Vitamin D and Skeletal Muscle

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Aging is associated with impairment in skeletal muscle mass and contractile function, predisposing to fat mass gain, insulin resistance and diabetes. At cell and animal levels, that VitD treatments had positive effects on the development of muscle fibres in cells in culture, skeletal muscle force and hypertrophy.

Keywords: skeletal muscle function ; vitamin D ; aging

1. Introduction

The process of aging is normally associated with a reduction in muscle mass, function and also with the development of frailty, which significantly reduces life expectancy [1][2][3]. The subsequent loss of skeletal muscle mass and strength is known as sarcopenia [2]. Metabolic diseases are generally part of this scenario, negatively impacting on skeletal muscle tissue [4]. However, studies indicate that there may be a variation across the population in relation to the rates of losing muscle mass over the years suggesting that diet and lifestyle may play a powerful influence on this process [5]. Different hormones and nutrients have been reported to influence skeletal muscle mass and VitD has been suggested to be one of them. So, it seems that the role of VitD lays beyond the bone and mineral metabolism as studies have been suggesting that supplementation with VitD has a potential positive effect on skeletal muscle function [6][7].

2. The Role of Vitamin D on Skeletal Muscle Function

2.1. Myotube Formation, Muscle Mass, Strength and Force

The ability of the muscle to respond to amino acid and insulin levels reduces with age, which increases anabolic resistance and might negatively influence protein absorption and digestion [8]. Muscle mass starts declining in the fourth decade of life and significant reduction can be observed by around 59 years of age [9]. Skeletal muscle anabolism seems to be enhanced by the effects of VitD and dietary protein [10]. This last study indicates that VitD may have both positive and negative effects on muscle homeostasis, (i.e., muscle regeneration and myofiber maintenance) depending on the dose used.

2.2. Muscle function and protein synthesis

It has proven that VitD3 in combination with insulin had an additive effect in the rate of protein synthesis in human myotubes [11]. These results confirm the stimulus of protein synthesis and hypertrophic effects of VitD3 in primary human cells, which might result in the prevention of skeletal muscle atrophy in humans. In summary, to date these results validate the likely role of VitD3 in preventing skeletal muscle atrophy and ensuring normal neuromuscular junction function. Despite previous reports, there are still insufficient evidence to establish if higher VitD3 doses are beneficial in the aging process or if the prevention of VitD3 deficiency is enough to preserve skeletal muscle function, protein synthesis and NMJ function.

2.3. Mitochondria and Lipid Metabolism

It is well known that intramuscular fat increases with age, which consequently reduces lean muscle mass used for energy metabolism [2]. Discovering strategies to preserve muscle mass in the elderly population is of public health importance. These changes in lipid metabolism seems to be connected to mitochondrial function in myotubes, as Schnell et al. have confirmed that 100 nM VitD3 for 24 h had significantly increased mitochondrial function, lipolytic genes (ATGL and CGI-58) and oxygen consumption rate (OCR) [12]. Similar outcomes were observed by Chang and Kim, as they found a significant increase in ATP levels and mitochondrial function gene expression after 100 nM of VitD3 treatment for 24 h, resulting in a protective effect on muscle fat accumulation and mitochondrial disfunction in C2C12 myotubes [13].

2.4. Glucose and Insulin Metabolism

In a healthy condition, skeletal muscle is accountable for ~85% of whole-body insulin-mediated glucose uptake, confirming its importance to insulin resistance development [14]. Recently increasing interest about the role of VitD deficiency and the association with hyperglycaemia and diabetes has been evident [15]. It has been suggested that VitD plays a significant role increasing translocation of the glucose transporter, GLUT4 to the plasma membrane. Overall, it appears that VitD3 has a direct effect on glucose and insulin metabolism in cell models in vitro and animal models. Preliminary evidence suggests that VitD3 has the potential to be a therapeutic target, possibly by improving the metabolic control in hyperglycaemia and diabetes conditions. However, clinical studies are necessary to investigate and clarify the precise molecular mechanisms and pathways by which VitD3 acts on glucose and insulin signalling and how it is related to skeletal muscle function.

2.5. Oxidative Stress, AGES

Oxidative stress can be described as an imbalance between the level of antioxidant capacity and the production of reactive oxygen species (ROS). Reactive oxygen species have been associated with a wide variety of conditions, such as obesity, hypertension, hyperglycaemia and dyslipidaemia [16]. Vitamin D deficiency and advanced glycation end products (AGEs) are found to be associated with the development of obesity, type 2 diabetes and sarcopenia [17][18]. Advanced glycation end products are a result of reactions of carbohydrates with proteins and its production is found to be higher in elderly and diabetic population, affecting bones and muscle tissue [19][20]. To the best of our knowledge, the results suggest that VitD3 might have beneficial effects on the reduction of ROS, on positive mitochondrial changes and on prevention of AGEs. In other words, VitD3 might be useful in the treatment of health complications related to the aging process and further studies should investigate its application in animal and clinical studies.

2.6. Muscle Mass, Strength and Function

Low total serum of [25(OH)D] seems to be linked to the aging process and also to the reduction in muscle performance [4].

3. Summary

The purpose of this review was to summarize the effects of VitD3 supplementation on skeletal muscle in cell, animals and in an aging population. Increasing total serum [25(OH)D] levels from insufficiency/deficiency status to normality does not appear to benefit muscle function, power or mass in older adults. Our review suggests that improvements in muscle performance in older adults cannot be guaranteed from VitD3 supplementation alone, at least over a short timeframe. Therefore, a combination of exercise, VitD supplementation and longer-term interventions may be more effective in increasing skeletal muscle health. Well-designed long duration double-blinded trials, standardised VitD3 dosing regimen, larger sample sized studies and standardised measurements may be helpful to determine favourable outcomes and future recommendations.

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