The Role of Vitamins and Mineral Elements in Management of Type 2 Diabetes Mellitus: A Review

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Abstract

Diabetes mellitus is a chronic endocrinological disorder characterized by high blood levels of glucose due to insufficient secretion of insulin by the pancreas or improper utilization of insulin by target cells. Diabetes is associated with serious complications and premature death. The major therapy option in diabetes mellitus is lifestyle management. Besides exercise, weight control and nutrition therapy, oral glucose lowering drugs and insulin injection are the conventional therapies for the disease. This review explores the role of various vitamins and mineral elements in management of type 2 diabetes mellitus. The literature regarding their modes of action in lowering blood glucose levels is also discussed in the review.

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Introduction

Diabetes mellitus is a chronic physiological metabolic disorder caused by inherited and/or acquired defect in production of insulin by pancreas, or by ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damages many of the body’s systems, in particular the blood vessels and nerves. In humans, it is due to a disorder of the pancreatic β-cells, in which insulin production is either lost or impaired, or from which a defective form of insulin is secreted.

A World Health Organization (WHO) study has shown that an estimated 30 million people worldwide had diabetes in 1985. A decade later, the global burden of diabetes was estimated to be 135 million. The latest WHO estimate for the number of people with diabetes worldwide, in 2000 was 177 million, and 3.2 million deaths per year was attributed to this disease. Due to population ageing and further urbanization, this is likely to increase to at least 370 million by 2030 and most of this increase will be in the developing countries. However, in Kenya for example, in 1995 it was estimated that, 1.0% of the population had diabetes and this rose to 1.06 % in 2000. It is estimated that by the year 2025, 132% of the population will be diabetic.

The major factors identified for developing diabetes are inherited genetic predisposition, environmental factors such as nutrition and chemical toxins. Excessive levels of glucagon can also lead to the development of hyperglycaemia. The currently accepted classification of diabetes mellitus are Type 1 (Insulin-Dependent) diabetes mellitus, Type 2 (Non-Insulin-Dependent) diabetes, specific diabetes type like brittle diabetes and gestational diabetes.

The various forms of diabetes management include nutrition, physical activity, acupuncture and hydrotherapy, mineral supplementation, conventional drugs and transplantation. Conventional drugs include exogenous insulin and oral hypoglycaemic agents whose drawbacks are high cost, toxicity and other side effects.

Nutrition is often said to be the cornerstone of diabetes care. The nutritional management of diabetes can affect long term health and quality of life. The goal for nutritional management is optimal metabolic control through a balance between food intake, physical activity, and if necessary, medication to avoid complications. In type 2 diabetes, nutritional goals aim for improved glycemic and lipid levels and weight loss when required. This review article explores the anticipated role played by various vitamins and minerals in management of type 2 diabetes mellitus.

Vitamins

Because diabetes is a state of increased oxidative stress, antioxidant vitamins are prescribed to people with diabetes. The following is a discussion of selected vitamins associated with lowering of blood glucose levels in type 2 diabetes patients.
i. **Vitamin E**: The purported effects of vitamin E on glucose control relate to the vitamin’s potent lipophilic antioxidant activity, with possible influences on protein glycation, lipid oxidation, and insulin sensitivity and secretion. Through unknown mechanisms, it also affects nonoxidative glucose metabolism.\(^{10, 11}\)

ii. **α-lipoic acid**: α-lipoic acid is a potent lipophilic antioxidant. It is a cofactor in many multienzyme complexes (for instance, Pyruvate dehydrogenase multienzyme complex) and may also play a role in glucose oxidation.\(^{12}\) In vitro α-lipoic acid enhances glucose uptake in muscle and prevents glucose-induced protein modifications.\(^{13}\)

iii. **Vitamins B\(_6\)**: Vitamin B\(_6\) supplementation offers significant protection against the development of diabetic neuropathy as diabetes patients with neuropathy are deficient in vitamin B\(_6\) and benefit from its supplementation.\(^{14}\) Individuals with long-standing diabetes or who are developing signs of peripheral nerve abnormalities are supplemented with vitamin B\(_6\). The neuropathy of a vitamin B\(_6\) deficiency is indistinguishable from diabetic neuropathy. Vitamin B\(_6\) is also important in preventing other diabetic complications because it inhibits glycosylation of proteins.\(^{15}\)

iv. **Vitamin C**: Vitamin C reduces glycosylation and provides antioxidant activity, which is beneficial to diabetics.\(^{16}\)

v. **Vitamin B\(_{12}\)**: A vitamin B\(_{12}\) deficiency is characterized by numbness of the feet, pins and needles sensations, or a burning feeling (symptoms typical of diabetic neuropathy).\(^{17, 18}\) Vitamin B\(_{12}\) supplementation has been used with some success in treating diabetic neuropathy. It is not clear if this is due to the correcting of a deficiency state or the normalization of the deranged vitamin B\(_{12}\) metabolism seen in diabetes patients.\(^{19}\)

vi. **Biotin**: Biotin improves glucose metabolism and nerve function. Biotin supplementation enhances insulin sensitivity and increases the activity of the enzyme glucokinase, the enzyme responsible for the first step in the utilization of glucose by the liver. Glucokinase concentrations in diabetes patients are very low. In one study, a dose of 16 mg/day of biotin resulted in significant lowering of fasting blood sugar levels and improvements in blood glucose control in type I diabetes patients.\(^{20}\)

### Minerals

Deficiencies of certain minerals, such as potassium, magnesium, zinc and chromium aggravate carbohydrate intolerance. The following minerals are discussed in relation to their potential to manage diabetes mellitus;

i. **Vanadium**: Prior to the discovery of insulin in 1922, vanadium was used for the control of blood sugar. Two small studies (one with six type 2 diabetes patients, and the next one with seven type 2 diabetic patients) showed that Vanadyl sulfate at a dose of 100 mg/day improves insulin sensitivity.\(^{21, 22}\)
Vanadium deficiency in human has not been documented. There are no accurate assays in clinical settings, and there is no recommended daily allowance.

Vanadium exists in several valency forms, with vanadyl (+5) sulfate and sodium metavanadate (+4) being the most common supplement forms. Its mechanism of action in glycemic control is thought to be primarily insulin-mimetic with up regulation of insulin receptors. In animal models, it facilitates glucose uptake and metabolism and enhances insulin sensitivity. Clinically, it enhances glucose oxidation and glycogen synthesis, and it modulates hepatic glucose output. Gastrointestinal discomfort, including diarrhea, nausea, and flatulence, are the side effects of administration of vanadium salts to patients. Organically chelated compounds, however, are thought to cause less gastrointestinal irritation than vanadium salts.

**ii. Chromium:** Chromium (Cr3+), a trace element in its trivalent form, is required for the maintenance of normal glucose metabolism. Experimentally, chromium deficiency is associated with impaired glucose tolerance, which is improved with supplementation. Most individuals with diabetes, however, are not chromium deficient. It is a part of glucose tolerance factor (GTF), a biologically active substance manufactured in the body that regulates glucose biotransformation and increases the number of insulin receptors, enhances receptor binding, and potentiates insulin action. Chromium picolinate is the preferred form because it is utilized more efficiently. Chromium administration decreases fasting and postprandial glucose and decreases fatigue, excessive thirst, and frequent urination. No recommended daily allowance (RDA) exists for chromium. A good supply of chromium is assured by supplemental chromium in addition to dietary sources. Good dietary sources are brewer’s yeast and barley flour, while refined sugars, white flour products, and lack of exercise deplete chromium levels.

**iii. Magnesium:** A deficiency of magnesium is significantly more common in type 2 diabetics than in the general population especially those with glycosuria, ketoacidosis, and excess urinary magnesium losses. Magnesium deficiency is associated with complications of diabetes, retinopathy in particular. One study observed that the patients with the most severe retinopathy had also the lowest levels of magnesium. Deficiency of magnesium potentially causes states of insulin resistance. Magnesium is a cofactor in various enzyme pathways involved in glucose oxidation, and it modulates glucose transport across cell membranes. It increases insulin secretion and/or improves insulin sensitivity and peripheral glucose uptake. It has no effect on hepatic glucose output and non-oxidative glucose disposal. Because it is an intracellular cation, it is difficult to measure accurately, and total body stores are rarely measured.

**iv. Calcium:** A daily intake of 1,000–1,500 mg of calcium, especially in older subjects with diabetes, is recommended. This recommendation is safe and reduces osteoporosis in older persons.
value of calcium supplementation in younger persons is uncertain. Calcium improves insulin sensitivity in some type 2 diabetic populations.

v. Manganese: Manganese is essential for human health. It is a cofactor of various enzymes that aid in cellular biochemical reactions. Such reactions include making and activating manganese superoxide dismutase (MnSOD) (an antioxidant enzyme) that helps protect the cell membranes and tissues from degeneration and disruption, helping the body to catabolize carbohydrates, lipids and proteins, and assisting in energy production. Manganese deficiency causes impaired glucose tolerance, impaired growth, impaired reproductive function, skeletal abnormalities, and altered carbohydrate and lipid metabolism.

vi. Potassium: Potassium supplementation yields improved insulin sensitivity, responsiveness and secretion; insulin administration induces a loss of potassium; and a high potassium intake reduces the risk of heart disease, atherosclerosis, and cancer.

vii. Zinc: Zinc is involved in virtually all aspects of insulin metabolism: synthesis, secretion and utilization. Zinc also has a protective effect against β-cell destruction and has anti-viral effects. Diabetics typically excrete excessive amounts of zinc in the urine and therefore require supplementation. This improves insulin levels in both type 1 and type 2 diabetes. In addition, zinc helps improve the poor wound healing observed in diabetes patients. Zinc is found in good amounts in whole grains, legumes, nuts, and seeds. The recommended level of supplementation for diabetics is at least 30 mg of zinc per day.

viii. Selenium: Selenium is an important component of selenoproteins, which are implicated in modulating oxidative stress and regulating thyroid hormone activity. Two recent studies undertaken to examine the relationship between serum selenium levels and the prevalence of diabetes among U.S. adults established that high serum selenium levels were positively associated with the prevalence of diabetes, that selenium supplementation did not prevent type 2 diabetes, and that it may increase the risk for the disease. Therefore, the indiscriminant use of selenium supplements should be discouraged until more randomized, controlled trials examine their effects on human health.

Conclusion

The adverse side effects associated with drug therapy in management of type II diabetes mellitus is accelerating reliance on nutritional approach to management of the disease. It is no wonder that research is currently also focused on analysis of mineral elemental composition of hypoglycemic plants. Supplementation of diets meant for diabetes patients with the aforementioned vitamins and minerals complements the other conventional interventions in the management of diabetes. However, it is necessary to study the effects of mega doses of these vitamins and minerals to diabetes patients.
People with poorly controlled diabetes are susceptible to multiple micronutrient deficiencies. Some of these micronutrients have potent antioxidant activity. It is not known whether the ingestion of antioxidant vitamins could delay or perhaps reverse the oxidative damage. People with diabetes should be educated about the importance of acquiring daily vitamin and mineral requirements from natural food sources. In select groups such as the elderly, pregnant or lactating women, strict vegetarians, or those on calorie-restricted diets, supplementation with a multivitamin preparation is advisable.

However, vitamin and mineral supplementation in pharmacological doses should be viewed as therapeutic intervention and, just as with medications, should be subjected to placebo-controlled trials to demonstrate safety and efficacy.

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