VITAMINS AND DIABETES MELLITUS

Ayasha Saiffi[1*], Dr. Sokindra kumar[1]

[1] Kharvel Subharti College of *Pharmacy, Subharti Puram, N.H. 58, Delhi–Haridwar By Pass Road, Meerut,*

**Corresponding author: Phone: 7838196139 and E-mail: ayashasaiffi@gmail.com*

Abstract

Objective: The aim of this study was to identify nutritional supplement commonly used in diabetes and evaluate the scientific evidence which support their use in patients with diabetes mellitus.

Methodology: reviewed papers, associated to the title were searched using key words, from PubMed, Medline, and other research related databases.
Major findings: Vitamin supplementation as well as pre and probiotics may be used in treating diabetes. Many people believe that dietary nutrients are effective and safer than drugs used in the treatment of diabetes, but they are not used to treat, prevent, cure and diagnosis of any eilments. Dietary supplements found in several forms ranges from vitamins, enzyme, minerals, micro and macronutrients, amino acids and botanicals.

Conclusion: The modern lifestyle and obesity leads to an increase in diabetes, generating a demand on antidiabetic medication. In affected patients, inadequate nutritional intake of required vitamins and minerals may worsen the diseases. Therefore, additional nutritional supplements and mineral can help individual meet their medical needs and requirements.

Keywords: Diabetes, obesity, Vitamins and oxidative stress.

Introduction

Diabetes mellitus is a metabolic disorder which affect about 400 million people globally [1]. This public heath issue leads to severe micro and macrovascular complications. Diabetes caused by either defecient insulin secretion or insulin ressistance[2]. Type 2 diabetes mellitus usually occurs in obese people and is related with hypertension and dyslipidemia[3].The types of diabetes are as follows:

1. Type I diabetes is because of immune-mediated destruction of β-cells of Pancrease that cause insufficient insulin production;

2. Type II diabetes is because of cellular insulin resistance, in this type of diabetes the targeted tissues are unable to respond to insulin due to genetics or lifestyle; and
3. Gestational diabetes, i.e glucose intolerance inpregnancy[4].

Pathophysiology of diabetes

Insulin and glucagon hormone maintain the glucose homeostasis in body[5]. Insulin is secreted by the beta cells of pancreas, it can act by either inhibiting the formation of glucose by glycogenolysis and gluconeogenesis or by enhance the intake of glucose by fat tissue, muscles and liver [6]. In low glucose concentration the alpha cells of pancreas secret glucagon, it can act opposite to insulin by increasing glycogenolysis and gluconeogenesis processes in liver[7]. Another hormone that involve in homeostasis are amylin (a 37 amino acid peptide), glucagon like Peptide – 1 (GLP-1) and Glucose dependent insulinotropic polypeptide (GIP) [8]. GLP and GIP helps in the synthesis and secretion of insulin[9]

Two main types of glucose transporters are used for the distribution of glucose to cell, which are classified as:

i)Sodium glucose co-transporter (SGLT)
ii)Facilitative glucose transporter (GLUT)

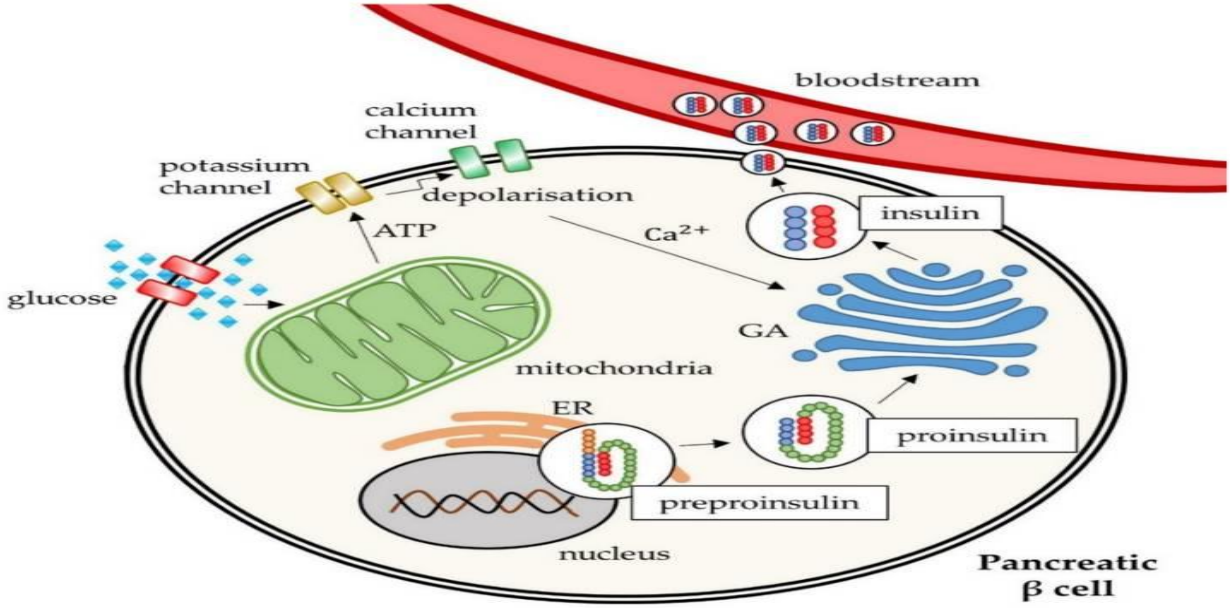

Figure 1Machenism of T2DM

List of Nutritional Supplements in Diabetes

- Omega-3fatty acids: Maintains blood sugar levels
- Alpha-lipoicacid: Prevents cell damage,improves the body's abilityto use insulin
- Micronutrients & Vitamins: Consider vitamin supplementation (B-group vitamins or folic acid) in metformin-treated patients
- Vitamin B: Nicotinamide can have beneficial effects on beta cells that can be helpful for those at high risk for T1DM. The machenism involve DNA repair enzyme poly-ADP-ribose polymerase and prevention of β-cell NAD depletion
- Vitamin C:Vit C is beneficial in oxidative stress caused in hyperglycemia.
- Vitamin E: It Has positive effect on insulin sensitivity.
- Vitamin K: It associated with insulin sensitivity and glucose metabolism
- Vitamin D: Direct effect on insulin secretion, mediated by nuclear vitamin D receptors also present in pancreatic β-cells[10]
- Protein: Important for building lean tissue mass and could have improve glucose control
- Branched chain amino acids: may benefit by stimulating insulin secretion and protein synthesis
- Creatine: creatine with exercise has the potential to provide some beneficial effects[11].
- Chromium: Chromium improves the action of insulin by improving tyrosine kinase activity on the insulin receptor
- Magnesium: magnesium itself can prevent the development of T2DM [12].

Vitamin A: Retinol binding protein (RBP), particularly RBP4, together with transtyrethin (TTR) transports retinol from the liver to peripheral tissues by binding with receptors and has been associated to fat metabolism and insulin sensitivity. high plasma concentrations of RBP4 have been seen in diabetic patients and lead to low uptake of glucose by skeletal muscle and high production of glucose in mice, with increase in insulin resistance [13].

Vitamins B:cobalamin, Thiamine, Riboflavin,biotin, Niacin, Folic acid, Panthotenic acid and Pyridoxine are usually categorized as B vitamins, and most of them have been related to type 2 diabetes mellitus

Vitamin D :A large number of evidence supports the relationship between vitamin D deficiency and T2D. Vitamin D shows direct and indirect effects on insulin secretion and sensitivity as well as systemic inflammation. vit D was reported to play an vital role in the maintenance of function of beta-cell of pancreas in vitro and in vivo studies. Vit D exert this action by the activation of the Vitamin DReceptor (VDR) expressed in the beta-cell of pancreas, as suggested by the fact that mice lacking VDR have impaired insulin secretion and stimulation of pancreatic islets results in increased insulin secretion after addition of 1,25(OH) 2 D 3 to the culture medium . In addition, when calcitriol is given a vitamin D response has been recognised in the human insulin receptor gene promoter, and

transcriptional activation of the gene has been identifed. Finally, vitamin D influence insulin secretion by acting on opening and closure of calcium channels. here, calcitriol act as chemical messenger by binding with receptors on the phosphobilipid layers of plasma membranes (VDR and 1,25D 3 -MARRS) maintaining calcium influx/efflux in beta-cells. Calcium is necessary for insulin secretion from pancreas; therefore, vitamin D deficiency through alterations in calcium flux in beta-cells may interfere with normal insulin release. Vitamin D in diabetes could also modulate the pathway of insulin ressistance. This effect on the regulation of extracellular and intracellular calcium levels may promote dephosphorylation of glucose transporter-4 leading to reduced insulin-stimulated glucose transport.Vitamin D in diabetes may also reduce the effects of systemic inflammation. vitamin D also reduce inflammatory cytokines that are linked with insulin resistance and activatecalbindin expression, a calcium-binding protein that protect from apoptosis . vitamin D reduced the accumulation of advanced glycation products, which are involved in the development of T2D complications and have also been associated with the development of insulin resistance. vitamin D concentration has been reported to be inversely associated with glucose status, insulin resistance, beta cell function, and risk of developing the metabolic syndrome. Several experimental studies have associated with deficiency of vitamin D level with the development of insulin resistance. higher concentration levels of vitamin D have been found to predict better beta cell function and lower glucose levels in subjects at risk for T2D. Data from observational studies also strongly support an association between low vitamin D status and incident T2D[14].

Vitamin E: Jain et al concluded that the vitamin E therapy in Diabetes prevents the development of late complications like retinopathy, foot ulcers and cardiovascular complications. A long term antioxidant therapy is beneficial, as it slows down the progression of the complications.[15]

Vitamin C: Vitamin C deficiency is observed in among diabetes mellitus patients. Deficiency of vitamin C levels has an impact on the serum MDA levels suggesting increased oxidative stress. The higher oxidative stress would have led to increase in glycated hemoglobin.ascorbic acid is used in the prevention of disease progression and their complications [16]

Vitamin K: Vitamin K is well known for its function in blood coagulation. Moreover, several human studies reported the beneficial role of vitamin K supplementation in improving insulin sensitivity and glucose tolerance, preventing insulin resistance, and reducing the risk of type 2 diabetes (T2 D). Both animal and human studies have suggested that vitamin K-dependent protein (osteocalcin [OC]), regulation of adipokine levels, antiinflammatory properties, and lipid-lowering effects may mediate the beneficial function of vitamin K in insulin sensitivity and glucose tolerance[17].

Table

Molecular mechanisms of action and clinical studies of in the management of DM.

Vitamins	Machenism of action	Clinical Studies	References
Vitamin C	Vitamin C enhances the immune system by stimulating IFN production and lymphocyte proliferation, enhancing neutrophil phagocytic capability . Vitamin C intake regulates fasting blood glucose (FBG) and glycosylated hemoglobin A1c (HbA1C) and improves insulin resistance	More clinical trials are needed to confirm whether Vitamin C shows promise as an effective therapeutic agent for diabetes mellitus.	Gillani S.W et al 2017 [18]
Vitamin D	Studies showed that Vitamin D promotes the conversion of proinsulin to insulin, increases insulin output, and enhances insulin action through the regulation of the calcium pool	A randomized control double-blind intervention study noted a significant improvement of insulin sensitivity in diabetic patients supplementing 4000 IU of Vitamin D for 6 months compared to placebo.	Von Hurst P.R et al 2010 [19]
Vitamin E	Animal models and human studies have demonstrated that vitamin E intake blocks LDL lipid peroxidation, prevents the oxidative stress linked to T2DM-associated abnormal metabolic patterns (hyperglycemia, dyslipidemia, and elevated levels of FFAs), and, subsequently, attenuates cytokine gene expression.	A recent report evaluated the effects of a combination of Vitamin C (1000 mg/day) and vitamin E (400 IU/day) for four weeks on insulin sensitivity in untrained and trained healthy young men and concluded that such supplement may preclude the exercise-induced amelioration of insulin resistance in humans.	Khodaeian M et al 2015 [20]

Conclusion

The modern lifestyle and obesity leads to an increase in diabetes, generating a demand on antidiabetic medication. In affected patients, inadequate nutritional intake of required vitamins and minerals may worsen the diseases. Therefore, additional nutritional supplements and mineral can help individual meet their medical needs and requirements. Despite the fact that vitamins have a significant impact on the risk of developing diabetes mellitus as well as its progression and complications, there is typically insufficient research to support the use of single or multiple vitamin supplementation in the general diabetic population. In order to ensure a proper nutritional status, the best advice should be to consume enough of the foods that contain necessary amounts of vitamins. With regard to some vitamins, using supplements poses the risk of excess or toxicity; nevertheless, when taking into account a person's entire diet, these adverse effects are essentially nonexistent. However, there is sufficient scientific evidence to suggest vitamin D supplementation in those with type 2 diabetes mellitus, who are being treated with metformin, to reduce the risk of its consequences. Consuming vitamin C, D, E, or a combination of all three has been linked to a lower risk of developing diabetes in the general population. For instance, it has been proposed that vitamins C, D, or E may have anti-diabetic qualities by controlling insulin secretion or sensitivity and causing anti-inflammatory, immunomodulatory, antioxidant, hypolipidemic, and hypoglycemic effects.

Acknowledgements: Declared none.

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