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CORONARY ARTERY DISEASE WITH PROSPECT OF FIBROBLAST GROWTH FACTOR-23 AND VARIOUS OTHER FACTORS -A NOVEL REVIEW PART II.

Medical Science

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ABSTRACT

Various factors play a role in Coronary Artery Disease like Insulin, Vitamin-D, Calcium, Phosphorous, and FGF-23 levels in blood. In continuation of the first part, present review explains the remaining part of relation of CAD with Vitamin-D, calcium, and phosphorous levels, in the blood.

KEYWORDS

Coronary Artery Disease, Vitamin-d, Calcium, And Phosphorous

INTRODUCTION

Abnormality in mineral metabolism mainly in phosphate and calcium might also lead to increased chances of CAD. Calcium is required in various body processes like blood clotting, muscle contraction, nerve impulse transmission, blood pressure regulation, hormonal regulation and enzyme activation. And it's been reported that there is a relationship between serum calcium level and increased risk of myocardial infarction[1]. Increase in arterial calcification can be attributed due to increase in phosphorous level in the body. In continuation of the first part, present review explains the remaining part of relation of CAD with Vitamin-D, calcium, and phosphorous levels, in the blood.

VITAMIN D

Vitamin D a lipid soluble prohormone. Vitamin D3 and cholecalciferol, are the two major precursors of vitamin D and are synthesized in the skin by sunlight and vitamin D2 or ergocalciferol [2,3], a plant derived, produced exogenously by irradiation of ergosterol, and enters the circulation through diet. Vitamin D3 is formed when 7-dehydrocholesterol in the skin is exposed to ultraviolet rays and converted to previtamin D3. This previtamin D3 is immediately converted to vitamin D [4]. Vitamin D is transported by the vitamin D binding protein to the liver where it undergoes hydroxylation to inactive form of vitamin D{(25(OH)D} and to kidneys where it is hydroxylated by the 1 alpha hydroxylase enzyme to active form of vitamin D {1,25(OH)D}. This enzyme is also expressed in a variety of extrarenal tissue, like osteoclasts, skin, colon, brain, keratinocyte, trophoblast of placenta and macrophages, which may be the cause of its wide-range of effects. Major inducers of alpha-1 hydroxylase enzyme are parathyroid hormone (PTH) and hypophosphatemia, and major inhibitors of this enzyme are calcium, fibroblast growth factor 23, and the enzyme's product $1,25(OH)_2D$.

Vitamin D plays an important role in maintaining an adequate level of serum calcium and phosphorus thus involved in bone homeostasis and metabolism. Vitamin D through its calcium regulation, influences various mechanisms associated with the pathophysiology of T2DM, including pancreatic β cell dysfunction and impaired insulin action [5-6]. Studies suggested that by optimizing vitamin D level could reduce insulin resistance [7]and decreases the risk of developing type 2 Diabetes mellitus [8,9]. Epidemiologic studies suggest a link between vitamin D and development of type 1 DM [10,11] Vitamin D3 receptors have strong immune-modulating effects. In some populations the development of type 1 DM is associated with polymorphisms in the vitamin D receptor gene [12,13]. However, the results from underpowered trials and post hoc analyses of larger trials on the effect of vitamin D supplementation on glycemic outcomes have been inconsistent [13-19].

Since the vitamin D receptors are also present in endothelium, Vitamin D may also have an impact on cardiovascular disease. vascular smooth muscle and cardiomyocytes. Framingham offspring studied vitamin D levels and incident cardiovascular events [20] and concluded that, participants who had low vitamin D levels were more likely to experience cardiovascular disease. The relationship remained significant among people with hypertension but not among those without hypertension.

On contrary, despite abundant evidence of the involvement of Vitamin D deficiency in the pathogenesis of CAD, very few well-conducted randomized controlled trials address this issue and also several randomized controlled trials where Vitamin D supplementation was evaluated in high-risk population in relation to improvement in cardiovascular outcome have failed to provide any conclusive results [21,22]. A systematic review conducted by Pittas *et al* [23] of longitudinal studies examining the relationship of Vitamin D supplementation on cardiometabolic outcomes (type 2 diabetes, hypertension, and CV disease) concluded that association of Vitamin D status and cardiometabolic outcome is uncertain. Out of the 13 trials, they examined four trials which showed that Vitamin D supplementation does not influence the cardiometabolic outcomes. Similarly, a recent randomized controlled trial examining the effect of Vitamin D supplementation on 24 h systolic ambulatory BP monitoring values and CV risk factors in hypertensive patients concluded that there is no significant effect of Vitamin D supplementation on BP and other CV risk factors; rather it increases triglyceride levels in the experimental group. [24].

CALCIUM AND PHOSHPORUS

Calcium and phosphorus have a role in numerous body functions, and are essential minerals found in the bone, blood and soft tissues. Phosphorus levels can affect calcium levels in the body, and vice versa. Parathyroid hormone, vitamin D and the kidneys all play their role in regulating calcium and phosphorus levels in the blood. Calcium and phosphorus are absorbed into the blood through the small intestine after eating foods that contain these nutrients. The bones will also release the nutrients to help maintain necessary blood levels. The parathyroid gland can sense an imbalance of calcium or phosphorus. If the calcium level is low, the parathyroid gland will release PTH, which tells the kidneys to produce more active vitamin D. This helps the body to absorb more dietary calcium and phosphorus through the intestine, tells the bone to release calcium and phosphorus into the blood and tells the kidneys to excrete more phosphorus in the urine.

Serum calcium and phosphorus also play an essential physiological role in energy production, membrane transport, and signal transduction [25]. Recent studies reported that higher serum calcium or phosphorus level could be associated with the pathogenesis of cardiovascular disease, including atherosclerosis, heart valve calcification, vascular calcification, and arterial stiffness. In patients with chronic kidney disease and in the general population, high serum phosphorus levels have been associated with mortality and cardiovascular events. Supporting evidence for an association between serum calcium and the risk of death and cardiovascular events is poor among individuals with chronic kidney disease (CKD). Also, current data on its association between serum calcium and phosphorus and cardiovascular risk remain controversial [25,26].

Coronary artery calcium (CAC) score determines the volume of calcium, it plays an important role in cardiovascular risk. Previous studies have shown association between CAC and CAD [27,28]

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