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Type 2 diabetes mellitus and vitamin metabolism

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Abstract

Type 2 Diabetes Mellitus (T2DM) is a disease characterized by chronic hyperglycemia and oxidative damage, leading to harm in tissues and organs. Studies have shown a relationship between increased oxidative stress, decreased insulin sensitivity, and the effectiveness of antioxidant therapy in managing T2DM. Early diagnosis, lifestyle changes, drug therapy, and vitamin supplements are essential in managing T2DM. Antioxidant vitamins, in particular, are crucial for reducing oxidative stress caused by T2DM and minimizing related complications.

Keywords: type 2 diabetes mellitus, antioxidant vitamins, insulin sensitivity, oxidative stress, glycemic control

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Introduction

According to the World Health Organization (WHO), Diabetes Mellitus (DM) is a chronic metabolic disease characterized by high blood sugar levels, which can lead to significant damage to the heart, blood vessels, kidneys, eyes, and nerves over time. The latest etiological classification by WHO identifies four clinical types of DM: Type 1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), DM due to other causes (e.g., infections, genetic disorders), and Gestational Diabetes Mellitus (GDM) [1].

T2DM results from the body's resistance to insulin or insufficient insulin production, often associated with lifestyle factors such as sedentary behavior, dietary habits, and obesity. Conversely, T1DM occurs due to the immune system's destruction of insulin-producing pancreatic cells [2].

The prevalence of T2DM is rising globally, posing significant health and economic challenges. Early intervention through lifestyle changes and pharmacological strategies can prevent complications. Vitamins with antioxidant properties have become increasingly important in mitigating oxidative damage in T2DM.

Antioxidants have been shown to reduce oxidative stress and prevent complications. A systematic review found that vitamins—especially vitamins C, D, and E—improve plasma oxidative stress markers and positively affect overall metabolic parameters [3].

Additionally, another meta-analysis evaluating the effects of vitamins highlighted their role in improving oxidative stress markers in T2DM. However, further studies are needed to assess their long-term benefits [4].

Prevention and Treatment

Environmental, genetic, and metabolic risk factors contribute to the development of T2DM. A family history of T2DM, obesity, advanced age, and a sedentary lifestyle are significant risk factors for the condition. Insulin resistance increases the likelihood of impaired glucose tolerance and the risk of developing T2DM. Preventing and delaying T2DM requires modifying environmental risk factors, such as increasing physical activity and reducing obesity. Awareness of T2DM risk factors is essential for early diagnosis and treatment, and screening high-risk populations can help reduce both macrovascular and microvascular complications [5].

In addition to lifestyle changes, certain oral antidiabetic drugs have been shown to delay and prevent hyperglycemia. Metformin, the most commonly used oral antidiabetic drug, belongs to the biguanide group. It enhances insulin sensitivity in peripheral tissues, reduces glucose variability, and suppresses hepatic glucose production [6].

Thiazolidinediones (TZDs) are insulin-sensitizing agents that improve pancreatic beta-cell function by increasing glucose uptake and insulin sensitivity in adipose tissues and skeletal muscles. Alpha-glucosidase inhibitors work by inhibiting the alpha-glucosidase enzyme, reducing carbohydrate absorption in the small intestine, and lowering postprandial glucose levels [7].

Diabetes and Vitamins

Vitamin A

Studies have shown a relationship between increased oxidative stress and decreased insulin sensitivity, demonstrating the efficacy of antioxidant therapy in T2DM management. Vitamin A, among all vitamins, has the strongest antioxidant capacity. Beyond its antioxidant properties, vitamin A exhibits pleiotropic effects on cell regulation, endocrine development, and pancreatic functions. Some studies have shown that serum vitamin A concentrations are lower in diabetic patients compared to healthy subjects [8].

Yamada et al. [9] investigated the relationship between serum antioxidant vitamin concentrations and T2DM. The study found that diabetic patients had significantly lower β-carotene and vitamin C concentrations compared to the control group, which were associated with diabetes. Evidence also suggests that daily vitamin A intake improves pancreatic β-cell function and may prevent or delay the progression from prediabetes to T2DM.

Another study by Manolescu et al. [10] reported that retinoic acid (RA) treatment reduced body weight, basal serum glucose, serum retinol, and RBP4 levels, increased insulin sensitivity, and lowered the retinol-to-RBP4 ratio. RA was suggested to be an effective antidiabetic agent for T2DM treatment.

Meerza et al. [11] conducted a study on mice, showing that vitamin A has both antioxidant and antihyperglycemic potential, supporting its use as a dietary supplement for T2DM patients.

Vitamin D

Various studies in different populations have highlighted the association of plasma vitamin D levels with cardiovascular diseases and diabetes. Vitamin D deficiency has been linked to the onset of coronary artery disease and the development of T2DM [12].

One study examined the effects of vitamin D supplementation on metabolic and oxidative stress markers in T2DM patients. Daily oral supplementation over 3–6 months improved HbA1c levels, and higher doses over three months significantly reduced advanced oxidation protein product levels [13]. Other studies reported that vitamin D supplementation improved HbA1c levels in overweight or obese T2DM patients with vitamin D deficiency [14] and that vitamin D3 supplementation improved glycemic control and reduced the dosage requirements of oral antidiabetic drugs [15].

Long-term studies of metformin's effects on vitamin D levels found no impact on serum 25[OH]D after 16 months of treatment [16]. Another study confirmed that vitamin D supplementation significantly reduced glycosylated hemoglobin levels in T2DM patients with vitamin D deficiency [17].

Vitamin E

Vitamin E is a potent antioxidant that reduces oxidative stress and inflammation, which play critical roles in the pathogenesis of diabetic complications. Its two main components, tocotrienols and tocopherols, exhibit anti-glycemic, anti-inflammatory, anticholesterolemic, cardioprotective, and neuroprotective properties. Tocopherols have been shown to have stronger antioxidant capabilities compared to tocotrienols [18].

Pramanik et al. [19] demonstrated that T2DM patients regularly taking riboflavin, niacin, pyridoxal phosphate, thiamine, α-tocopherol, and ascorbic acid along with oral antidiabetic drugs had reduced markers of lipid peroxidation, increased serum levels of intracellular antioxidants, and slower progression of diabetic retinopathy. A study on tocotrienol-rich vitamin E showed improved nerve conduction parameters in T2DM patients, highlighting its potential for addressing diabetic peripheral neuropathy [20].

Vitamin K

Vitamin K-dependent proteins play a significant role in the pathological calcification of bones and the vascular system. Despite optimal treatment, cardiovascular risk remains high in T2DM patients, who are also more prone to fractures and arterial calcifications [21].

Vitamin K1, naturally found in green leafy vegetables, suppresses arterial calcification through the carboxylation of matrix GLA protein. Observational studies have linked vitamin K deficiency with increased arterial calcification burden and cardiovascular events. Three months of combined K1/D vitamin supplementation in T2DM patients prevented the development of new calcified lesions in coronary arteries and the aorta [22]. Another study evaluated the clinical effects of vitamin K4 supplementation in T2DM patients and found improvements in triglyceride levels, insulin resistance, and the dosage of oral antidiabetic drugs [23].

Vitamin C

In vitro and in vivo studies emphasize the beneficial effects of vitamin C on the cellular functions of the immune system. Vitamin C supports neutrophil migration, oxidative bursts, phagocytosis, and microbial killing in infected tissues. In T2DM patients with poor glycemic control, 1,000 mg/day of vitamin C was shown to enhance oxidative bursts and PMN phagocytosis [24]. Another study explored the combined effects of metformin with acetylsalicylic acid and ascorbic acid on cardiovascular risks associated with diabetes, reporting significant improvements in glucose metabolism, lipid profile, and reductions in long-term diabetes complications [25].

Vitamin B12

Diabetic neuropathy (DN) is one of the most common microvascular complications of diabetes and is often underdiagnosed in clinical practice. DN in DM patients is thought to result from metabolic events such as hyperglycemia, accumulation of advanced glycation end products, and oxidative stress. Vitamin B12 levels are frequently low in DM patients receiving metformin therapy.

Supplementing with 1 mg of oral methylcobalamin for 12 months increased plasma B12 levels and improved sudomotor functions, neurophysiological parameters, pain scores, and quality of life in DN patients [26]. In a study examining the relationship between long-term metformin use and vitamin B12 deficiency in patients with T2DM, prolonged use of metformin was biochemically associated with B12 deficiency and anemia. The study emphasized the necessity of periodically monitoring B12 levels in patients receiving metformin therapy [27]. In another study, the relationship between metformin dosage and vitamin B12 deficiency in T2DM patients was investigated. The findings indicated that a 1 mg increase in daily metformin dosage resulted in a slight decrease in vitamin B12 levels, but no association was found between the duration of metformin use and B12 deficiency [28].

Discussion

T2DM represents a complex interplay of genetic, lifestyle, and metabolic factors, leading to chronic oxidative stress and organ damage. The findings highlight the therapeutic value of vitamin supplementation in T2DM management. Antioxidant vitamins not only reduce oxidative damage but also support glycemic control and decrease the incidence of complications. Despite promising results, further randomized controlled trials are needed to determine the optimal doses and long-term effects of vitamin therapies across diverse populations.

Conclusion

This study has reviewed the literature on T2DM and vitamin metabolism, compiling the findings to contribute to the body of knowledge on the subject.

In conclusion, T2DM causes irreversible damage to tissues and organs through oxidative stress, while antidiabetic agents can lead to deficiencies in certain vitamins. Early diagnosis, lifestyle modifications, and medication are crucial for the management and treatment of T2DM, and vitamins play a significant role in managing the condition and preventing complications. Each vitamin contributes through distinct biochemical mechanisms to the prevention of major and minor complications caused or exacerbated by diabetes.

In particular, antioxidant vitamins are emphasized as essential in reducing oxidative stress caused by T2DM and minimizing related complications. Studies have demonstrated that the appropriate use of vitamin supplements can enhance the quality of life for individuals with T2DM and serve as a valuable strategy in slowing disease progression. Research in this area continues to pave the way for the development of new strategies to manage T2DM more effectively.

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