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### VITAMIN D DEFICIENCY AND ITS RELATIONSHIP WITH TYPE II DIABETES MELLITUS

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All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0). Abstract: Hypovitaminosis D exceeds 50% of the Brazilian population, causing major implications for public health in the country. Low vitamin D levels are associated with worse glycemic control. Therefore, the aim of this study is to review the literature on the effect of vitamin D on glycemic control. It has been observed that a low concentration of vitamin D is associated with a decrease in both production and sensitivity to insulin. In patients with type II diabetes, there is a high prevalence of hypovitaminosis D. In this sense, studies with diabetics who underwent vitamin D supplementation still show contradictory data on the effectiveness of supplementation in glycemic control. Thus, it is of paramount importance to carry out research in the area for a reliable result that can cause a direct response in the population.

**Keywords:** Vitamin D, Diabetes Melittus, Glucose, Supplementation.

#### INTRODUCTION

Vitamin D is considered a prohormone, which plays a key role in calcium and phosphate balance and bone structure (BANDEIRA et al. 2015). In addition, it also has receptors in the most diverse cell types such as hematopoietic cells, epidermal cells, neurons, osteoblasts, myocytes, among others (SCHUCH et al., 2009).

Vitamin D can be found in two forms D2 (ergocalciferol) that comes from the diet, through the consumption of foods such as fish, egg, tuna, oil and is also available in its D3 form (cholecalciferol), synthesized by the skin through exposure to solar radiation (VILAR, 2021).

To become active, vitamin D undergoes a hydroxylation process (the vitamin molecule receives an OH in its structure) and is called 25-hydroxyvitamin D (25OHD) (BANDEIRA et al., 2015). In the kidney, this molecule will undergo a second hydroxylation, becoming called 1,25 dehydroxyvitamin D (1,25(OH)2D), the active version of the vitamin.

In recent decades, several studies have shown an association between low 25OHD concentration and increased risk of cancer, cardiovascular disease, glucose metabolism disorders, neurodegenerative diseases and death (AUTIER et al, 2013). However, it is interesting to note that even in tropical countries such as Brazil, the prevalence of hypovitaminosis D exceeds 50% of the population and can increase the risk of various health complications (RAMOS, 2018). Specifically, regarding glycemic control, hypovitaminosis D is associated with both insulin resistance and pancreatic beta-cell dysfunction (SCHUCH et al., 2009). However, the physiological mechanisms that explain the link between vitamin D and glycemic control are not completely understood. Thus, the aim of this study is to review the literature on the effect of vitamin D on glycemic control.

#### METHODOLOGY

A bibliographic survey was carried out in the Scielo, Pubmed and Google Scholar databases. In these environments, we searched for articles published between 2000 and April 2021, using descriptors such as: Vitamin D, Diabetes Mellitus, Calbindin, Glucose, Vitamin D Receptor, Supplementation. Additionally, consultations of printed and online books were carried out to build and complement the information and discussions on the subject.

#### **RESULTS AND DISCUSSION**

Vitamin D contributes to the maintenance of glucose homeostasis through indirect mechanisms. One study compared vitamin D concentrations in 120 people with diabetes mellitus and 120 healthy individuals. It was observed that among diabetics the prevalence of low level of low 25(OH)D3 was higher than among healthy individuals. Furthermore, an inverse relationship was identified between glycated hemoglobin and 25(OH)D3 levels in the patient group, implying that 25(OH) D3 levels may affect glucose control in type 2 diabetes mellitus (KOSTOGLOU-ATHANASSIOU et al, 2013)

The mechanism of action of the vitamin, in the control of glycemia, seems to be due to the existence of Vitamin D receptors in the  $\beta$ -cells (insulin producers), which can affect the synthesis of insulin, as well as having a role in the binding proteins of calcium to the pancreatic tissue (CHRISTAKOS et al, 2003)

Firstly, the active form of vitamin D (1,25-dihydroxyvitamin D) has as one of its purposes to increase the synthesis of calbindin (calcium binding protein) which in turn helps maintain calcium homeostasis in some tissues. Thus, the presence of 1,25-dihydroxyvitamin D increases the production of calbindin, especially calbindin-D28k, which acts by taking calcium to the beta-pancreas cells. a low synthesis of calbindin and consequently there would be a low production of insulin, considering that the Beta-pancreatic cells need calcium to depolarize and release insulin. Thus, calbindin controls insulin release by regulating intracellular calcium (CHRISTAKOS et al, 2003). Therefore, optimal levels of calcium and vitamin favor the increase of calbindin, contributing to the release of insulin by regulating intracellular calcium, aiming at glycemic control (PITTAS et al, 2006).

Secondly, vitamin D in its active form (1,25OH2D) can act directly on  $\beta$  cells, which operate from the bloodstream, by binding to the set of vitamin D receptors (VDR), causing an increase in the transcriptional activation of the insulin receptor gene, there is then an overall increase in these receptors in the cells. Thus, it causes an increase in extracellular

glucose uptake. In addition, vitamin D can promote greater longevity of  $\beta$  cells by modulating generation (through inactivation of nuclear factor-kB [NF-kb]) and through cytokines (MITRI J.; PITTAS, A.G. 2014).

## VITAMIN D SUPPLEMENTATION IN DIABETICS

Vitamin D supplementation by patients with type 2 diabetes mellitus is a subject that has been gaining great repercussion lately, since, according to the Pan American Health Organization, diabetes affects about 60 million people throughout the American continent (OPAS, 2021). Considering this high prevalence, strategies to improve glycemic control are of great relevance (BELL, 2011).

A recent meta-analysis showed that daily doses of more than 2000 IU/day were consistently associated with improved glycemic indices (LI et al., 2018). However, the findings are still contradictory. For example, in the study carried out by Pittas and collaborators (2019) more than 2000 participants were analyzed, who were randomized into two groups, G1 received supplementation of 4000UI per day and G2 received placebo. The authors noted that supplementation did not result in a significantly lower risk of diabetes than placebo (PITTAS et al, 2019).

#### FINAL CONSIDERATIONS

In conclusion, it can be observed that there is an association between vitamin D concentration and parameters related to diabetes. Considering the relevance of protective strategies for this disease, it is necessary to carry out more studies to identify the real effect of vitamin D on glycemic control, as well as the optimal dosage of this vitamin to obtain these effects.

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