

Vitamin D and Its Metabolic Functions

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Abstract

Vitamin D is one of the most important vitamins for humankind and %95 of its requirements are acquired by synthesising solar rays on skin. While lack of vitamin D can lead to many diseases, especially cancer, the ones who get vitamin D in an appropriate level, can reduce this risk if they exercise. If, also, vitamin D level is high, obesity risk will be minimized because of eating less thanks to leptin hormone. Vitamin D receptors exist in approximately 40 tissues. The most important effect of vitamin D, which dissolves in fat, is on bone mineralization phosphorus metabolism and calcium. People whose vitamin D level is low, should take nourishment by sources rich in vitamin D instead of helper pills.

Keywords: Vitamin D, Energy, Energy Metabolism, Leptin, Obesity, Exercise

Vitamin D ve Metabolik Fonksiyonları

Özet

Vitamin D, insan için en önemli vitaminlerden biridir ve ihtiyacının %95'i güneş ışınlarının cilde sentezlenmesiyle karşılanır. Vitamin D eksikliği özellikle kanser gibi bir çok hastalığa yol açabileceği için, yeterli bir seviyede vitamin D alanlar eğer egzersiz yaparlarsa bu riski azaltabilirler. Aynı zamanda vitamin D seviyesi yüksek olursa, leptin hormonu sayesinde daha az yemek yeneceği için obezite riski minimuma inecektir. Vitamin D reseptörleri yaklaşık olarak 40 dokuda vardır. Yağda çözünen vitamin D'nin en önemli etkisi kemik mineralizasyonu fosfor metabolizması ve kalsiyum üzerinedir. Vitamin D seviyesi düşük olan kişiler, yardımcı ilaçlar yerine vitamin D açısından zengin olan kaynakların besinlerinden yararlanmalıdır. Vitamin D eksikliğinin kanser, metabolik sendromlar, bulaşıcı, otoimmün ve kardiyovasküler gibi bir çok hastalıkla ilişkisi olduğu bildirilmiştir. Gözlemsel çalışmalarda, endüstrileşmiş ülkeler de dahil olmak üzere dünyanın kuzey bölgelerinde vitamin D eksikliğinin çok yaygın olduğu anlaşılmıştır.

Anahtar Kelimeler: Vitamin D, Enerji Metabolizması, Leptin, Obezite, Egzersiz

Introduction

It's known for a long time that vitamin D takes part in duty of calcium-phosphorus homeostatis and bone metabolism. In the situation of vitamin D deficiency results in the increase of bone resorbtion and secondary hyperparathyroidism completed with ritex and osteomalacia. On the other hand vitamin D is necessary for muscle health, while muschle health is necessary for exercising. It's observed that muscle strenght increases by support of vitamin D1. In the studies about Vitamin D since the beginning of 1980's, it's found out that Vitamin D has an important effects on cell differentiation, proliferation inhibition other than calcium homeostatis of VDR and bone metabolism. Being also important for healthy mineralization of skeleton system, %95 of vitamin D requirement is met by synthesising solar rays on skin. The rest of it is acquired by foods. Its synthesised on skin form is called vitamin D3, taken from foods form is called vitamin D2. However, enviromental factors, geographical situation, season conditions, melanine density on skin, protecting creams and clothing style block acquiring enough vitamin D from the Sun (Muszkat, 2010; Holick, 2002). One should be exposed to sun and leave his hands and face out, he can take advantage of sun rays. Among nourishments that have vitamin D, we can say that animal foods liver and fatty fish, pasta, grains, fruit juice, milk and others have it. Vitamin D is an important vitamin for a healthy life. If not taken enough in diet lists, vitamin D deficiency can exist very easily. In the situations of vitamin D deficiency, there are some symptoms about musculoskeletal system and this results in some musculoskeletal diseases (Holick, 2002; Holick, 2004; Reginato, 1999). Because of being among the vitamins that melt in fat and synthesized in an endogeny biological environment, vitamin D is a group of sterols that have hormones and hormone precursors and has the most important effect on calcium phosphorus metabolism and bone mineralization (Bringhurst, Demay, Krane, Kronenberg, 2005).

Vitamin D receptors are the member of the nuclear hormone receptor super family that includes thyroid hormones, steroids and retinoic acid receptors. In the construction of VDR here are the ligand binding field to which active vitamind D is connected, the bulge field sized with two fingers and binds receptor to DNA and a zinc atom that make these in a stabile situation. There are vitamin D receptors in approximately 40 tissues such as heart, pancreas, muscles, immune system cells, brain and bowel cells (Ozkan, Doneray, 2011; Nemere, Carson, 1998; De Luca, Cantorna, 2001). The normal level of vitamin D is called as serum vitamin D level that blocks the development of ricets or osteomalasi, makes in a normal level of parathormon (PTH) by resulting calcium of diet in absorbtion in an optimal level. Vitamin D levels in 32 ng/mL for matures and 20 ng/mL for children are accepted as normal (Misra, Pacaud, Petryk, Collett-Solberg, Kappy, 2008).

Vitamin D deficiency leads to secondary hyperparathorism by unbalancing calcium. Both for children and matures, the number of the ones who suffer from vitamin D deficiency is approximately %50. Therefore vitamin D deficiency is accepted as epidemy worldwide. Births out of term, dark skin, malnutrition, not having enough sun rays and old age take part in risk factors. Also the causes are absorbtion deficiency, 25 hydroxylation defect, hydroxylation defect in 1.25 and decrease in the level of serum vitamin D binding proteins (Holick, 2004; Javorsky, Maybee, Padia, Dalkin, 2006).

Patients who should be observed for vitamin D level are the ones that have bone diseases, musculosketor symptom and have risk factor for vitamin D deficiency. Among the causes of osteomalasi which is a bone disease, there are decreasing of synthesis on skin, decreasing bio-availability, increasing of catabolism, decreasing of 25(OH)D synthesis, increasing 25(OH)D

progress, decreasing 1.25(OH)₂D vitamin synthesis, and osteomalasi originating from tumor and genetical diseases. Vitamin D deficiency usually doesn't show indications therefore "vitamin D deficiency" term is used for patients who are determined to have very low vitamin levels. Osteomamasi having indications like pain in skeleton system, myasthenia can be in a very complicated situation. In radiological observations, decreased bone density, broken and fake broken can be seen (Javorsky, Maybee, Padia, Dalkin, 2006).

Usually being in the highest level in the end of the summer and in the lowest level in the beginning of spring, vitamin D has basic jobs like ensuring calcium and phosphorus absorption from bowels and protecting calcium and phosphorus levels of organisms with PTH. When decreased under a critical level or had an insufficient calcium absorption from bowels, PTH level increases. PTH effect and 1-alpha-hydroxylase enzyme are activated and 1.25(OH)₂D level increases. To make a normal calcium level, PTH and 1.25(OH)₂D effect and calcium from bones are mobilised and during this process, bone mineralisation failures (Pelajo, Lopez-Benitez, Miller, 2010; Hatun, Bereket, Çalıkoğlu, Özkan, 2003).

Vitamin D and Leptin

There's a relationship between Vitamin D and leptin. The ones who have a normal level of Vitamin D stop their appetites and energy expenditure, so thanks to leptin receptors they don't put on weight too much and the risks of obesity, thick bell and diseases originating from them will be minimized. In a study, it's found out that rats that have lack of VDR, have decrease in their fat mass and serum leptin levels but increase in their energy expenditures. These changes independent from age are accompanied with uncoupling protein-1(UCP-1), increase in gene expression and non-fat phenotype (Schwartz, Woods, Porte, Seeley&Baskin, 2000; Narvaez, Matthews, Broun, Chan, Welsh, 2009)

If there are enough vitamin D in blood stream, fat cells slow their fat forming and storing processes down. When vitamin D level is low, the amount of parathyroid (PTH) and calcitriol hormones is increased. When these hormones are in a high level, body will turn into a glutton organism and store fats instead of burning them. This situation increases %40 of the risk of person's being obesity (Holick, 2004; Zemel, Reddy, Sowers, 1991)

Vitamin D and Obesity

Obesity is a health problem which results from overstorage of fat. In studies, we can see that fatness of children and adolescence age also increases. Fatness problem exist because of combination of genetic facts and environmental facts. Obese have lower 25(OH)D level when compared with people who have a normal weight (Arslanoglu, 2009; McGill, Stewart, Lithander, Strik, Poppitt, 2008). In many studies with matures, the connection between vitamin D and obesity is observed. As a consequence, it's reported that obesity is a risk factor for vitamin D deficiency. Total body fat is in a relationship with 25(OH)D which shows vitamin D and it's explained that the cause of vitamin D deficiency is accumulation of fat tissue¹⁹. In observational studies, the relationship of low serum 25(OH)D level and obesity, diabetes mellitus and metabolic syndrome are determined. These are; vitamin D's being soluble in fat and stored in fat tissue, having an opposite relationship between body fat rate in big cohort studies and BMI and vitamin D level, stating that vitamin D modulates insulin synthesis and secretion, showing VDR expression in fat tissue. It's reported that active vitamin D regulates

calcium exchange in rat models and β cells as invitro. On the other hand, there are very good reports about active vitamin D's modulating intracellular ionised calcium signalitation in adipositis and increasing lipogenesis by inhibiting uncoupling protein-2 (UCP-2) and decreasing lipolysis (Rosen, Adams, Bikle, 2012).

Discussion

The most important discussion subject is about boundary value of vitamin D. Plasma 25-OH-D3 is the best clinical indicator because it states vitamin D total which is taken with cutaneous synthesis and diet. In some studies, it's reported that 15 ng/mL which is the sub limit of this value is not enough for providing appropriate skeleton integrity. In another study, at least 20 ng/mL serum 25-OH-D3 level is needed to reach optimum parathyroid level in over 49 age people. However in some studies, when serum 25-OH-D3 level is over 28 ng/mL, PTH level be in the lowest gap (Thomas, Lloyd-Jones, Thadhani, 1998; Malabanan, Veronikis, Holick, 1998; Holick, 2003). In early ages, children who have vitamin D deficiency, have triple increase of diabetes development risk in their later life. However an opposite relationship between vitamin D intake in early ages and type-1 diabetes development risk (Hyppönen, Läärä, Reunanen, Järvelin, Virtanen, 2001; Harris, 2002). Although Turkey is rich in sunlights, vitamin D deficiency affects babies and children in adolescence era. This rate is between %8 and %21. At the same time there are many similar studies are done in different communities to determine vitamin D deficiency in children (Akman, Tumer, Hasanoglu, Ilhan, Cayci, 2011; Gordon, DePeter, Feldman, Grace, Emans, 2004).

Epidemiological studies about rheumatoid atric (RA) show that there's a relationship between vitamin D deficiencies in matures and RA and vitamin D deficiency in patients with RA is very common. However, reports researching the relationship between vitamin D level of patients with RA and disease activity are very different from each other. While in some the connection is determined, in some not (Patel, Farragher, Berry, Bunn, Silman, Symmons, 2007; Rossini, Maddali, La Montagna, 2010; Braun-Moscovici, Toledano, Markovits, Rozin, Nahir, Balbir-Gurman, 2011).

Patients with musculoskelon system pain and low back pain and who are diagnosed with somatisation are determined to have vitamin D deficiency and with treatment, symptoms are fixed within 3 months. A published editing puts forward that because of having the same symptoms with vitamin D deficiency, FM is wrongly diagnosed to these patients. With this, Block reports that there's no relationship between nonspecific musculoskelon system pains including vitamin D deficiency and FM (Holick, 2002; Torrente, Pecoud, Favrat, 2004; Block, 2004). Devarage team found a relationship between vitamin D level and prediabetes in their study. Pittas and his friends followed 25(OH)D levels and glucose intolerance up in women during 20 years in their study which is called "Nurses He-alth Study" and found an opposite relationship between vitamin D and calcium intakes and the risk of type 2 diabetes development and the ones who at least consume 3 portion milk have lower diabetes risk compared to the one who consume 1 portion in a day (Devaraj, Jialal, Cook, 2011; Pittas, Chung, Trikalinos, 2010).

Ecological studies show a negative relationship between going far away from Equator and hypertension and cardiovascular diseases. Vitamin D metabolites' antihypertrofive and anti-proliferative effects on cultural cardiomyosystesis are reported (Fleck, 1989; O'Connell, Berry, Jarvis, 1997). Vitamin D harmonises with datas that report an opposite relationship

between vascular calcification 25(OH)D levels by inhibiting bone morphogenetic protein-2 expression. Among diabetes hemodialysis patients, the ones who have lower 25(OH)D levels are claimed to have sudden cardiac death.

Conclusion

In some studies, although obesity has lower vitamin D compared to healthy people, having no increase in PTH level makes us think that it originates from the increase of vitamin D's storage in fat tissue more than insufficient absorption. It's reported that vitamin D deficiency is connected with many chronic diseases like cancer, metabolic syndrome, infectious, autoimmune and cardiovascular diseases etc. In observational studies, vitamin D deficiency is very common in northern parts of the world including industrialized countries. Those who can't get enough from sun rays and have vitamin D deficiency should be treated by eating foods rich in vitamin D. It's known that BMI and 25(OH)D levels have a negative relationship. 25(OH)D deficiency is observed in obesity very commonly. Connected with low serum 25(OH)D level, diabetes, KHD and other serious problems' levels should be determined and the ones who have low levels should be treated. By showing an antiproteinuric and anti-inflammatory effect, Vitamin D metabolites immune modulator, RAAS suppression provides a renoprotective effect. In clinical studies on CKD patients, it's reported that low vitamin D and heart failure and other heart diseases are each independent risk factors. Vitamin D and obesity relationship is uncertain and most of the reports are observational. Cardiovascular diseases are among the most important reasons of patients who have newly renal impairment. However, vitamin D deficiency exists as an independent risk factor for development of newly renal impairment. However in the studies on those who have chronic kidney disease low vitamin D situation for heart failure, heart diseases, coronary vascular calcification and cardiovascular mortality is an independent risk factor. One of the doctors of Minnesota University, Dr Shamalar Sibley found out that those who have enough vitamin D have more tendency to lose weight compared to those who have vitamin D deficiency in his study about decreasing calories' effect on hormones. Besides those who consume vitamin D very much have a thinner waist than those who consume much less. Those whose vitamin D levels are better feel full although they eat less and if had enough vitamin D, less fat will be stored and especially much more fat will be burned in waist area. Because vitamin D, which works with calcium, decreases stress hormone, cortisol that results in fatness in waist.

Therefore it's very beneficial that those who have vitamin D deficiency should be reinforced. On the other hand, although it's very important to have sun rays between the hours 10-15 at which sun rays are very dense, especially in summer sun rays come to earth with very right angle and it may lead to skin cancer, one should be very careful. When vitamin D test is made (25-hydroxyvitamin D test), those whose values under 40 nanogram per milliliter should take vitamin D. Those whose BMI is over 25 need more vitamin D and those whose BMI is over 30 and more need at least double vitamin D compared to those normal weights. It's true that we should take vitamin D foods rich in vitamin D instead of pills. Those whose vitamin D levels are normal have lower risks for obesity, musculoskeletal system diseases, osteoporosis, cardiovascular diseases cancer and osteolysis when they are older, if they exercise regularly.

Conflicts of interest

None declared by authors.

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