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Possible action mechanisms of vitamin D supplementation in combating obesity and obesity-related issues of bone health: a mini review

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Abstract

Vitamin D is necessary for maintaining the bone function, and its deficiency is linked with the development of obesity. Moreover, bone health is correlated with obesity through many mechanisms by modulating bone marrow mesenchymal stem cells to differentiate as adipose cells, inflammatory response, glucose metabolism, oxidative homeostasis, energy metabolism and gut microbiota. Based on previous studies, vitamin D, obesity, and bone health are linked with each other at multiple levels. However, our knowledge of the associations of vitamin D with coexisting abnormalities, such as bone health-related issues and obesity, is still in its infancy. The complex relationships still need to be investigated and elucidated further. Therefore, in this review, the relationships between vitamin D, obesity and bone health have been discussed. This review identified that evidence proving the capacity to reduce or prevent obesity-related disorders by targeting vitamin D intakes is mainly unknown. However, the inverse relationships of vitamin D levels with obesity and bone health-related issues are apparent.

Keywords: vitamin D; obesity; bone health; vitamin D deficiency; vitamin D receptor.

Practical Application: Vitamin D supplementation can be used to combat with obesity development in human and also ameliorate bone loss issue, especially in obese population.

1 Introduction

Vitamin D in the endocrine system can maintain the balance of calcium in the body and bone health. Its lack may cause bone lesions, such as rickets. In addition, vitamin D also appears to exert a multiple effects in inhibiting fat production and regulating the inflammatory response of adipose tissue. Low vitamin D levels are linked to obesity, according to a growing body of evidence (Ding et al., 2012). In addition, studies have shown that obesity is linked to an increase in the quantity of adipose tissue in bone marrow, which may damage bone structure and properties of bone materials, leading to bone loss (Ambrosi et al., 2017; Boskey & Imbert, 2017). Fat in bone marrow can stop osteoblasts from proliferating and stimulate bone resorption, destroying bone homeostasis (Xiao et al., 2010; Lee et al., 2015). The interaction between obesity and bone health also leads to functional impairment and an increase in disease risk in numerous people worldwide (Compston & Genant, 2010; Cao, 2011; Ilich et al., 2014; Mishra et al., 2016). Previous researches suggested that there are multiple levels of correlations between vitamin D, obesity, and bone health. However, our knowledge of the association of vitamin D with coexisting abnormalities, mainly bone health-related issues and obesity, is still in its infancy. The complex relationships still need to be investigated and elucidated further. Therefore, in this review, the relationships between vitamin, obesity and bone health, and bone health and obesity have been discussed. Moreover, several molecular mechanisms that are possibly involved in these relationships on and the status of current in vitro/ in vivo and clinical research on the impact of vitamin D on obesity and bone health has been reviewed. Some research directions have been put forward, which may be considered for future investigation.

2 Possible links among vitamin D, obesity, and bone health

2.1 Obesity and bone health

When excessive quantity of high-fat diet (HFD) is consumed, the energy intake exceeds energy expenditure (EE), which leads to the storage of excessive energy in white adipose tissue (WAT), the main pathological feature of obesity (Wu et al., 2013). Obesity is an important factor associated with the development diseases including diabetes, liver disease etc., and with the deterioration of bone health (Ouchi et al., 2011; Ambrosi et al., 2017; Boskey & Imbert, 2017). Mesenchymal stem cells (BM-MSC) in bone marrow can differentiate into osteoblasts. Its differentiation is regulated by many factors, can secrete proteins and hormones, and can affect osteoblasts and adipocytes (Tencerova et al., 2019). The disruption of the balance between osteoblast and adipocyte differentiation is a critical factor in the progression of obesity and bone loss (Gautam et al., 2017). The differentiation

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potential of BM-MSCs is closely related to the changes in micro-environment (Tencerova & Kassem, 2016). Similar to aging, obesity is associated with significant metabolism changes in the micro-environment (Tencerova et al., 2019). The pathogenetic relationships and molecular mechanisms connecting obesity and bone loss are also tightly correlated. Obesity has been linked to an increase in oxidative stress (Marseglia et al., 2014) and chronic inflammation in previous research (Alvehus et al., 2010). Moreover, HFD-induced obesity has negative effects on glucose homeostasis and energy metabolism, since it is linked to oxidative stress and fatty liver tissue inflammation (Tewari et al., 2015; Villarroya et al., 2017). However, researchers have also reported that chronic inflammation has adverse effects on the bone, which causes imbalance in bone metabolism, leading to bone loss (Redlich & Smolen, 2012; Kanazawa, 2017; Napoli et al., 2017). Previous data further revealed that the bone is an organ associated with energy metabolism (DiGirolamo et al., 2012; Cheung et al., 2014). Moreover, experiments show that bone cells and bone morphogenetic cells in bone will produce dysfunction under the condition of high glucose metabolism disorder, and then induce osteoporosis (Kanazawa, 2017). Impaired glucose status can also inhibit the expression of some key genes and lead to increased adipogenesis and decreased osteogenesis (Keats & Khan, 2012). Further, reactive oxygen species (ROS), which cause oxidative stress, are also important signal molecules that regulate bone remodeling (Domazetovic et al., 2017). In conclusion, it is worth noting that obesity-related conditions, such as increased oxidative stress and chronic inflammation, as well as impaired glucose homeostasis and energy metabolism, are all associated with bone loss, As shown in Figure 1.

2.2 Vitamin D and obesity

Vitamin D is a circulating pre-hormone that is active in the body. The inactive vitamin D is obtained through diet (containing oily fish and milks) and exposure to sunlight. However, the main source of vitamin D is exposure to UV-B light rather than a healthy diet (Haussler et al., 2013). UV-B radiation (wavelength 290-315 nm) boosts vitamin D production in the skin by converting 7-dehydrocholesterol to cholecalciferol, a precursor to vitamin D3 (Cronise et al., 2014; Calton et al., 2016). The activation of vitamin D involves complex processes. Pre-vitamin D3 is converted to vitamin D3 via thermal isomerization and delivered to the liver. Hydroxylation in the liver by the enzyme, vitamin D-25-hydroxylase, results in the conversion of the pre-vitamin to 25-hydroxy vitamin D (25(OH)D), the major circulating form and vitamin status indicator of this vitamin; in this form, this vitamin is stored and is fat-soluble. The storage mainly occurs in the adipose tissue (Wortsman et al., 2000; Heaney & Holick, 2011). When needed by the body, the 25(OH)D undergoes further hydroxylation to form the biologically active form of the vitamin, as shown in Figure 1. 1,25-dihydroxyvitamin D (1,25(OH)2D), in the kidney, which acts in vivo via the vitamin D receptor (VDR) (Wei & Christakos, 2015; Migliaccio et al., 2019).

Obesity and vitamin D deficiency are both prevalent worldwide. Vitamin D insufficiency is more common in obese

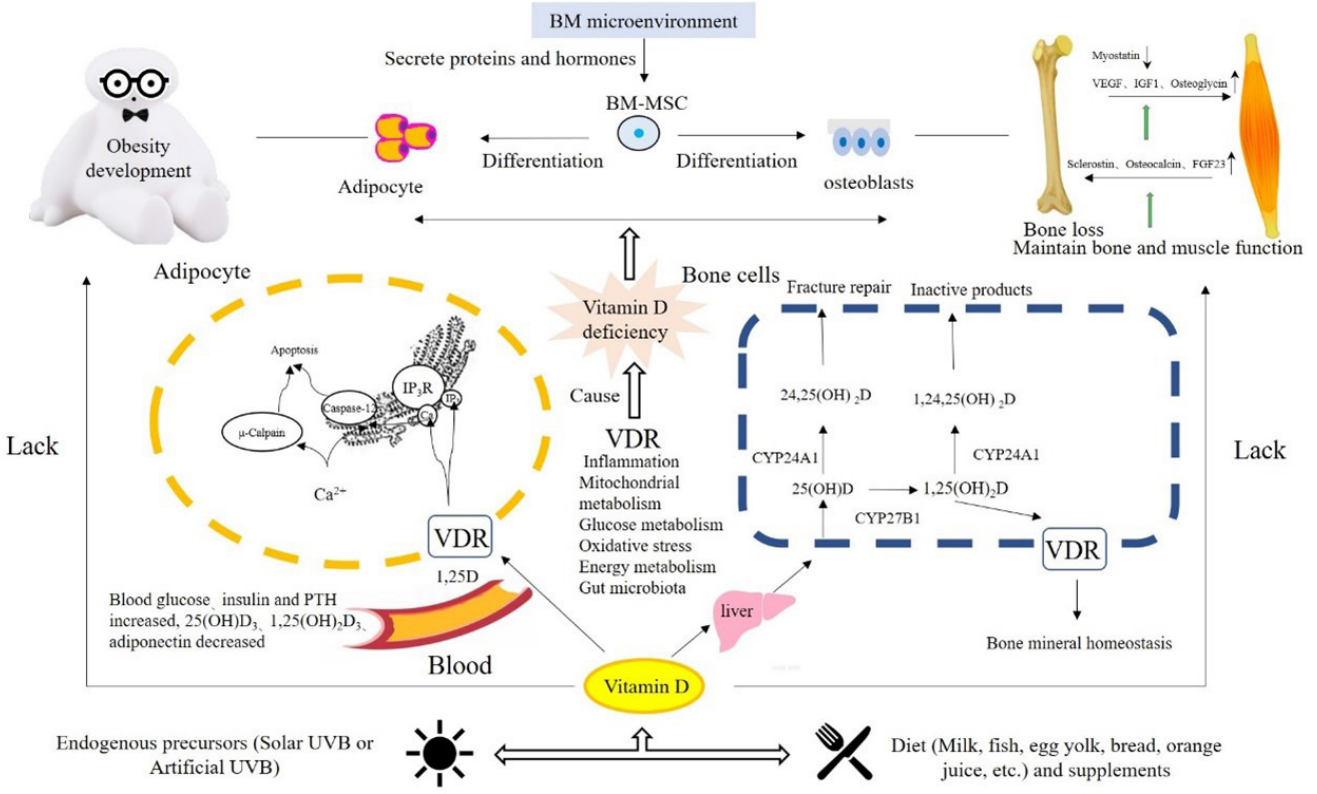

Figure 1. The relationship between Vitamin D, Obesity and Bone. describes the main functions of vitamin D and its relationship with obesity and bone. At the same time, it also summarizes the relationship between the three deficiencies.

children and adolescents than in their non-obese peers; the risk of vitamin D adequacy is twice as high in the former group than in the latter (Plesner et al., 2018). Considering that the level of 50-75 nmol/L is not sufficient, an increase in the threshold of vitamin D adequacy in adults to 75 nmol/L has been suggested to improve its potential health benefits (Holick et al., 2011). Vitamin D deficiency in obese patients is thought to be caused by a variety of factors. The following four recommendations, which are most frequently cited, may explain why people with obesity have low vitamin D levels (Migliaccio et al., 2019). Exposure to sunshine due to outdoor activity, which is lower among patients with obesity than among their emaciated peers, is considered to be a reason (Vanlint, 2013). Obese people may have less outdoor activities than non-obese people, so their skin is exposed to the sun for a shorter time, resulting in reduced vitamin D synthesis (Vanlint, 2013). Previous evidence has suggested that the negative feedback from an elevated 1,25(OH)2D concentration in individuals with obesity might decrease 25(OH)D concentration, while recent studies showed the opposite (Lagunova et al., 2011). Data supporting this cause remain equivocal and inconclusive. The third reason is provided by studies on human and animal models: adipose tissue can contribute to the isolation of vitamin D in patients with obesity (Wortsman et al., 2000; Hossein-Nezhad & Holick, 2013). The fourth reason may be that the serum and adipose tissue concentrations of 25(OH)D are closely correlated. In obese patients, a large amount of adipose tissue forms an expanded vitamin D pool. High levels of vitamin D needs to saturate this larger reservoir, and this higher storage capacity increases the risk of low 25(OH)D concentrations in patients with obesity (Drincic et al., 2012; Carrelli et al., 2017). Vitamin D deficiency, on the other hand, contributes to the development of obesity, and vitamin D supplementation can help to reduce obesity. After dietary intervention for vitamin D deficiency, the production of 1,25(OH)2D, also called calcitriol, could increase lipolysis in adipocytes, reduce the expression and activity of adipogenic genes, increase the expression of lipolytic genes, and lower lipid content of adipocytes (Figure 1) (Chang & Kim, 2016; Cheng et al., 2016). As a result, vitamin D replenish men is critical in preventing the enlargement of adipose tissue.

2.3 Vitamin D and bone health

Adequate serum vitamin D concentration is required to maintain bone health during growth (Turer et al., 2013). Vitamin D is essential for the musculoskeletal system's calcium and bone metabolism to remain consistent. Its deficiency leads to rickets in children, or osteoporosis and osteocalcin in adults (Suda et al., 2003). Vitamin D has long been considered to be important the regulation of calcium and phosphate homeostasis. Therefore, its effect on bone function is crucial (Antinozzi et al., 2017; Hassan-Smith et al., 2017). Vitamin D targets the stomach, kidney, and bone(where vitamin D stimulates stored bone calcium mobilization) to maintain calcium and phosphorus balance (DeLuca, 2004; Holick et al., 2011).

Low vitamin D levels are linked to muscle pain, an increased risk of sarcopenia, and associated falls in both active and inactive individuals. Several randomized controlled trials showed that vitamin D supplementation improves muscle strength in both physically active and inactive people, demonstrating the importance of vitamin D for the maintenance of skeletal muscle function and overall health (Salminen et al., 2015; Chiang et al., 2017). In children with low-energy forearm fractures, vitamin D deficiency and ineffectiveness are widespread, especially in obese children and children with fractures that require surgical treatment (Hosseinzadeh et al., 2020).

In the biological process of bone development and mineralization, vitamin D plays a critical function. Previous studies have found an unfavorable association between serum concentration of vitamin D and bone mineral density (Pekkinen et al., 2012). A previous study revealed that vitamin D supplementation can improve bone mineral density and bone mass in people with low levels of serum vitamin D (Winzenberg et al., 2011). However, according to a recent study, high-dose vitamin D supplementation has adeleterious effect on bone mineralization in adults (Burt et al., 2019). Thus, the link between vitamin D status and bone health remains unclear. A large number of prospective studies are needed to further evaluate the association between vitamin D status and bone health (Figure 1).

2.4 Vitamin D and food

People can obtain vitamin D from foods (milk, fish, eggs, fruits, etc.), such as yogurt with vitamin D, which can not only promote bone growth and inhibit obesity, but also contain a large number of lactic acid bacteria. In basic research, it is found that Lactobacillus plantarum B719 fermented dairy products (FMP-B719) have anti osteoporosis effect, it can promote the proliferation and mineralization of mouse MC3T3-E1 cells, improve the bone mass of proximal femur in osteoporosis rats and the strength of femur in ovariectomized rats (Lee et al., 2020). Lactobacillus mf27 and Lactobacillus casei 393 can inhibit the formation of osteoclasts and increase the bone trabecular volume of ovariectomized and lipopolysaccharide (OVX-LPS)-induced intestinal bone Dysbiosis (OVX-LPS) rats, and selectively regulate the composition of intestinal microbiota, improve intestinal barrier function, and improve intestinal bone axis (Eor et al., 2020). Yogurt supplemented with vitamin D can promote bone health.

Fruit puree have a large content of vitamin D. It is found that obese rats who eat a low-fat diet supplemented with fruit puree can reduce the weight of obese rats, control blood lipid metabolism, reduce the levels of total cholesterol and triacylglycerol, reduce the expression of inflammatory markers, reduce liver injury and improve the morphology of liver, eating fruit puree may help to control and improve obesity complications caused by lipoprotein changes (Morales-Avila et al., 2020). Vegetables and fruits are also important sources of vitamin D and contain anthocyanins. Eating vegetables and fruits can inhibit lipid absorption, increase energy consumption, regulate lipid mechanism, control food intake and regulate intestinal microbiota, reduce/regulate insulin resistance and fasting insulin level, and inhibit obesity (Yildiz et al., 2020).

3 Mechanisms associated with the role of vitamin D in obesity and bone health

As mentioned above, bone and adipose tissue are interrelated, and the increase in obesity aggravates the decrease in bone mass (Gendelman et al., 2014). Previous studies have found that there is a significant association between serum vitamin D levels and various components of aberrant body composition, manifested as osteoporosis and obesity (Pekkinen et al., 2012; Calton et al., 2015; Migliaccio et al., 2019). Several molecular mechanisms have been postulated to elucidate the role of vitamin D in obesity and bone health. However, several underlying mechanisms associated with vitamin D-related pathways, and their regulation and role in obesity and bone loss, or modes of translation of these pathways into clinical improvements are unclear and still need further investigation (Figure 1).

3.1 VDR and inflammation

Calcitriol, a hormone form of vitamin D, exerts its immunomodulatory properties and functions by activating VDR, which regulates gene transcription and protein synthesis (Ceglia & Harris, 2013); thus,it may play a role in the relationship between obesity, bone health, and inflammation. Vitamin D has been shown to inhibit the synthesis of Il8, Il6, and Mcp1, which is correlated with inflammation response (Mutt et al., 2012; Calton et al., 2015). Calcitriol has direct effects on inflammation-related pathways, such as the NF-κB pathways along with mitogen-activated protein kinase (MAPK) pathways, which have been shown to occur in adipocytes (Mutt et al., 2012; Mutt et al., 2014). 1,25(OH)2D exhibits anti-inflammatory effects by promoting the secretion of anti-inflammatory cytokines and reducing the secretion of pro-inflammatory cytokines from macrophages. It has been shown that 1,25(OH)2D/VDR suppresses NF-κB activities, which leads to a decrease in the expression of pro-inflammatory cytokines, as well as inhibition of cell proliferation and cancer-associated inflammation (Dimitrov et al., 2014; Christakos et al., 2016). The blockage of the nuclear factor of activated T cells, sequestration of Runx1, and induction of the transcription factorFoxp3 are all involved in the inhibition of IL-17 transcription by 1,25(OH)2D/VDR. Foxp3 is also involved in the development and function of regulatory T lymphocytes (Christakos et al., 2013) .

VDR and vitamin D metabolic enzymes are also present in reproductive tissues, which will affect the production of female sex hormones and steroids. The high serum 25 (OH) D level may be related to endometriosis. For men, vitamin D was found to be positively related to semen quality and androgen status. In addition, vitamin D treatment may rause testosterone levels. Men with testicular disease showed low expression of cyp21r, low level of 25 (OH) D and osteoporosis. The risk allele may be more prevalent in men than in women; therefore, more men may experience a faster decline in skeletal muscle mass than women (Lerchbaum & Obermayer-Pietsch, 2012). Therefore, the relationship between genetic variants of VDR and inflammatory response needs to be investigated further.

3.2 VDR and mitochondrial metabolism

The function of mitochondrial, that is, production of energy in the form of ATP, is crucial for skeletal muscle cells because of high energy requirements of these cells (Deepa et al., 2016). VDR can also be transferred to the mitochondria of the skeletal muscle cells, and this receptor potentially affects cellular bioenergetics directly (Girgis et al., 2013).

Currently, it has been suggested that vitamin D regulates mitochondrial metabolism by increasing the expression of electron transport chain proteins and tricarboxylate cyclases via genomic and non-genomic mechanisms (Silvagno & Pescarmona, 2017). Treatment with vitamin D enhances the expression levels of MAPK13, MYC, as well as endothelial PAS domain-containing protein 1 mRNA, which encodes for a protein that controls mitochondrial biogenesis (Ryan et al., 2016) . However, little research has been done on the precise role of vitamin D in mitochondrial metabolism.

3.3 Glucose metabolism

Previous studies in children showed that the serum concentration of vitamin D was inversely associated to waist circumference, systolic blood pressure, insulin resistance (IR), and fasting serum glucose level (Aypak et al., 2014; Reyman et al., 2014). Vitamin D appears to interfere with insulin secretion both directly, by binding to VDR, and indirectly, by regulating calcium concentration in extracellular space (Song et al., 2013). Moreover, vitamin D concentration was found to be positively connected to insulin secretion and negatively related to blood glucose level. In obese teenagers, vitamin D supplementation resulted in a reduction in IR (Belenchia et al., 2013).

Insulin release by pancreatic-cells is triggered by high blood glucose levels (Gilon et al., 2014). The regulation of intracellular Ca^{2+} concentration is one of the molecular mechanisms by which vitamin D modulates insulin secretion by pancreatic β-cells. 1,25(OH)2D reduces the expression of the L-type Ca^{2+} channels, which decreases the intracellular Ca^{2+} concentration, thereby altering calcium signaling. Another study discovered that vitamin D regulates intracellular Ca^{2+} levels through calbidin, a cytosolic Ca^{2+}-binding protein implicated in insulin secretion stimulation (Johnson et al., 1994) .

Insulin production and secretion were found to be reduced after glucose loading in mice lacking a functioning VDR (Zeitz et al., 2003). Insulin sensitivity improvement caused by vitamin D is linked to insulin signaling. The number of IRs on the surface of insulin-responsive cells rises as a result of 1,25(OH)2D-mediated transcriptional activation of the IR gene. Thus, calcitriol maintains insulin sensitivity by upregulating the IR gene, which ensures appropriate insulin signaling (Green et al., 2008).

3.4 Oxidative stress

Another possible mechanism by which vitamin D is linked to obesity and bone loss is its ability to ameliorate oxidative stress (OS). OS was reported to be linked to a variety of illnesses, including aging and cancer development (Poolsup et al., 2016). In animal models of Parkinson's disease, supplementation with

vitamin D reduces oxidative stress (Wang et al., 2001). As a neuro-protective hormone, vitamin D can interact with ROS and nitric oxide synthase species. Nanomolar concentrations of calcitriol were found to protect neurons against the effects of superoxide and hydrogen peroxide in a prior investigation (Kalueff et al., 2004) . Vitamin D has been reported to initiate potential antioxidant defense by increasing glutathione concentration (Buell & Dawson-Hughes, 2008). In addition, it has been proposed that vitamin D may have a direct effect on the central nervous system by crossing the blood-brain barrier and activating receptors in brain cells (Pozzi et al., 2013).

With the suppression of the antioxidant pathway, levels of the redox-sensitive transcription factor, nuclear factor-erythroid-2-related factor 2 (Nrf2) increase (Reuter et al., 2010). l,25(OH)2D regulates expression of Nrf2, which controls many antioxidants and detoxifying enzymes (Hayes & Dinkova-Kostova, 2014). Vitamin D supplementation reduced 8-hydroxy-2'-deoxyguanosine, an oxidative damage marker in lymphocytes and lung cancer cells, in clinical trials (Halicka et al., 2012). Previous studies also demonstrated that the capacity of vitamin D, as a very powerful antioxidant, can prevent zinc-induced oxidative stress, and that a vitamin D analog can have antioxidant benefits via activating the Nrf2-Keap1 antioxidant pathway (Nakai et al., 2014).

3.5 MSCs, energy metabolism and exercise

Vitamin D can regulate VDR, thereby affecting energy metabolism (Wong et al., 2011), and may also potentially regulate adipogenesis and preadipocyte differentiation (Ding et al., 2012). Adipogenesis and osteogenesis are both regulated by different signaling pathways. The Wnt signaling pathways are mainly involved, and Wnt exhibits both pro-osteogenic and antiadipogenic properties (Rao & Kuehl, 2010). On the other hand, RUNX2 is considered to be the major regulator of osteogenesis (Vimalraj et al., 2015).

Regular training is beneficial to inhibit fat production and bone absorption. Resistance exercise has been observed to interfere with adipogenesis in estrogen deficient rats (Duarte et al., 2017). Mechanical loading signals can activate the expression of osteogenic and chondrogenic genes, which impedes adipogenesis by activating the Wnt-β-catenin pathway (Pagnotti et al., 2019). Physical activity enhances the expression of Pgc1, a transcriptional coactivator involved in mitochondrial biogenesis as well as oxidative metabolism, in muscle tissue; this, in turn, regulates the expression of Fndc5 gene (Bostroem et al., 2012) . A recent study demonstrated that irisin impairs adipogenesis and promotes osteogenesis in visceral fat tissue. Moreover, irisin induces the expression of transcriptional regulators related to beige adipocytes in subcutaneous WAT, including Ucp1, Prdm16, Tmem26, Cd137, and Pgc1α. All of these factors lead to an increased in EE, which helps to reverse obesity-related IR (Li et al., 2019). In addition, we observed the up-regulation of Runx2, osterix, and osteopontin expression and the enhancement of mineralization when iridin was added to osteoblasts during differentiation in vitro. Study also exhibited that the down-regulation of Runx2 expression by vitamin D promotes osteoblast maturation from MSCs (Posa et al., 2018).

3.6 Gut microbiota

Studies have shown that intestinal microorganisms may affect obesity and weight gain by affecting metabolic, host gene expression as well as inflammatory pathways, and the intestinal brain axis. Various intervention studies and treatments in animals and humans have found that body weight and metabolic function are improved through changes in microbiota composition (Maruvada et al., 2017). In addition, the intestinal microbiome can affect remote target organs by regulating nutrient absorption, regulating the immune system or the translocation of bacterial products. Molecular products and activated T cells enter the systemic circulation, and they can migrate to remote target organs, including bones. The change of intestinal flora will affect the change of bone phenotype (Hernandez et al., 2016). Vitamin D deficiency reduces the diversity of animal microbial community, and vitamin D can induce the expression of several tight junction proteins ZO-1, Occludin, and Claudin in intestinal epithelial cells, preserving the intestinal barrier's integrity. It can target mucosal immune system and maintain ilc3 (producing IL-22 and CD8αα). In addition, vitamin D inhibits the function of Th1 and Th17 cells in the intestine. Vitamin A and vitamin D work together to control the function of intestinal barrier, ILC3 and T cells, all of which influence the microbiota in the gut (Cantorna et al., 2019).

4 Current research status: role of vitamin D action in obesity and bone health

4.1 In vitro and in vivo studies and perspectives

A previous in vitro study reported that increasing vitamin D levels stimulates the skeletal muscle cells differentiation and results in myoblasts maturation, which leads to an increase in myotube fiber diameter (Van der Meijden et al., 2016).

Another in vitro study showed that a high level of 1,25(OH)2D inhibits the proliferation of keratinocytes via VDR-mediated genomic mechanisms (Tang et al., 2012) promotes differentiation of keratinocytes by increasing intracellular calcium levels via nongenomic mechanisms (Barrea et al., 2017).

In a rat muscle model, vitamin D deficiency caused a reduction in superoxide dismutase and catalase enzymes, which resulted in oxidative stress. In C_2C1_2 muscle cells, vitamin D therapy might reverse oxidative stress parameters, boost total protein degradation, and lower levels of muscular atrophy gene markers (Bhat & Ismail, 2015).

Ghazaleh et al. evaluated the vitamin D's protective effects on HFD-induced obesity in rats and found that vitamin D inverted HFD-induced OS and neuro-inflammation by elevating SOD and GPX levels and reducing MDA concentrations and inflammatory biomarker levels (Hajiluian et al., 2018).

In addition, studies have shown that vitamin D (VD) plays a protective role in skeletal muscle. 1,25-(OH) 2-vitamin D3 (VD3) improves C2C12 skeletal muscle cell apoptosis induced by palmitic acid and increases the expression of VDR receptor in a dose-dependent manner. Both VD3 treatment and VDR overexpression improve C2C12 muscle cell apoptosis, endoplasmic

reticulum stress Inflammation and glucose uptake, VD inhibits AMPK/SIRT1 mediated ER stress by increasing VDR expression, and further improves skeletal muscle loss and insulin resistance in mice (Li et al., 2021).

However, studies to assess the effects of vitamin D supplementation on obesity and bone health are scarce; hence, further studies are needed.

4.2 Clinical studies and perspectives

Patients with low serum vitamin D levels have been shown in certain trials to improve their health after taking vitamin D supplements. Chanet et al. proved that the use of breakfast supplements of vitamin D enhances the subsequent synthesis of muscle protein and muscle mass in healthy older men (Chanet et al., 2017). Bone health is linked to increased muscle mass. Men, but not women, with hypovitaminosis, defined as serum 25(OH)D level of < 20 ng/mL, had a low mean value of appendicular skeletal muscle mass index, according to a prior study using a countrywide sample of Koreans aged 40 years (Ko et al., 2015).

Kim et al. used data obtained from 5908 (2485 men, 3423 women) individuals aged ≥ 50 years to analyzed the relationship between serum vitamin D levels and the number of abnormalbody composition, including osteosarcopenic obesity, low bone mass and muscle mass with concurrent high fat mass. They found that a high serum vitamin D level in middle and late life was linked to reduced odds of occurrence of multiple abnormalities in body composition, especially osteosarcopenic obesity, which indicates that maintaining adequate levels of vitamin D may be beneficial to health (Kim et al., 2017).

In addition, a current study used a double-blind randomized placebo-controlled experiment to assess the influence of a 26-week vitamin D supplementation program on body mass reduction, body composition, and bone mineral density in children who were overweight or obese and were having undergone an integrated 12-month fitness program, via a double-blind randomized placebo-controlled trial. They found no difference in the level of change in body mass index (BMI) change. Supplementing with vitamin D had no effect on body weight loss in children and adolescents with vitamin D deficiency (Brzezinski et al., 2020). The authors also stated that one dose of vitamin D (1200 IU) was administered to each participant irrespective of body mass and age, and the 26-week study may be too short for assessing the effect of vitamin D. Another study reported that the effect of administering seven drops of 1750 IU/day and 50,000 IU/month of vitamin D were equivalent., Patients showed normal vitamin D levels at the end of this study, as well as enhanced calcium levels, as well as decreased bone turnover and waist circumference (Dalle Carbonare et al., 2018).

5 Conclusion

This study reviewed the relationship between vitamin D and coexisting abnormalities, mainly bone health and obesity. The possible mechanisms by which vitamin D supplementation help combat obesity and obesity-related bone health were also reviewed. However, there are still some gaps in the knowledge in this area. There is a paucity of evidence proving the potential to alleviate or prevent obesity-related disorders by adjusting vitamin D intakes (Dinca et al., 2016). Furthermore, the associations among obesity, bone loss, and vitamin D are usually unclear, which can be attributable to the significant heterogeneity between studies, making the comparison between studies difficult. Despite these limitations, the inverse relationships between vitamin D levels and obesity and bone health-related issues are apparent.

Conflict of interest

The authors declare that there is no conflict of interest.

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