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Mini Review

Endogenous Vitamin D Levels and Athletes - A Brief Review

Koundourakis NE* and Margioris AN
Department of Clinical Chemistry - Biochemistry, University of Crete, Greece

***Corresponding author:** Koundourakis NE, Department of Clinical Chemistry - Biochemisty, School of Medicine, University of Crete, Heraklion, Greece

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Abstract

In the last decades a lot of interest has risen regarding the functions of vitamin D. Vitamin D is primarily synthesized endogenously following cutaneous exposure to Ultraviolet B Radiation (UVB). Apart from the classic role in skeletal health and calcium and phosphorus homeostasis, vitamin D exerts a host of other physiological effects. To date, there is strong evidence suggesting that vitamin D affects the neural and muscular tissues, the cardiovascular system, body composition status, and energy homeostasis. This evidence indicates that vitamin D may have a role in the maintenance and enhancement of exercise performance capacity in athletes and other physically active individuals. Observational studies have been reported that vitamin D levels correlate with grip and quadriceps strength, aerobic fitness, and several parameters of neuromuscular performance, although these findings are not universal. These discrepancies could be related with the observations that vitamin D seems to affect performance capacity mainly when athletes are in a deficient state (i.e. levels below 20 ng/ml). Paradoxically, a growing number of studies report a high prevalence of vitamin D insufficiency or downright deficiency even in regions with extensive sunlight in athletes from several sport disciplines, in both high and low latitudes. Vitamin D exerts its effects via Vitamin D Receptors (VDRs) which are present in a variety of tissues of the human body. In addition, numerous VDR binding sites throughout the genome controlling hundreds of gene have been reported. The VDR acts either as a nuclear receptor which mediates the so-called genomic effects or via a non-nuclear receptor mediating non-genomic actions. The aim of this non-systematic mini review is to present the hypothetical mechanisms via which this secosteroid may affect the ability to perform efficiently during exercise, and furthermore to evaluate the existing literature regarding the relationship between endogenous vitamin D levels and exercise performance indices in athletes.

Keywords: Vitamin D; Athletes; Exercise performance

Abbreviations

VDRs: Vitamin D Receptors; VDR: Vitamin D Receptor; CSA: Cross Sectional Area; RAAS: Renin-Angiotensin-Aldosterone System; VO_{2max}: Maximal Oxygen Consumption; SJ: Squat Jump; CMJ: Countermovement Jump; BMI: Body Mass Index

Introduction

Vitamin D is a secosteroid produced mainly in the skin after exposure to ultraviolet radiation while small amounts originate from a limited range of dietary sources [1-3]. Although this secosteroid has long been known for its classic role in skeletal health and both calcium and phosphorus homeostasis, to date the vitamin D system is considered to influence nearly every biological function of the human body [3]. This is due to the recent discovery that VDRs are present in a variety of tissues of the human body and furthermore the findings that there are numerous VDR binding sites throughout the genome, controlling hundreds of genes [4-6]. This discovery has opened new ways of research related to vitamin D biological effects and molecular pathways indicating a pleiotropic role of this secosteroid. Sufficient levels of this micronutrient have been reported to confer adaptive and performance benefits in non-athletic and athletic population via multiple direct and indirect mechanisms [4-7]. The aim of this non-systematic mini review is to provide a substantial review of the literature regarding the effects of vitamin D on several physiological systems of the body that are related with the ability to perform efficiently during exercise. Furthermore, this mini-review presents the recent evidence examining the possible association between vitamin D serum levels and neuromuscular and aerobic performance indices in athletes.

General Biochemistry and Physiology

Vitamin D is produced in the skin under the influence of ultraviolet radiation converting 7-dehydrocholesterol to pre-vitamin D3 [1,3]. In the dermis pre-vitamin D3 is converted to vitamin D3 (cholecalsiferol) before its subsequent conversion to 25-hydroxy vitamin D (25(OH) D) in the liver [1-3]. In the kidneys hydroxylation of 25-hydroxy vitamin D takes place to calcitriol (1, 25-dihydroxy vitamin D (1, 25(OH) 2D), its biologically active form [8]. Dietary intake also provides small quantities of vitamin D2 (ergocalciferol) which follows the same hydroxylation pathway. After hydroxylation vitamin D is transported in the blood bound to a vitamin D binding protein [9]. Like all steroid hormones calcitriol acts as a molecular switch to signal genetic transcription. More than 1000 human genes

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are direct targets of calcitriol [10]. The pleiotropic effects of vitamin D are mediated by the VDRs which are expressed in a large number of human cell types indicating the potential for widespread effects [4-7,9]. Although the VDR principally acts as a nuclear transcription factor, a nonnuclear receptor mediating non-genomic actions has been also described [12]. There is evidence that vitamin D affects the cardiovascular and the musculoskeletal systems [4,5,7], and that also regulates fat oxidation, various endocrine systems, and the brain [12,13].

Vitamin D Deficiency in Athletes

A surprisingly high prevalence of vitamin D insufficiency or deficiency has recently been reported worldwide. This prevalence of vitamin D insufficiency is a global problem in both high and low latitudes [14]. Athletes from several sport disciplines have been found to have vitamin D levels below 20 ng/ml at percentages greater than 37% [4,7,14-16]. Similarly, English [17] and Greek [18] professional soccer players were found to be 65% (<20ng/ml) and 55, 22% (<30ng/ml) vitamin D insufficient in winter (at 53°N) and May (at 35, 7°N) respectively. These findings are further supported by the observation that 84% of 342 Qatar soccer players were vitamin D insufficient (<30 ng/ml) in July, despite the favorable latitude (25, 4°N) of the study [19].

It should be mentioned that the literature lacks a unified normal range for serum levels of vitamin D. There has been much debate regarding the cut-off point for diagnosing vitamin D deficiency [4]. According to the Endocrine Society, normal levels of vitamin D are 30-60 ng/ml, insufficiency is defined as levels of 21-29 ng/ml and deficiency is defined as levels below 20 ng/ml [20]. Based on this most scientists define vitamin D insufficiency as levels lower of 30 ng/ml [21]. Notably, it has been suggested that it may be necessary to increase serum levels above the concentration of 20 ng/ml of vitamin D in order to avoid the proposed negative effects of its deficiency [14,22,23].

Vitamin D and Skeletal Muscle Physiological Function

Vitamin D has been suggested that it should be a potent modulator of skeletal muscle physiology and function [5]. As mentioned, vitamin D exerts its actions by binding to the VDR. Although the expression of the VDR in skeletal muscle tissue has been questioned [24], recent data strongly indicate that it is present in skeletal muscle [25]. VDR acts as a nuclear receptor and the molecular mechanisms of vitamin D action in muscle tissue include genomic and non-genomic effects [5,6]. The effects of vitamin D on the genome regulate muscle calcium and phosphate transport across the cell membrane, but have also been found to have anabolic properties. Vitamin D binds to its nuclear receptor resulting in de novo protein synthesis [5-7], it influences myogenesis, muscle cell proliferation and differentiation [26]. In addition, vitamin D is related with positively altered CSA of the skeletal muscle fibers, and increased diameter and number of type II muscle fibers [5-7]. In the non-genomic level vitamin D regulates calcium transport and intracellular calcium levels [25], parameters that are of vital importance for muscle contraction and thus, human movement.

Implications for Neuromuscular Performance

The proposed genomic and non-genomic effect of vitamin D on skeletal muscle may also affect athletic performance. In particular, any increases in muscle protein synthesis and myogenesis leading to increased muscle mass could result in positive altered muscle strength [18]. Increased anabolism after exercise training could promote recovery from exercise stress [27]. Lastly, hypertrophy of type II muscle fibers could result in enhanced neuromuscular performance [4,18]. It should be mentioned that this type of fibers are crucial for explosive type human movements, which are of great importance in majority of the athletic events.

Cardiovascular System and Vitamin D

Over the last years several studies have elucidated that VDR and vitamin D metabolizing enzymes are expressed in the heart and vascular smooth muscle cells, arterial vessels, endothelial and other cells that affect systemic blood pressure [5,6]. These findings indicate that the cardiovascular system is another target tissue for vitamin D. A vast body of literature introduces a number of pathways by which vitamin D might influence the cardiovascular system. In particular, it has been observed that vitamin D affects the structural remodeling of both the cardiac and vascular tissues [4,6,7], alters myocyte contractility [6], and down-regulates the RAAS [6] which is responsible for vascular resistance, blood pressure, electrolyte and intravascular fluid volume homeostasis. [6,26]. Moreover, low vitamin D levels have been linked with increased arterial stiffness, endothelial dysfunction, and in a deficient state it has been found to stimulate systemic and vascular inflammation, enabling atherogenesis [28-32]. Notably, there is evidence showing that among individuals with peripheral artery disease, low vitamin D status was associated with a faster decline of functional performance [33], providing an indirect link between its levels and performance capacity in this type of population.

Implications for Aerobic Performance

The well documented association between vitamin D insufficiency with left ventricular hypertrophy and several indices of vascular health, including arterial stiffness and endothelial function, could have implications for aerobic performance [28]. Indeed, a linear association between vascular health and arterial stiffness with endurance capacity has been reported [34]. In addition, it is well documented that the most accurate measure of aerobic capacity, VO_{2max}, is regulated by cardiac output, increased peripheral vessel resistance, arterial oxygen content and its extraction, and furthermore, by the ability of the cardiovascular system to provide nutrients to the exercising muscle through the circulation [7]. Since low serum vitamin D levels may result in myocardial hypertrophy, increased blood pressure, endothelial dysfunction and peripheral vascular resistance [34,35], this secosteroid could in turn affect aerobic capacity and VO_{2max} due to decreased cardiac output, and reduced oxygen and nutrients supply to the exercising muscles. These converging lines of evidence could support the idea that inadequate vitamin D levels could negatively influence cardiorespiratory fitness. Lastly, there is evidence showing that vitamin D has the ability to affect the oxidative capacity of the muscle and its metabolism. Treating severe 25(OH) D deficiency has

been associated with improved mitochondrial oxidative capacity in skeletal muscle [6,36]. This finding also indicates that vitamin D could affect aerobic capacity by an indirect control of muscle metabolism.

Vitamin D Levels, Athletic Population and Exercise Performance

The first evidence regarding the possible association between vitamin D and performance has come from early studies [37,38]. It has been reported [37] that cardiovascular fitness, muscle endurance, and speed were enhanced after exposure to ultraviolet radiation. In 1944 German investigators showed that irradiated students showed a 13% improvement in performance on a bike ergometer under ultraviolet radiation, whereas the performance of the control subjects was unchanged [38]. American researchers found that even a single dose of ultraviolet irradiation tended to improve the strength, speed, and endurance of college women [18,37].

In accordance are the findings of a recent study from our laboratory [18]. A linear relationship between vitamin D levels and muscle strength as evaluated by SJ and CMJ, sprinting ability (10 m and 20 m), and VO_{2max} was observed in non-supplemented professional soccer players. Our results are comparable with others showing that vitamin D levels are related with neuromuscular performance capacity in athletes and young physical active individuals [39-42]. However, these findings are not universal. No associations were observed between vitamin D levels and grip strength in hockey players [43], swimming performance in adolescence swimmers [44], and isokinetic peak torque during knee flexion and extension in soccer players [45]. The authors attributed the lack of an association between vitamin D and the examined exercise performance parameters to the different exercise modes employed [43,45], since vitamin D could preferentially affect muscle groups that were not evaluated in these studies. Notably, in the study by Hamilton et al. [45] the soccer players with vitamin D levels <20ng/ml exhibited significantly lower torque in hamstring and quadriceps muscle groups indicating that although vitamin D concentrations above >20ng/ml may not affect performance, there is the possibility that lower levels could impair the ability to perform efficiently during exercise.

Although VO_{2max} and aerobic capacity, based on large epidemiologic cross-sectional investigations, are clearly related with vitamin D serum levels [41,46], the evidence regarding athletic population is limited and inconsistent in nature. A recent study in professional soccer players reported that VO_{2max} was significantly related with the vitamin D status [17]. Similar findings were observed in young physical active individuals [41]. The authors also reported that the individuals who had 25(OH) D levels above the limit of 35 ng/ml which was used as a cut off value, had significantly higher (20%) VO_{2max} values. On the contrary, vitamin D status was not associated with VO_{2peak} as a measure of cardiorespiratory fitness during a skating treadmill test in junior and collegiate male hockey players [43]. The authors suggested that this result should be related with the fact that none of their players were vitamin D deficient. In support to this hypothesis Wilson et al. 2013 [47] suggested that deterioration in aerobic capacity result only in vitamin D deficient individuals.

Vitamin D, Adiposity and Exercise Performance

There is evidence suggesting that vitamin D affects both neuromuscular performance capacity and cardiovascular fitness via indirect mechanisms [4-7]. In particular, a close association between vitamin D levels and adiposity has been observed [4,5,7]. Studies in both athletic and non-athletic populations have shown that low levels of vitamin D are inversely correlated with body fat percentage and BMI [48-50]. In addition, it is well documented that body fat percentage is inversely related with both neuromuscular and aerobic performance capacity [51]. Therefore, based on these observations it could be hypothesized that vitamin D might affect exercise performance indirectly via its effects on human adiposity and body composition status.

Conclusion

This review has investigated the importance of vitamin D in the regulation of a range of physiological systems, its proposed effects on athletic performance, and has provided novel insights into how vitamin D mediated mechanisms may alter this kind of performance. Recent evidence postulates that vitamin D is strongly related with a functional cardiovascular and neuromuscular system and also affects body composition status. Based on the available literature it is clear that vitamin D plays an important role in ability to perform efficiently during exercise while its deficiency may result, apart from deterioration in performance, in several health issues. However, there is limited evidence based on correlation studies showing an association between vitamin D levels and neuromuscular and aerobic performance in athletes. Further research is needed to establish whether vitamin D may benefit the athletic performance or not. The magnitude of the effect in athletes may be less pronounced than that of the ones observed in epidemiologic studies. Regarding the optimum levels of this secosteroid the presented evidence indicates that values of serum vitamin D concentration above 30 ng/ml are required for functional performance.

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