Role of Vitamin D in Prediabetic Individuals – Update

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ABSTRACT

Vitamin D deficiency and diabetes have one common trait of being pandemic. Association between insulin sensitivity and serum 25-OHD levels is clear. Patients with diabetes and Vitamin D deficiency have increased insulin resistance. Vitamin D supplementation may decrease the incidence of diabetes mellitus and may improve the metabolic control in the diabetes state.

Keywords: Deficiency, Prediabetes, Vitamin D

INTRODUCTION

Unequivocal evidence supports the primary association of vitamin D with bone health. Recent evidences suggest role of vitamin D in optimal functioning of many organs and tissues throughout the body. It has also been documented to play important role in the prevention and management of diabetes mellitus, myocardial infarction, stroke and congestive heart failure.[1,2] Epidemiological evidences show a close association between vitamin D deficiency and diabetes mellitus progression.[3] Recent studies have provided the information that it is beneficial and rational to give vitamin D in patients suffering from type 2 diabetes mellitus (T2DM).[1,3] Rational drug prescribing is defined as the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost.[4]

The present update outlines the beneficial properties vitamin D against progression of prediabetes to type 2 diabetes mellitus.

Vitamin D deficiency and Prediabetes

Prediabetes refers to impaired fasting glucose and/or impaired glucose tolerance in individuals. Prediabetic individuals are at increased risk of developing T2DM. In India, there is high prevalence of T2DM. It has been forecasted that by 2030, India would bear maximum burden of this disease in the world. It has been estimated that between 33% and 66% of people with pre-diabetes will progress to T2DM over a period of 3-6 years. During that time, they may also be at increased risk of coronary heart disease. Risk factors for prediabetes include obesity (BMI>30kg/m2); a high waist circumference measurement (>80 cm in women and 94 cm in men); a sedentary life style; a close family history of T2DM; a history of gestational diabetes in women; and being >40 years (or >25 years for some black and minority ethnic groups).

For most people in prediabetes stage, healthy lifestyle modifications or pharmacologic interventions have been shown to be effective in preventing or delaying the onset of T2DM. Several clinical evidences support this hypothesis that individuals at risk of developing T2DM have lower serum concentration of 25(OH)D. The results from two nested case-control studies collected by Finnish Mobile Clinic have suggested that high 25(OH)D status provide protection against T2DM.[5,7]

Vitamin D and insulin sensitivity

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Local production of 1α, 25(OH) 2D3 may be an important autocrine link between vitamin D status and pancreatic function. Vitamin D plays a crucial role in the endocrine functioning of pancreas due to presence of vitamin D-dependent calcium-binding protein and cytosol receptor for the hormonal form of vitamin D, 1,25(OH)2D3 in the pancreas. Studies have reported that vitamin D play an important role in insulin secretion and insulin resistance. 25(OH)D concentration is independently associated with both insulin sensitivity and beta cell function among individual at risk of type 2 diabetes mellitus, thereby indicating that vitamin D may play a role in pathogenesis of T2DM. These findings suggest that vitamin D may have an important role in regulating glycemic control, which may also contribute to beneficial effect on CV outcomes.\textsuperscript{[8-9]}

**Mechanisms for the effects of vitamin D**

Presence of vitamin D receptors on pancreatic \(\beta\) cells, Vitamin D activating 1α hydroxylase expressed in pancreatic \(\beta\) cells, presence of vitamin D response element in the insulin gene, presence of vitamin D receptor in skeletal muscle and the fact that 1,25(OH)D increases transcription of insulin receptor genes and also suppresses the renin gene reducing hyperglycaemic induced increases in renin levels in pancreatic \(\beta\) cells and blockade of renin angiotensin activity has been proposed as a novel target for diabetes treatment. Protective effects of vitamin D in diabetes, maybe due to well-known effects of vitamin D such as its anti-inflammatory properties, its effects on calcium and phosphorus metabolism and regulation of the insulin receptor gene. It seems that vitamin D increases calcium content of the cells, in turns leads to increased transport of glucose into the muscle. Vitamin D also regulates nuclear PPAR (Peroxisome proliferative activated receptor) that has an important role in the insulin sensitivity. Vitamin D deficiency is associated with increase in inflammation. Vitamin D attenuates the expression of proinflammatory cytokines involved in insulin resistance such as interleukins, IL1, IL6, TNFa, also down regulates NFk\(\beta\) (Nuclear factor) activity.\textsuperscript{[10,11]}

**Preventing the progression of prediabetes with Vitamin D supplementation**

Traditionally, synthesis in the epidermis from sun exposure and foods (sun dried mushrooms and oily fish) are two main sources of vitamin D. The institute of Medicine guidelines have recommended a dose of vitamin D3 up to 4,000 IU daily as safe. For vitamin D deficient individual’s treatment should be initiated with 50,000 IU of vitamin D3 weekly for a period of 8 to 12 weeks. Maintenance therapy can be continued once the initial repletion phase is complete (Fig.1).

Several cross-sectional and prospective studies in various populations show inverse association between circulating 25(OH)D and fasting plasma glucose (FPG) level, impaired glucose tolerance (IGT), HbA1c, metabolic syndrome, and incidence of prediabetes. A small number of clinical trials have suggested beneficial effect of vitamin D supplementation in prediabetes, including improved insulin secretion, basal fasting insulin sensitivity and postprandial peripheral insulin resistance. Vitamin D deficiency may, therefore be involved in the pathogenesis of diabetes, and a better understanding of mechanism involved could lead to the development of preventive strategies.

**CONCLUSION**

Vitamin D plays an important role in lowering risk of prediabetes progressing to T2DM. This provides a rationale for the use of vitamin D as a therapeutic adjunct in prediabetic individuals.

**What this study adds:**

1. **What is known about this subject?**
   Vitamin D play an important role in the prevention and management of diabetes mellitus, myocardial infarction, stroke and congestive heart failure. Epidemiological evidences show a close association between vitamin D deficiency and diabetes mellitus progression.

2. **What new information is offered in this study?**
   This update emphasizes that vitamin D supplementation has benefits in terms of glycemic parameters and highlights that vitamin D is beneficial and should be recommended to prevent the progression from prediabetes to diabetes.
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