Research Progress on the Role of Vitamin D in Preventing Gestational Diabetes

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Abstract. Research on the prevention and treatment of gestational diabetes mellitus (GDM), which poses a major threat to the health of both mothers and children, has to increase as living standards have increased. Numerous investigations into the pathophysiology of GDM, such as chronic insulin resistance, islet beta cell dysfunction, and other factors, have been carried out recently. Numerous studies have also examined the relationship between vitamin D and GDM, concluding that vitamin D deficiency may be linked to the development of GDM and that vitamin D supplementation can help GDM patients. The results of the research, however, are conflicting because of the influence of numerous factors, making it impossible to say if vitamin D supplementation is a prerequisite for the prevention and management of GDM. This article reviews the research progress on the prevention of GDM by analyzing the relationship between vitamin D and GDM. Future research should expand sample sizes, integrate multiple influencing factors, and investigate the precise relationship between vitamin D and GDM to develop more authoritative prevention and treatment strategies.

Keywords: Vitamin D, gestational diabetes, medical nutrition therapy.

1. Introduction

A common pregnancy complication that falls under the category of high-risk pregnancy is GDM, which is defined as an increase in blood sugar that occurs when a pregnant woman with insufficient insulin secretion is unable to compensate. Following childbirth, some people recover on their own, but those with GDM are more likely to acquire type 2 diabetes. The incidence of GDM in China is 14.8%–23.2% [1], and it is still increasing. The global prevalence rate is currently 10.4%–25.0% [2]. Its pathogenesis is more complex, pregnant women will appear in the pregnancy period, polydipsia, polyuria, weight loss, easy fatigue, dizziness and other symptoms. In addition, diabetes will also increase the incidence of complications during pregnancy, such as excessive amniotic fluid, macrosomia, premature rupture of membranes and other adverse consequences, so GDM will seriously harm the health of mother and child, must be paid attention to.

Studies have shown that medical nutrition therapy (MNT), as a common intervention method for GDM patients, combined with exercise, can achieve significant effects such as sugar control and adverse pregnancy risk inhibition [3]. In another study, according to the characteristics of maternal energy requirements and blood sugar control requirements during pregnancy, reasonable collocation of the intake of various nutrients, trace elements and vitamins during pregnancy can also significantly reduce the blood sugar level of pregnant women with gestational diabetes and improve the pregnancy outcome [4]. GDM is characterized by insulin-island beta cell dysfunction in the context of chronic insulin resistance during pregnancy. At present, studies have shown that vitamin D, folic acid and vitamin B12 can significantly improve patients' insulin sensitivity [5-6].

Therefore, this paper will review the research progress on the prevention of gestational diabetes by analyzing the research status of vitamin D and gestational diabetes, aiming to lay a foundation for subsequent research and provide a theoretical basis.

2. Vitamin D Status

2.1. Introduction to Vitamin D

Vitamin D is a fat-soluble cholesterol-like hormone, also known as calcitol, which is a large group of substances containing cyclopentahydroenanthrene structure and having the biological activity of calciferol, the most common being vitamin D2 and vitamin D3. 80%-90% of vitamin D is converted from UV absorption by human skin, and the remaining 10%-20% is from dietary absorption, such as cod liver oil, mushrooms and liver, so the main source of vitamin D supplement is sun-irradiated skin synthesis, food and supplement addition [7]. Vitamin D is considered to be a pleiotropic prohormone with widely distributed receptors that regulate immune response and have anti-inflammatory effects [8].

2.2. Vitamin D's Mechanism of Action in the Human Body

The health of the human body is closely associated with vitamin D2 and D3. Vitamins D2 and D3 are prohormones that are active after being hydroxylated twice: First, 25-hydroxyvitamin D (25[OH] D) is formed in the liver, and then the bioactive hormone calcitriol (1, 25 (OH) 2D) is formed in the kidney, and is used in the small intestine, bone and other target organs, participating in the maintenance of intracellular and extracellular calcium concentration and the regulation of metabolism. In addition, vitamin D has immunomodulatory and anti-inflammatory effects. Vitamin D3 is the primary form of vitamin D that is available to the body. 1,25 (OH)2D is the most important active component of vitamin D3, which can be obtained by sunlight (produced by chemical reaction of cholesterol in the skin and directly absorbed into the blood) and diet (absorbed into the blood by lymphatic vessels along the brush border of the small intestine under the action of bile) [9]. It has been demonstrated by studies that there exist more than 40 metabolites of vitamin D. Despite the fact that most of them have a short half-life during circulation, the half-life of 25[OH] D is within the range of 21 - 30 days. Thus, detecting the serum 25[OH] D stands out as the best approach to assess vitamin D [10]. The National Institutes of Health concluded [11] that if an individual's serum 25[OH] D is≥50 nmol /L, vitamin D can be considered adequate. Serum 25[OH] D is also commonly used clinically as an indicator to measure vitamin D levels in the body. Currently, vitamin D has been under investigation as a prospective candidate for the treatment or prevention of cancer and autoimmune disorders such as T1D [12].

3. Pathological Process of GDM

3.1. Pathogenesis of GDM

GDM is a type of spontaneous hyperglycemia during pregnancy, according to IADPSG criteria: Receiving a fasting blood glucose (FPG) test reading≥92 mg/dL at the first prenatal visit indicates GDM [13]. The body of the mother goes through a series of physiological changes during a healthy pregnancy to help the fetus develop, including the adaptation of the cardiovascular, kidney and metabolic system, and insulin sensitivity is an important metabolic adaptation during pregnancy. During the first trimester, insulin sensitivity increases, but as pregnancy progresses, the increases in local hormones and those secreted by the placenta can bring about a condition of insulin resistance [14]. This slight state of insulin resistance is able to boost the production of endogenous glucose and the breakdown of fat reserves, which will result in further rises in blood sugar levels and the concentrations of free fatty acids (FFA) [15]. Animal evidence shows that, in order to keep glucose homeostasis, pregnant women make compensations for these changes by means of the hypertrophy and proliferation of pancreatic beta cells as well as an increase in GSIS. Under normal circumstances, the mother's insulin sensitivity can be restored to the pre-pregnancy level within a few days after delivery [16], while the vast majority of 80% of GDM patients show β-cell dysfunction in the context

of CIR, in which the normal insulin resistance during pregnancy is partially superposition [17]. As a result, affected women tend to have more severe insulin resistance than healthy pregnant women.

3.2. Influencing Factors of GDM

Chronic insulin resistance (IR), obesity, islet beta cell dysfunction and other factors may lead to the development of gestational diabetes. As antagonistic insulin-like substances increase in pregnant women, insulin sensitivity decreases, maternal glucose and free fatty acid concentrations increase, and insulin secretion increases in order to maintain normal blood sugar levels. If insulin secretion is excessive, Ca2+ and reactive oxygen signaling is too strong, the function of islet beta cells is impaired, and islet cells die, leading to the occurrence of GDM [18].

4. Application Progress of VD Adjuvant Therapy for GDM:

4.1. Correlation between VD and GDM

Pregnancy is a special stage in the life course, with a high demand for vitamin D. During pregnancy, the synthesis of 1, 25(OH) 2D in the kidneys increases, and the serum level of 1, 25(OH) 2D in women in late pregnancy stage is twice that of non-pregnant or postpartum women [19]. But during pregnancy, a decrease in outdoor activity and sun exposure, as well as an increase in fat mass at the end of pregnancy, can lead to insufficient intake of the required vitamin D. Testing for 25[OH]D is the best way to assess vitamin D status. Some studies have found that 25[OH] D concentration is related to the age of women during pregnancy, BMI during pregnancy, seasonal changes and other influencing factors. The prevalence of vitamin D deficiency was significantly higher in pregnant women over 35 years of age and in pregnant women during childbirth. According to the studies of LAN Xulan, Liu Zhao and Ma Ziwen et al., lack of vitamin D in pregnant women can induce GDM. The level of 25[OH] D is closely related to blood glucose, glycated hemoglobin and insulin resistance in GDM patients [20-22].

4.2. Preventive Effect

Vitamin D participates in regulating Ca-P metabolism as well as IST, and it plays a significant role in maintaining the normal metabolism of blood glucose.Vitamin D deficiency or insufficiency may affect fat metabolism, low-grade inflammatory response, immune response, oxidative stress, mitochondrial function and other pathways, resulting in abnormal GLM, affecting insulin sensitivity, and increasing the risk of insulin resistance. During pregnancy, the synthesis of 1, 25(OH) 2D in the kidneys of pregnant women increases, and serum 1, 25(OH) 2D levels in women in the third trimester are twice as high as in non-pregnant or postpartum women [23]. It can be concluded that the need for vitamin D intake is higher during pregnancy. In addition, studies have shown that oral vitamin D3 intervention in GDM patients can increase the level of 25-hydroxyvitamin D and decrease the value of insulin resistance index, suggesting that vitamin D3 supplementation is conducive to improving insulin resistance. The reasons were analyzed to be related to reducing fat accumulation in adipocytes, alleviating leukocyte infiltration in adipose tissue, improving specific immune dysfunction, enhancing serum total antioxidant capacity, and regulating mitochondrial regulatory function [24], which may reduce the risk of GDM.

During pregnancy, it is recommended to boost the amount of outdoor activities, lengthen the duration of sun exposure, and ingest natural foods with a high vitamin D content. The intention behind this is to prevent the possible consequences of vitamin D deficiency or insufficiency on metabolic pathways, especially those related to fat cell metabolism, low-grade inflammatory response, immune response, oxidative stress, and mitochondrial function. These impacts could lead to abnormal GLM and an elevated risk of insulin resistance.

4.3. The Impact of Vitamin D Supplementation in Preventing GDM

Vitamin D can affect glucose homeostasis in the body, GDM with functional pancreatic changes, and the anti-inflammatory characteristics of vitamin D contribute to the restoration of physiological insulin secretion, if vitamin D deficiency, can affect insulin secretion. Vitamin D supplementation can also promote duodenal absorption and enhance kidney's ability to absorb calcium, which is conducive to insulinactivated intracellular signaling. If vitamin D is deficient, it is not conducive to intracellular calmodulin regulation and affects insulin receptor drive of peripheral cells. In addition, vitamin D mediates pancreatic beta cells to secrete insulin. Therefore, the monitoring of vitamin D-related indicators should be strengthened during pregnancy [25].

Studies have shown that 25-OH-VD deficiency can be regarded as a solitary risk determinant for the initiation of GDM. If 25-OH-VD deficiency leads to significant abnormalities in blood sugar and insulin, GDM will be caused [26]. As the principal form of vitamin D in the organism, 25-OH-VD is a widely recognized evaluation index of vitamin D. If the level of 25-OH-VD is normal, it indicates that vitamin D is sufficient, can rapidly induce the function of pancreatic β cells and promote insulin transcription and synthesis, so vitamin D has a certain role in preventing and treating GDM. Therefore, vitamin D supplementation can reduce fasting blood glucose, glycated hemoglobin and serum insulin levels and improve glucose metabolism in women with GDM. Studies have found that the positive rate of glucose stimulation test and glucose tolerance test in pregnant women supplementing vitamin D in early and mid-term pregnancy is significantly higher than that in pregnant women supplementing 5000IU vitamin D daily, and compared with pregnant women who do not supplement vitamin D, the risk of GDM in pregnant women supplementing vitamin D D1 ~ 399IU or more than 400IU a day is significantly reduced. However, inconsistent research results were also reported. For example, a study conducted by Indian scholars included 559 pregnant women and a serum 25- (OH) D detection conducted by PARK et al., 523 pregnant women from South Korea [27, 28] both found that vitamin D was not associated with GDM. The differences in research results are related to the influence of various factors such as sample size, race, region, season, age and lifestyle differences in different studies. More high-quality experimental studies on vitamin D and GDM can be carried out in the future.

5. Conclusion

This article reviews the research progress on the prevention of GDM by analyzing the research status of vitamin D and GDM. This paper introduced the pathogenesis and pathological process of GDM, expounded the correlation and mechanism of action of vitamin D, and emphatically discussed the application progress of vitamin D adjuvant therapy for GDM, including the correlation between the two, the preventive effect and the effect of vitamin D supplement. By reviewing a number of literatures, we can thereby deeply fathom the origin and development of GDM and affirm that supplementing with vitamin D can better the situation of those with GDM, laying a theoretical foundation for subsequent studies on the prevention and control of GDM by regulating vitamin D levels. Nevertheless, currently, the majority of research is merely centered around the correlation between vitamin D and GDM, while the comprehensive consideration of other possible influencing factors of GDM is inadequate, which cannot determine whether vitamin D supplementation can be used as a necessary condition for the prevention and treatment of GDM. Follow-up studies can expand the sample size, comprehensively consider a variety of influencing factors, and deeply explore the precise connection between vitamin D and GDM, so as to form a more authoritative prevention and treatment strategy and better improve the incidence of GDM.

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