Genet 2010; 19: 2739–2745.

[6] Al-Daghri NM, Al-Attas OS, Alkharfy KM, Khan N, Mohammed AK, Vinodson B, et al: Association of VDR-gene variants with factors related to the metabolic syndrome, type 2 diabetes and vitamin D deficiency. Gene 2014; 542: 129–133.

[7] Al-Daghri NM, Guerini FR, Al-Attas OS, Alokail MS, Alkharfy KM, Draz HM, et al: Vitamin D receptor gene polymorphisms are associated with obesity and inflammosome activity. PLoS One 2014; 9:e102141.

[8] Almesri N, Das NS, Ali ME, Gumaa K, Giha HA: Independent associations of polymorphisms in vitamin D binding protein (GC) and vitamin D receptor (VDR) genes with obesity and plasma 25OHD3 levels demonstrate sex dimorphism. Appl Physiol Nutr Metab 2016; 41: 345–353.

[9] Ambika Ashraf , et al (2009) .Threshold for Effects of Vitamin D Deficiency on Glucose Metabolism in Obese Female African-American Adolescents. The Journal of Clinical Endocrinology & Metabolism, Volume 94, Issue 9, 1 September 2009, Pages 3200–3206, https://doi.org/10.1210/jc.2009-0445

[10] Anderson D, Holt BJ, Pennell CE, Holt PG, Hart PH, Blackwell JM: Genome-wide association study of vitamin D levels in children: replication in the Western Australian Pregnancy Cohort (Raine) study. Genes Immun 2014; 15: 578–583.

[11] Bahrami A, Sadeghnia HR, Tabatabaeizadeh SA, Bahrami-Taghanaki H, Behboodi N, Esmaeili H, et al: Genetic and epigenetic factors influencing vitamin D status. J Cell Physiol 2018; 233: 4033–4043.

[12] Barja-Fernández S, Aguilera CM, Martínez-Silva I, Vazquez R, Gil-Campos M, Olza J, et al: 25-Hydroxyvitamin D levels of children are inversely related to adiposity assessed by body mass index. J Physiol Biochem 2018; 74: 111–118.