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A MULTIDIMENSIONAL STUDY ON METABOLIC IMPACT ON VITAMIN-D AND MUSCLE FUNCTION

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ABSTRACT
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. We still don't know whether the vitamin D receptor exists in fully developed human skeletal muscle or what its role is in the body, and we don't know what effects or processes vitamin D activities have on human skeletal muscle. The primary objective of this study is to develop a strain of vitamin D-deficient rats in order to examine the rate of protein breakdown in that species. Oxidative stress has been related to a wide range of diseases that cause muscular atrophy. Oxidative stress alters the normally stable equilibrium between oxidant production and antioxidant activity. Oxidants may come from a variety of sources, including the enzymes and chemicals that produce them (NO). In addition, the function of several proteolytic mechanisms in vitamin D deficiency-induced muscle atrophy is investigated. By the end of the research, we will know that a lack of vitamin D leads to increased ubiquitin protein pathway activity, which in turn leads to breakdown of muscle protein. Loss of muscle mass is associated with a rise in atrophy marker genes and a fall in myogenic genes due to increased muscle protein breakdown.

KEYWORDS: Multidimensional, Metabolic Impact, Vitamin-D, Oxidative stress

INTRODUCTION

Multiple studies in recent years have shown that vitamin D, specifically the hormone-active form 1',25-dihydroxyvitamin D [1',25(OH)2D; calcitriol], has effects beyond those on the skeleton. Multiple studies have shown these results. Among them include vitamin D hormone's effects on cell division and proliferation, as well as its profound effects on the cardiovascular, focused sensory, endocrine, and immune systems. Vitamin D is a catchall word for two distinct substances, both of which have significant physiological roles in humans. Both vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) belong here; ergocalciferol is generated by certain plants but mostly in organisms, while cholecalciferol is synthesised by the human skin in response to sunlight by the action of UV radiation on 7-dehydrocholesterol. Several factors, such as age, UV exposure (distance, season, use of sunscreens, and clothing), and nationality (skin pigmentation), all have a role in the final outcome of these photographs. All of these problems may interfere with the body's capacity to produce vitamin D in its accessible form.

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Lack of vitamin D3 production is associated with both a sedentary lifestyle and bad habits in general, both of which lead to ill health. On the other hand, too much exposure to sunlight may turn pre-vitamin D and vitamin D3 into harmless photoproducts. Several different body systems work together to produce vitamin D in its active form. First, vitamin D3 must undergo two separate hydroxylation reactions, one in the liver and one in the kidneys. 1,25-dihydroxyvitamin D3 (calcitriol), the end product, is created as a result of the flow to its target tissues and functions in a genomic or nongenomic fashion..

VITAMIN D DEFICIENCY

In the last several years, interest in vitamin D has increased dramatically. More than 80% more enquiries for estimations of blood vitamin D concentration were made between 2000 and 2010, and the number of transactions for vitamin D enhancements grew several times during the same time period. While instances of vitamin D poisoning are uncommon, they do happen. Therefore, both patients and doctors need to understand the dangers of vitamin D excess and how to effectively manage it. Controversy exists over whether or not vitamin D deficiency and adequacy should be described in terms of the ratio of 25(OH)D2 to 25(OH)D3 concentrations. Current recommendations state that a vitamin D level of less than 20 ng/mL (50 nmol/L) constitutes a deficit. Rather than 20 ng/mL (50 nmol/L), most studies have demonstrated that concentrations of 25(OH)D between 30 and 50 ng/mL (75 and 125 nmol/L) or 40 and 60 ng/mL (100 and 150 nmol/L) are necessary for human health (Pludowski et al. 2018). However, people who are deficient in vitamin D should think about the vitamin's bioavailability and, therefore, the protein that binds to vitamin D. (VDBP). Although VDBP binds 85-90% of circulating 25(OH)D and 1,25-dihydroxyvitamin D3, the remaining unbound 25(OH)D is deemed bioavailable (either free or bound to albumin). The remaining 90%-15% of the total quantity of absolute 25(OH)D is made up of free 25(OH)D, which accounts for 1% of the total amount of circulating vitamin D. Bioavailable 25(OH)D is present in the inexactly bound fraction and the free fraction because albumin's affinity for 25(OH)D or 1,25(OH)2D3 is less stable than that of VDBP. Vitamin D bioavailability may vary widely between individuals with a VDBP genetic mutation or VDBP-KD mouse models with low 25(OH)D blood levels. Similarly, ethnic disparities in the population at large have an impact on VDBP. VDBP and serum 25(OH)D levels in Black people were lower (38.10.5 nmol/L) than in White people (64.40.9 nmol/L), although the levels of bioavailable 25(OH)D in Black and White people were similar (2.90.1 and 3.10.1 ng/mL, respectively). Vitamin D toxicity may occur with excessive vitamin D intake. Symptoms such as nausea, heaviness, muscle weakness, polyuria, nephrocalcinosis, and renal failure owing to hypercalcemia were indicative of vitamin D overdose in these patients..

MUSCLE WASTING

Several disorders, such as diabetes, cancer, uraemia, and congestive heart failure, have the serious side effect of causing muscle wasting (15). Muscle wasting is associated with insufficient vitamin D in both humans and animals (8, 16–18). Muscle atrophy occurs when the balance between protein

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breakdown and synthesis is altered (19). Proteolytic pathways in skeletal muscle have been identified as the ATP-ubiquitin-subordinate system, the lysosomal system, and the cytosolic calcium-actuated system (19). Some research suggests that disorders characterised by muscular atrophy are caused by an overactive ATP-subordinate ubiquitin proteasome pathway (UPP) (15, 20 – 22). At its heart is the 26S proteasome, a multisubunit, multicatalytic proteolytic complex in eukaryotes that degrades proteins outside of lysosomes. The 26S proteasome is made up of two different complexes: the supervisory 19S subunit and the cooperative 20S subunit (23). There are three types of proteolytic activity that have been linked to the 20S subunit: chymotrypsin-like (5), trypsin-like (2), and caspase-like (3). (1). To designate proteins for degradation, the 26S proteasome interacts with chains of the 76-amino-acid polypeptide "ubiquitin," which are tagged by a set of three enzymes called E1, E2, and E3 (23, 24). The substrate specificity provided by E3 ligases makes the cycle of protein degradation in cells very well-controlled. (23). The polyubiquitin-labeled protein is degraded to peptides and recycled as soon as ubiquitin reaches the 20S synergist centre. Atrogin-1 (muscle atrophy F-box protein) and MuRF1 (muscle ring finger protein) are two muscle-specific E3 ligases that are crucial for the therapy of muscle atrophy, according to recent studies.

It is unclear what function different proteolytic systems play in vitamin D deficiency-related muscle protein degradation. The presence or absence of VDR in the skeletal muscles of many animals remains unclear (12-14, 27-28). Therefore, it is unclear whether the muscle anomaly associated with D-deficiency is the consequence of decreased vitamin D activities in muscle through the VDR or the effect of systemic abnormalities such as hypocalcemia or high PTH in the blood. Calcium's importance in maintaining healthy muscle and gastrointestinal function is well-documented (29, 30). Calcium's involvement in preventing vitamin D deficiency-related muscular atrophy is uncertain. Because of the known link between vitamin D deficiency and muscle atrophy, the current research set out to investigate the part that vitamin D and calcium play in this condition.

VITAMIN D AND MUSCLE FUNCTION

Osteomalacia was formerly assumed to be a deficiency in vitamin D or another substrate required for the formation of the mineral hydroxyapatite, which is what bones are made of (calcium and phosphate). Younger patients, on the other hand, often have more severe symptoms, including weakness, discomfort, and hypotonia in their muscles. In adults, severe and prolonged vitamin D deficiency (20 nmol/l) may cause a waddling gait, proximal myopathy, and even the requirement for a wheelchair. Muscle wasting due to a lack of vitamin D has been recognised for some time. In his 1645 description of the condition, Whistler said that newborns with rickets had "adaptable, waxy" bones and "heavy, boring" muscles. Subtle changes in muscle function, such as an increased risk of falling, slower muscular atrophy over time, and worse performance in sports, may be seen in those with milder and maybe less persistent vitamin D insufficiency. In this part, we will talk about the many clinical studies and new ideas in biochemistry that

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investigate the molecular effects of vitamin D on skeletal muscle..

1.5.1 Vitamin D and Muscle

- **Physical performance**

For over eighty years, experts have recommended that people who work outside in the sun take measures to boost their fitness. Although variations in vitamin D levels due to exposure to ultraviolet light are not explicitly discussed in these trials, they may have contributed to the observed effects on muscular function. In 1944, German researchers observed that medical interns' performance on a cycle ergometer increased by 13% after being exposed to UV light for a month and a half. A Russian research from 1938 found that college students who were exposed to UV radiation had much faster sprint speeds. (7.4 percentage points vs. a gain of 1.7 percentage points in the control group). An American research including 11 male undergraduates revealed a 19% improvement in cardiovascular endurance after a course of UV radiation..

- **Falls**

Loss of muscle mass and function is known as sarcopenia, and it is a common side effect of ageing. It has been associated with a higher risk of mortality, disability, and falls in the elderly. It is possible that the development of sarcopaenia in institutionalised old people is aided by their vitamin D deficit. As a result of age-related declines in skin's viability for UV-mediated vitamin D synthesis and diminished renal activation of 250HD, levels of vitamin D receptor (VDR) decline in the kidneys and muscles. Weakened muscles from a lack of vitamin D may leave the elderly more susceptible to falls and other injuries. Many people's body mass index (BMI) and vitamin D production decline with age because to obesity. The likelihood of an old person sustaining serious injuries, being hospitalised, and remaining frail rises dramatically after a fall. A broad variety of chronic illnesses that induce weakness and deconditioning contribute to falls in addition to sarcopenia, impaired engine function, postural unsteadiness, visual impedance, and so on.

LINKING BETWEEN VITAMIN D AND ADIPOSE METABOLIC DISORDERS

Adequate vitamin D consumption is necessary for the prevention of rickettsiosis and for the intestinal absorption of calcium and magnesium. In response to ultraviolet (UV) irradiation, the skin produces 7-dehydrocholesterol, the primary source of vitamin D in the body. The 1, 25-dihydroxyvitamin D3 [1, 25(OH)2D3] active form of vitamin D3 plays a crucial role in calcium homoeostasis and metabolism. This variant affects target gene transcription. Vitamin D deficiency or insufficiency is still common, especially in developing countries. Researchers showed that 87.6 percent of 734 youngsters (between the ages of 12 and 18) had vitamin D deficiency. Calcium and bone mineralisation aren't the only things vitamin D is involved in; it also plays a part in adipose tissue, adipogenesis, glucose-insulin balance, cell formation, and more.

Adipose tissue plays a crucial role in energy homoeostasis and glucose metabolism. Fat tissue is an endocrine organ that secretes hormones and fatty acids and proteins. This structure contains many different kinds of cells, including adipocytes at various stages of

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development, fibroblasts, macrophages, and immune cells. Adipose tissue is dominated by a certain kind of cell called adipocytes. Adipose tissue transcription factors (peroxisome proliferator-activated receptor (PPAR), CCAAT enhancer-binding protein (C/EBP), and Kruppel-like factor proteins) are essential for controlling the development of preadipocytes into mature adipocytes. Adipose tissue, where the vitamin D receptor (VDR) is also located, is a potential source of vitamin D abundance. A transcription factor for the vitamin D receptor that has been activated (VDR) Previous studies using animal models have indicated that vitamin D inhibits adipogenesis in 3T3-L1 preadipocytes. Due to its function in regulating insulin synthesis, glucose levels, and inflammation, a deficiency in vitamin D has been associated to obesity, MS, T2DM, and fatty liver disease.

Therefore, we investigated the metabolic issues related to vitamin D deficiency and its association with fat tissue (diabetes, nonalcohol fatty liver, and cardiovascular diseases). This study looked at vitamin D supplementation, vitamin D metabolism in adipose tissue, and increased or reduced vitamin D activation as a means of proving the connection between vitamin D and metabolic disorders. Vitamin D modulation in adipose tissue, vitamin D's effect on adipogenesis, and the metabolic diseases it's related with were also investigated.

VITD AND ADIPOGENESIS

Uncertainty persists over 1,25(OH)2-D's role in adipogenesis. Preadipocytes undergo development into functional adipocytes in a process known as adipogenesis. Increased expression of lipogenesis-related genes like fatty acid synthase (FASN), fatty acid binding protein (FABP), and peroxisome proliferator-activated receptor gamma (PPAR-), the primary transcription factor involved in adipogenic differentiation, is how 1,25(OH)2-D stimulates adipogenesis in human cells. 1,25(OH)2-D, on the other hand, suppresses adipogenesis in mouse 3T3-L1 pre-adipocytes by sequestering the nuclear receptor retinoic X receptor (RXR) and downregulating the transcription factors C/EBP, C/EBP, and PPAR-. However, 1,25(OH)2-D increases FASN and lipoprotein lipase (LPL) expression in human subcutaneous preadipocytes, a process that may be mediated through PPAR- upregulation.

Due to the presence of 1-hydroxylase in mature adipocytes, vitD, both 25(OH)-D and 1,25(OH)2-D, may promote adipogenic differentiation into mature adipocytes. 1,25(OH)2-D also suppresses the expression of uncoupling proteins in vitro, enhances adiponectin production, and upregulates the expression of typical adipocyte genes like leptin. Therefore, VDR directly suppresses the production of uncoupling protein-1 (UCP1), the essential enzyme for uncoupling fatty acid oxidation in brown adipose tissue (AT) (BAT). In reality, this procedure takes place on a cellular level without the involvement of 1,25(OH)2-D, the physiological ligand for the VDR hormone. Leptin, on the other hand, may increase the production of fibroblast growth factor 23, a negative regulator of renal 1-hydroxylase, completing the negative feedback loop. On the other hand, 1,25(OH)2-D has been shown to suppress leptin release in human adipocytes in vitro. Indeed, further research is needed to determine if or how

vitD supplementation affects leptin levels in individuals.

CONCLUSION

When it comes to calcium homeostasis and bone mineralization, vitamin D has long been regarded as an essential nutrient. It has been shown that vitamin D has a significant impact on the function of muscles. There is a favourable link between 25(OH)D3 levels and physical performance in the elderly, as well as a negative correlation with the risk of falls. The structure and function of skeletal muscle may be affected by vitamin D, which is well-known. A lack of vitamin D is associated with a decrease in muscle mass and strength, regardless of age. Vitamin D deficiency has been reported to cause mostly type II muscle fibre atrophy in skeletal muscle biopsy samples. Vitamin D supplementation has been found in human trials to prevent muscular atrophy. Systemic illnesses such as autoimmune disorders, diabetes, cancer, and AIDS are all associated with skeletal muscle wasting/atrophy. Protein degradation and synthesis pathways in the muscle are imbalanced, resulting in muscular atrophy. There are three primary proteolytic systems in the skeletal muscle, which all play a role in protein breakdown. Three pathways are involved: the ubiquitin-proteaseasome, the lysosomal, and the calpain In both animals and humans, a lack of vitamin D has been linked to muscle atrophy. Vitamin D insufficiency causes muscle atrophy, however no research have examined the role of these three proteolytic processes.

[1] 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.

[2] 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.

[3] Bartelt and J. Heeren, "Adipose tissue browning and metabolic health," Nature Reviews Endocrinology, vol. 10, no. 1, pp. 24–36, 2014.

[4] Basit, Sulman. (2013). Vitamin D in health and disease: A literature review. Br J Biomed Sci. 70. 161-72. 10.1080/09674845.2013.11669951.

[5] Battault, Sylvain & Whiting, Susan & Peltier, Sébastien & Sadrin, S & Gerber, G & Maixent, jean michel. (2012). Vitamin D metabolism, functions and needs: From science to health claims. European journal of nutrition. 52. 10.1007/s00394-012-0430-5.

[6] Battault, Sylvain & Whiting, Susan & Peltier, Sébastien & Sadrin, S & Gerber, G & Maixent, jean michel. (2012). Vitamin D metabolism, functions and needs: From science to health claims. European journal of nutrition. 52. 10.1007/s00394-012-0430-5.

[7] Benjamin EJ, Dupuis J, Larson MG, Lunetta KL, Booth SL, Govindaraju DR, et al: Genome-wide association with select biomarker traits in the Framingham

Heart Study. BMC Med Genet 2007; 8(suppl 1):S11.

[8] Best, Cora & Riley, Devon & Laha, Thomas & Pflaum, Hannah & Zelnick, Leila & Hsu, Simon & Thummel, Kenneth & Foster-Schubert, Karen & Kuzma, Jessica & Cromer, Gail & Larson, Ilona & Hagman, Derek & Heshelman, Kelly & Kratz, Mario & de Boer, Ian & Hoofnagle, Andrew. (2020). Vitamin D in human serum and adipose tissue after supplementation. The American Journal of Clinical Nutrition. 113. 10.1093/ajcn/nqaa295.

[9] Bhat, Mehrajuddin & Kalam, Ramesh & Qadri, Syed & Madabushi, Seshacharyulu & Ismail, Ayesha. (2013). Vitamin D Deficiency-Induced Muscle Wasting Occurs through the Ubiquitin Proteasome Pathway and Is Partially Corrected by Calcium in Male Rats. Endocrinology. 154. 10.1210/en.2013-1369.

[10] Bienertová-Vašku J, Zlámal F, Pohoralá A, Mikeš O, Goldbergová-Pávková M, Novák J, et al: Allelic variants in vitamin D receptor gene are associated with adiposity measures in the central-European population. BMC Med Genet 2017; 18: 1–9.

[11] Bikle, Daniel. (2018). Vitamin D Biochemistry and Physiology. 10.1007/978-3-319-73742-3_1.