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Editorial

Vitamin D Deficiency and Heart Failure: Possible Mechanisms and Predictive Value

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Abstract

Serum deficiency of 1α, 25-Vitamin D (DVD) is common co-morbidity for various cardiovascular conditions and metabolic diseases. The potential spectrum of biological effects of 1α, 25-Vitamin D3 is very wide – from maintenance of calcium homeostasis and to improve mental function. Growing evidences appear to be suggested that DVD may exiting cardiovascular disease, such as arterial hypertension, atherosclerosis, myocardial infarction, stroke, as well as has negative effects on cardiovascular outcomes due to heart failure (HF), fibrillation/flutter, thromboembolism, atherothrombosis, and dyslipidemia. The aim of the mini review is accumulation data regarding role of DVD in patients with asymptomatic and symptomatic HF as well as cardiovascular disease subjects at high risk of HF.

Keywords: Vitamin D; Deficiency of 1; 25-dihydroxycholecalciferol; Cardiovascular disease; Heart failure; Cardiovascular outcomes; Supplementation of Vitamin D

Introduction

Serum deficiency of 1α, 25-Vitamin D (DVD) is common co-morbidity for various cardiovascular conditions and metabolic diseases [1, 2]. Growing evidences appear to be suggested that DVD may exiting cardiovascular disease, such as arterial hypertension, atherosclerosis, myocardial infarction, stroke, as well as has negative effects on cardiovascular outcomes due to heart failure (HF), fibrillation/flutter, thromboembolism, atherothrombosis [3,4]. Indeed, the great proportion of subjects with exiting cardiovascular disease have been demonstrated DVD when compared with the general population [5, 6]. Although The Framingham Offspring Study and the Third National Health and Nutritional Examination Survey showed a link between Vitamin D3 intake and cardiovascular risk factors, the innate exact molecular mechanisms leaded to worsening of HF associated with DVD are still unclear. The aim of the mini review is accumulation data regarding role of DVD in patients with asymptomatic and symptomatic HF.

Biological role of 1α, 25-Vitamin D3

The active form of vitamin D (1α, 25-Vitamin D3; 1,25-dihydroxycholecalciferol; 1,25-dihydroxy-vitamin D3) has been closely associated with metabolic control, cell and tissue growth, differentiation, suppression of proliferation, induction of apoptosis, and regulation of adaptive and innate immune responses, especially integrity of cartilage, bone and calcium homeostasis [7]. Therefore, 1α, 25-Vitamin D3 has powerful adipogenic and anti-inflammatory properties, lipophylic capacity, and it is able to modulate the synthesis of apo-A lipoproteins [8]. It is known that 1α, 25-Vitamin D3 regulates metabolism via classical steroid hormone receptor-mediated gene transcription and by initiating rapid membrane-mediated signaling pathways [9]. Overall, the potential spectrum of biological effects of 1α, 25-Vitamin D3 is very wide – from maintenance of calcium homeostasis and to improve mental function. In context of the paper it is important to discuss the role of 1α, 25-Vitamin D3 as a marker of cardiovascular outcomes in HF patients and subjects at high risk of cardiac dysfunction.

1α, 25-Vitamin D3 and Inflammation

Vitamin D deficiency in humans is frequent and has been associated with inflammation. There are data that DVD has been induced a progression of cardiovascular disease through activation of inflammation because the 1α, 25-Vitamin D3 has anti-inflammatory properties [10]. In fact, serum inflammatory cytokines, such as interleukin-6, tumor necrosis factor-alpha and interferon-γ, have been shown to impact to alteration of receptor's expression for 1α, 25-Vitamin D3 in skeletal and cardiac muscle has been reported to result in significant effects on metabolism, calcium signaling and fibrosis in these tissues [10]. Overall, dysregulation of nuclear receptor signaling pathways in cardiovascular disease is common for their progression. In this context, altered expression of 1α, 25-Vitamin D3 receptors probably may have a pivotal role in translation of inflammation state to the tissue repair worsening. There are data clarified that decreased 1α, 25-Vitamin D3 may lead to insulin resistance, which is considered a key player in the development of myopathy, sarcopenia, and cachexia in HF [11]. Because expression of 1α, 25-Vitamin D3 receptors has been decreased with age [12], elderly and senior subjects are vulnerable population for DVD-related progression of cardiovascular disease.

Vitamin D and Vascular Repair

The role of the active hormone 1, 25-dihydroxycholecalciferol (1, 25-dihydroxy-vitamin D3; 1α, 25-Vitamin D3) in the cardiovascular system is controversial. It is well known that high doses of 1α, 25-Vitamin D3 may induce vascular calcification, increase a risk of atherothrombosis and improve glucose metabolism [13, 14]. Recent studies have been shown a closely positive correlation between DVD and glycated hemoglobin, low-density lipoproteins, body mass

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index, markers of endothelial dysfunction, such as asymmetric and symmetric dimethylarginine, and inverted correlation with fasting glucose [15, 16]. Therefore, 1α, 25-Vitamin D3 may involve in maturation and differentiation of progenitor cells different origin that plays a pivotal role in vascular reparation [17]. In animal model Gupta GK et al [18] found that significant down-regulation of receptors in proliferating smooth muscle cells in neointimal lesions could be due to atherogenic cytokines, including tumor necrosis factor-alpha and inflammatory interleukins. According opinion of investigators these findings could be explained a potential mechanism for uncontrolled growth of neointimal cells in injured arteries leading to rest enosis and worsening vascular remodeling. Given these facts it might be suggested that DVD links lipid and glucose metabolism and contributes vascular reparation. However, potential independent role of serum 1α, 25-Vitamin D3 as marker of vascular remodeling is still not understood.

Serum 25-hydroxy Vitamin D and Cardiovascular Outcomes

Currently the relationship between 1α, 25-Vitamin D3 level, dose of Vitamin D3 supplements, and total mortality rates remains to be under investigated [19]. In population-based cohort ESTHER study survival status among patients (total of 9949 men and women, aged 50 to 74 years) od generally population were collected after 2, 5, and 8 year's follow-up period [20]. Authors reported that comparing subjects with 1α, 25-Vitamin D3 levels below 30 nmol/L and above 50 nmol/L resulted in a hazard ratio of 1.27 (95% confidence interval = 1.05-1.54) for total cardiovascular events and 1.62 (95% confidence interval = 1.07-2.48) for fatal cardiovascular events in a model adjusted for important potential confounders. Therefore, increased cardiovascular risk at 1α, 25-Vitamin D3 levels below 75nmol/L was found. Authors concluded that DVD associates with moderately increased risk of cardiovascular disease. In fact, it is surprise that the observed association is much stronger for fatal than for nonfatal events obtained. Dror Y et al [21] reported that 1α, 25-Vitamin D3 in the 20-36 ng/mL range was associated with the lowest risk for mortality and morbidity in patients with acute coronary syndrome. However, low and high serum level of 1α, 25-Vitamin D3 was identified as predictors of increased mortality. Prevalence of DVD in small patient population with takotsubo cardio myopathy was found too [22]. Although deficiency of serum 1α, 25-Vitamin D3 appears to be frequently, it does not understand whether DVD is phenotypic marker at high cardiovascular risk or factor contributed innate pathogenetic mechanisms of disease progression.

Chronic Heart Failure and 1α, 25-Vitamin D3 Deficiency

There are evidences regarding tightly association DVD and poor prognosis in chronic HF patients [23-25]. Indeed, Fall T et al [23] found that higher circulating 1α, 25-Vitamin D3 was to be associated with better left ventricular pump function. Therefore, biomarkers of cardiac remodeling appear to be closely associated with 1α, 25-Vitamin D3 level that probably may take into consideration in the field direct effecting DVD on clinical outcomes [26]. On the other hand, in small population-based cohort Hoorn Study the significant interrelation between 1α, 25-Vitamin D3 and myocardial structure was not found [27].

In final, there are attempts to treat the patients with HF aimed improving clinical status and outcomes, but obviously they are not always sufficient. Indeed, the possible therapeutic benefits of vitamin D supplementation are very attractive. Schroten NF et al [28] reported that six weeks of supplementation with 2,000 IU VitD3 increased 1α, 25-Vitamin D3 levels and decreased plasma rennin activity and plasma rennin concentration. No significant changes in serum N-terminal pro-B-type natriuretic peptide and markers of fibrosis were observed. Large clinical trials are needed to be clarifying the effect of Vitamin D supplementation in DVD subjects with HF and cardiovascular disease.

Conclusion

I conclusion, recent investigations have shown that DVD was to be associated with cardiovascular diseases as well as the presence of comorbidities, such as diabetes mellitus, dyslipidemia, and hypertension. Although DVD in HF population is frequently presents, lack of strongly evidence regarding vitamin D supplementation and improving cardiovascular mortality in various patient cohorts. More important that DVD is considered a powerful tool for risk stratification of the patients with HF and other cardiovascular disease, while so many speculations regarding how does it work in real clinical practice are existed.

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