International Journal of Research in Medical Sciences
Rosyid FN. Int J Res Med Sci. 2022 Apr;10(4):973-979
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20220997

Review Article

Micronutrient deficiency in type 1 and 2 diabetes mellitus: diagnosis and therapy

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Received: 02 February 2022
Accepted: 02 March 2022

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ABSTRACT

Diabetes is a group of metabolic diseases characterized by increased blood glucose levels (hyperglycemia) due to decreased insulin secretion and/or activity. Chronic hyperglycemia in diabetics is associated with long-term damage, dysfunction and failure of multiple organs such as the eyes, kidneys, nerves, heart and blood vessels. Micronutrients consist of vitamins and minerals that the body needs in small amounts for cellular metabolism. Micronutrients function as cofactors in enzyme-catalyzed reactions and if they are deficient, they can result in impaired metabolic function that can lead to more serious disease conditions. Micronutrients are beneficial for metabolism, gene expression and influence the development or progression of a chronic disease, including diabetes. Metabolic changes in diabetes are very complex, if not controlled properly can develop into complications such as neuropathy, nephropathy, cardiopathy, dyslipidemia and retinopathy. The micronutrients needed by DM patients are vitamin B complex consisting of B1 (thiamin), B2 (riboflavin, B6 (pyridoxine), B12, niacin, biotin, pentothenic acid, as well as folic acid and vitamin C. Minerals that need to be given as therapy in DM patients namely chromium, magnesium, manganese, selenium, vanadium and zinc.

Keywords: Micronutrient, Diabetes, Diagnosis

INTRODUCTION

Agriculture provides all the nutrients needed to sustain life on earth. Meanwhile, the agricultural system is not developed so that it cannot meet the nutritional needs of humans in the world. Therefore, it is very important to build links between agriculture, nutrition and health in order to find sustainable solutions to nutritional deficiencies.[1]

Micronutrients consist of vitamins and minerals that the body needs in small amounts for cellular metabolism. Micronutrients function as cofactors in enzyme-catalyzed reactions and if they are deficient it can result in impaired metabolic function that can lead to more serious disease conditions. The use of dietary supplements needs to be considered, including for diabetes. Currently, attention is focused on dietary supplements that are beneficial in various diseases such as: coronary heart disease, cancer, osteoporosis and other chronic diseases as well as degenerative diseases such as diabetes, Parkinson's and Alzheimer's.[2,3]

Micronutrients are nutrients needed by humans and other living things throughout life in small amounts, to regulate various physiological functions, which organisms themselves cannot produce. This includes dietary minerals in amounts that are generally less than 100 mg/day compared to the macrominerals required in larger amounts. Trace elements include at least iron, cobalt, chromium, copper, iodine, manganese, selenium, zinc and molybdenum. Micronutrients also include vitamins, which are organic compounds needed as nutrients in small amounts by organisms.[4]

Patients with poorly controlled Diabetes Mellitus will be more susceptible to micronutrient deficiencies so counseling should be given about the importance of fulfilling vitamins and minerals from food according to their needs.[5] Micronutrient deficiencies such as zinc, chromium, magnesium, copper, manganese and vitamin B-6 are associated with glucose intolerance.[6] Many studies discuss the benefits of micronutrients for diabetics, but there is not much evidence to show that micronutrient supplementation is very important for the body's needs.[1]Medical nutrition therapy is the basis for the management of diabetes mellitus, but there is still nothing clear about its management, for example the role of micronutrients in the pathogenesis and complications of diabetes[7]. Seeing this background, the authors are interested in discussing micronutrient deficiencies in type 1 and type 2 diabetes, diagnosis and therapy.

MICRONUTRIENTS

Micronutrients are vitamins and minerals that the body needs in small amounts for specific functions. Vitamins and minerals function as essential coenzymes and cofactors for metabolic reactions and cellular reactions such as glycolysis, the citric acid cycle, protein and fat metabolism.[8] Meanwhile, according to O'Connel, micronutrients are useful for metabolism, gene expression and influence the development or progression of a disease.[9] Chronic changes including diabetes. Metabolic changes in diabetes are very complex, if not controlled properly it can develop into complications such as neuropathy, nephropathy, cardiopathy, dyslipidemia and retinopathy.[10]

The micronutrients needed by DM sufferers are vitamin B complex consisting of B1 (thiamin), B2 (riboflavin, B6 (pyridoxine), B12, niacin, biotin, pentothenic acid, as well as folic acid and vitamin C. carbohydrate metabolism and plays a role in the mechanism of nerve impulses vitamin B2 as a mediator in the transfer of energy from carbohydrates, proteins and fats to ATP vitamin B6 plays a role in the transmission of nerve impulses, amino acid metabolism, hemoglobin formation also plays a role in the stability of the integrity of the nervous system Niacin in addition to functioning in nervous tissue and the gastrointestinal tract also plays a role in the formation of energy and skin integrity. Biotin plays a role in the production of fatty acids and the conversion of nutrients into energy. Minerals that need to be given as therapy in DM patients are chromium, magnesium, manganese, selenium, vanadium and zinc.[11]

Zinc is a ubiquitous micromineral in human/animal tissues and is involved in the function of various enzymes in metabolic processes. Zinc is required for the activity of more than 90 enzymes related to carbohydrate and energy metabolism, protein degradation/synthesis, nucleic acid synthesis, heme biosynthesis, CO transport (carbonic anhydrase) and other reactions. The most obvious influence is metabolism, function and maintenance of the skin, pancreas and male reproductive organs. In the pancreas, zinc has to do with the amount of protease secretion needed in digestion. It is also related to insulin, although it does not play a direct role in insulin activity.[12]

In addition, chromium plays a role in insulin activity, so it can improve glucose intolerance. Selenium is an essential micromineral with a wide range of requirements and toxicity. Selenium is important for human and animal metabolism; said that after the discovery of enzymes that require Se for its activity, namely: glutathione peroxidase and iodothyronine 5'-deiodinase, besides that Se also functions for the immune and reproductive systems. Magnesium plays a role in the components of bone and intracellular fluid, neuromuscular transmission, activating several enzymes, metabolism of carbohydrates and fats. Manganese is also associated with a large number of enzymes in several metabolic processes, including pyruvate and acetyl-CoA carboxylase and isonitrate dehydrogenase in the Krebs's cycle and mitochondria; mitochondrial shape; superoxide dismutase which protects mitochondrial membrane, besides that it also plays role in bone development (organic matrix) and reproduction.[13]

DIAGNOSIS OF MICRONUTRIENT DEFICIENCY IN TYPE 1 AND TYPE 2 DM

The diagnosis of micronutrient deficiency in type 1 and type 2 diabetes is as follows:

Zinc

Zinc deficiency can cause : anorexia, impaired taste and smell, stunted growth, hypogonadism, inhibited wound healing, impotence in renal dialysis patients, depression, lability of mind, lack of concentration, tremor, nystagmus, diasrthria, jitteriness, photophobia, night blindness, blepharitis, skin lesions (fingers, perineum, nasolabial parietal, folds), paronychiae with monilial superinfection, nails (stops growing, disappears with Beau's line), hair growth stops or alopecia and diarrhea.[14]

Chromium

Chromium deficiency can cause impaired glucose tolerance, increased triglyceride and cholesterol concentrations in serum.[15]

Selenium

Selenium deficiency can cause muscular dystrophy, reproductive disorders, decreased food intake, subcutaneous edema and mineralization of the kidneys.[16]

Magnesium

Magnesium deficiency can cause muscle weakness, hyperritability, convulsions, anorexia, vomiting,

decreased bone mineralization, weight loss, and calcification of the aorta.[5]

Manganese

Manganese deficiency causes impaired glucose tolerance and pancreatic cell granulation (in guinea pigs), impaired lactation and fetal development (rats) as well as fatty liver.[10]

Vitamin E

Vitamin E deficiency will cause symptoms including steroid pigment deposits, low vitamin E in plasma and adipose tissue, creatinuria, muscle weakness, and increased creatinine phosphokinase activity (all of which are indications of muscle cell damage). The same symptomology can be seen in conditions where there is abnormal absorption (malabsorption) of fat in the intestines and steatorrhea (loss of fat in the stool), cystitis, pancreatic fibrosis, biliary atresia or cirrhosis, sprue and chronic pancreatitis.[17]

Vitamin C

Deficiency of vitamin C can interfere with the synthesis of food in the liver, the signs of deficiency do not appear. Toxicity does not cause toxicity.[6]

Vitamin D

Vitamin D deficiency can cause rickets, costochondral enlargement, osteomalacia, osteoporosis. Toxicity Hypercalcemia, calcinosis, anorexia, lameness.[18]

Thiamine (B1)

Vitamin B1 deficiency can cause anorexia, weight loss, ataxia, polyneuritis, ventriflexion (cats), paresis (dogs), cardiac hypertrophy (dogs) and bradycardia. Toxicity can cause decreased BP, bradycardia and arrhythmias.[19]

Riboflavin (B2)

Vitamin B2 deficiency can cause growth retardation, ataxia, collapse syndrome (Dogs), dermatitis, purulent ocular discharge, vomiting, conjunctivitis, coma, corneal, bradycardia, fatty liver (Cat). Toxicity does not cause severe pain.[20]

Pyridoxine (B6)

Vitamin B6 deficiency will cause an increase in the excretion of several amino acid metabolites that normally will be further degraded, especially the tryptophan metabolites, methionine and glycine. (Urea excretion will also be increased, which may be due to a decrease in non-essential amino acids resulting in a decrease in NH_3back and N-amino). B6 deficiency can also cause the excretion of xanturenic acid, quinurenin, and hydroxyquinurenin (from tryptophan) in the urine, but it can also cause anorexia, growth retardation, weight loss, microcytic hypochromic anemia, renal tubular atrophy, calcium stones.[18]

Cobalamin (B12)

Vitamin B12 deficiency can cause stunted growth (cats), methylmalonic aciduria, anemia. Toxicity can cause impaired reflexes (decreased vascular reflexes).[21]

Niacin

Niacin deficiency can cause anorexia, diarrhea, stunted growth, ulcers of the palate and buccal mucosa, necrosis of the tongue (dogs), ulcers of the tongue (cats), cheilosis, uncontrolled salivation convulsions.[22]

Biotin

Biotin deficiency can cause hyperkeratosis, alopecia (cats), dry secretions around eyes, nose and mouth (cats), hypersalivation and anorexia. Toxicity may be non-toxic to dogs and cats.[23]

MICRONUTRIENT DEFICIENCY THERAPY IN TYPE 1 AND TYPE 2 DIABETES MELLITUS

Micronutrient deficiency therapy needed by patients with type 1 and type 2 diabetes is as follows:

Zinc

The relationship between zinc and insulin was first recognized by Scott and Fischer who found that the normal human pancreas contains significant amounts of zinc, but only very little in the diabetic pancreas.[24] Increased zinc in diabetic patients will increase urinary excretion resulting in polyuria. Diabetic patients, excretion of zinc in the urine is higher when compared to non-diabetics.[8]

Zinc is an efficient antioxidant and has an important role in the function of various enzymes and insulin metabolism.[25] Zinc is found mainly in cereals, meat, seafood, and dairy products.[7] About 90% of zinc is found in skeletal muscle and bones, and less than 0.1% circulates in the plasma.[26]

Zinc has an important role in metabolic diseases (e.g., insulin resistance, metabolic syndrome, diabetes), therefore zinc plays a major role in the stabilization of insulin hexamers and insulin storage in the pancreas. Zinc is an antioxidant against oxidative stress, where oxidative stress is the cause of insulin resistance and diabetes.[27] Zinc helps store insulin in beta cells, and insulin secretion increases to reduce zinc concentration in beta cells, there will be a decrease in insulin levels if there is a deficiency zinc.[25]

Chromium

Chromium is one of the elements found in the earth's crust and oceans, it is available in several oxidative forms, namely as metallic chromium (Cr^0), trivalent (Cr3+) and hexavalent (Cr6+). Trivalent chromium (Cr3+) is found in most foods and nutritional supplements with a low level of toxicity.[5] Trivalent chromium (Cr3+) is required for normal glucose metabolism, so chromium deficiency can lead to impaired glucose tolerance. There is no accurate biochemical indicator in determining chromium status because chromium is a supplement so the performance will be effective for people with deficiency. Adequate intake for chromium is 25 g for women and 35 g for men.[15]

According to Cefalu, most of the literature on both animal and human studies indicates that chromium is an essential element for insulin action.[15] According to Anderson, chromium supplementation has an effect on glucose and insulin in patients with type 2 diabetes.[28] Anderson's study showed that supplementation of 200 g/day during a 4-month study did not show an effect but the effect appeared in subjects with supplementation of 1000 g/day. The need for chromium is related to the degree of glucose intolerance, which is 200 g/day, if the intolerance is higher then more than 200 gm/day is needed. Intake of chromium 8 µg/kgBW/day is more effective than 4 µg/kgBW/day for people with gestational diabetes. Chromium's mechanism of action is to increase insulin action.[28]

Selenium

Selenium is a component of enzymes catalyzing redox reactions and acts as an antioxidant in the form of selenoproteins containing selenocysteine.[13] Known selenoproteins are glutathione peroxidase, thioredoxin reductases and iodothyronine deiodinases Food sources of selenium are fish, eggs, and meat from animals that are fed a lot of food. selenium, and grains grown in high-selenium soils. Selenium is an anion, is relatively well absorbed from the diet and its homeostasis is regulated by excretion, mainly in the urine and through respiration.[29]

Selenoproteins have a role in the transport of selenium to tissues and selenium deficiency is rare, but if selenium deficiency occurs in diabetes, there will be an increase in oxidative stress.[45,46] Selenium is a strong antioxidant and has anti-inflammatory effects in patients with insulin resistance and diabetes.[12]

Selenium can inhibit hyperglycemia or hyperinsulinaemia caused by the expression of adhesion molecules and also reduce inflammation, C-reactive protein and L-selectin.[29] This mechanism is via tyrosyl phosphorylation of cellular and ribosomal proteins usually involved in post-insulin receptors. Battell et al showed that sodium selenate increased glucose tolerance in a mouse model of streptozotocin-induced diabetes.[13] In mice, selenate causes decreased gluconeogenesis and inhibits phosphorylation of phosphotyrosine by 50%. Studies in type 1 diabetic rats have shown that selenium can protect against mitochondria from oxidative stress.[16]

Magnesium

Magnesium is an essential cofactor for >300 enzyme reactions involving energy metabolism and nucleic acid synthesis.[23] Magnesium is a micromineral that plays an important role in glucose homeostasis and insulin action.[30] Magnesium is a micronutrient that is often deficient in diabetics. Decreased magnesium levels and increased urinary loss of magnesium are common in patients with type 1 and 2 diabetes. Magnesium deficiency is associated with hypertension, insulin resistance, glucose intolerance, dyslipidemia, increased platelet aggregation, cardiovascular disease, complications of diabetes and pregnancy but it is not clear whether this status low magnesium will directly cause these disorders.[23] It is estimated that there are 2 main factors, namely gastrointestinal factors and renal factors. Gastrointestinal factors include autonomic neuropathy which results in reduced Mg intake due to nausea, vomiting, diarrhea, and esophageal dysfunction. Renal factors that influence is increased loss of Mg through the urine due to hyperglycemia (osmotic diuresis), ketoacidosis, and hypoalbuminemia; decreased Mg reabsorption due to insulin deficiency/resistance; and low-quality diets also contribute to hypomagnesaemia in diabetic patients. Magnesium acts as a cofactor in all ATP transfer reactions, which indicates that magnesium has very important role in insulin receptor phosphorylation. An intracellular Mg depletion can lead to defective tyrosine kinase function at insulin receptor.[5]

Manganese

Manganese deficiency, a cofactor for several enzymatic systems results in glucose intolerance in animals.[14] Pancreatectomy and diabetes are associated with reduced levels of manganese in the blood, while manganese supplementation can improve glucose utilization caused by manganese deficiency in animals.[10] In humans, manganese plays a role in the pathogenesis of diabetes.[24] Observations in diabetic patients compared to normal control groups showed that the excretion of manganese in the urine was high and the concentration of manganese in the blood and hair decreased.[10] However, it must be determined whether diabetes causes the excretion of manganese in urine. High and decreased concentrations of manganese in the blood and hair, or manganese deficiency contribute to the development of intolerance. The pathogenesis and therapeutics of manganese are not fully understood and need further research.

Nicotinamide

Nicotinamide is one of two forms of vitamin B3 (niacin), the other being nicotinic acid. The active forms of

nicotinamide are adenine dinucleotide (NAD) and phosphate derivative (NADP). This coenzyme plays an important role in the function of hundreds of enzymes and the metabolism of carbohydrates, fats and proteins. The dietary recommended intake for niacin is expressed in terms of niacin equivalent (NE) because niacin can be synthesized by the body in the form of tryptophan. The recommended dietary adequate is 14 mg NE for women and 16 mg NE for men. Torable Uptake Level Intake is 35 NE/day for adults. The effect of nicotinamide supplementation is being investigated, especially focusing on the progression of type 1 diabetes, while for type 2 diabetes only a small number of studies have been conducted but the results are inconsistent. Nicotinamide was most effective in subjects with recently diagnosed diabetes and in subjects with positive islet cell antibodies but not diabetes. Nicotinamide helps protect -cell function in patients with type 1 and 2 diabetes. The effectiveness and safety of long-term use of nicotinamide supplementation is unclear and monitoring of liver enzymes and platelet function is necessary. Consuming adequate amounts of niacin-rich foods such as fortified dry grains, cereals, meat, fish and dried beans is safer. The effectiveness and safety of long-term use of nicotinamide supplementation is still unclear and it is necessary to monitor liver enzymes and platelet function. Consuming adequate amounts of niacin-rich foods such as fortified dry grains, cereals, meat, fish and dried beans is safer. The effectiveness and safety of long-term use of nicotinamide supplementation is still unclear and it is necessary to monitor liver enzymes and platelet function. Consuming adequate amounts of niacin-rich foods such as fortified dry grains, cereals, meat, fish and dried beans is safer.[2]

Vitamin E

Vitamin E is a fat-soluble vitamin that functions as an antioxidant. Low vitamin E levels are associated with an increased incidence of diabetes. Diabetics have an increased need for antioxidants due to increased production of free radicals with hyperglycemia. Vitamin E works by neutralizing the production of free radicals during cell metabolism, protecting cell membranes and lipoproteins from oxidative damage. Therefore, vitamin E can prevent and treat diabetic complications such as nephropathy and neuropathy by reducing protein glycation, fat oxidation and inhibiting platelet aggregation.[17]

Vitamin C

Research has shown that vitamin C supplements have benefits in people with type II diabetes. The study included patients who were not given vitamin C for the first week, then 1g/day for 4 weeks, followed by 3 gm/day for 4 weeks. The results showed that giving high doses of vitamin C helped to control blood sugar levels and improve anti-oxidant status. In addition, giving vitamin C supplements (about 1000 mg a day) can help prevent or reduce the occurrence of cataracts and neurological disorders that often occur in people with diabetes. It is suspected that vitamins can inhibit glycosylated proteins, so that they can prevent complications due to diabetes.[19,26]

Vitamin D

Vitamin D has attracted much attention over the last few years in relation to its possible role in chronic disease. This vitamin is fat-soluble and has a half-life of about 15 days. Vitamin D comes from food, produced in the body by the help of UV rays from the sun.[6] Obesity has a risk of vitamin D deficiency, because fat binds to vitamin D and prevents its absorption into the blood. Dark skin is less efficient at making vitamin D. There are currently no recommendations for taking this vitamin, other than in pregnant and lactating people, and the elderly (10gper day) and infants and children under 5 years (7-8.5 gm/day). Vitamin D deficiency is thought to affect glucose metabolism, decrease beta cell function, increase insulin resistance and glucose intolerance. Meta-analysis results Song et al found that there is a strong association between type 2 diabetes and low serum vitamin D levels.[17] Rashidi et al conducted a study on 100 people with type 2 diabetes. The sample was given a 50 000 IU vitamin D3 supplement for a week until 8 weeks. The results of this study showed that there was a significant decrease in fasting blood glucose levels and insulin resistance.[31]

B vitamins

The B complex vitamins consist of B1 (thiamin), B2 (riboflavin, B6 (pyridoxine), B12, niacin, biotin, pentothenic acid, and folic acid and vitamin C. B vitamins are cofactors of enzymes in carbohydrate metabolism and play a role in the mechanism of nerve impulses Vitamin B2 as a mediator in the transfer of energy from carbohydrates, proteins and fats to ATP vitamin B6 plays a role in the transmission of nerve impulses, amino acid metabolism, hemoglobin formation also plays a role in the stability of the integrity of the nervous system Niacin in addition to functioning in nervous tissue and the gastrointestinal tract also plays a role in the formation of energy and skin integrity. Biotin plays a role in the production of fatty acids and the conversion of nutrients into energy.[6]

CONCLUSION

Micronutrients consist of vitamins and minerals that the body needs in small amounts for cellular metabolism. Micronutrients function as cofactors in enzyme-catalyzed reactions and if they are deficient, they can result in impaired metabolic function that can lead to more serious disease conditions.

Diabetes is a group of metabolic diseases characterized by increased blood glucose levels (hyperglycemia) due to

decreased insulin secretion and/or activity. Chronic hyperglycemia in diabetics is associated with long-term damage, dysfunction and failure of multiple organs such as the eyes, kidneys, nerves, heart and blood vessels.

Micronutrients are beneficial for metabolism, gene expression and influence the development or progression of a chronic disease, including diabetes. Metabolic changes in diabetes are very complex, if not controlled properly can develop into complications such as neuropathy, nephropathy, cardiopathy, dyslipidemia and retinopathy.

The micronutrients needed by DM patients are vitamin B complex consisting of B1 (thiamin), B2 (riboflavin, B6 (pyridoxine), B12, niacin, biotin, pentothenic acid, as well as folic acid and vitamin C. Minerals that need to be given as therapy in DM patients namely chromium, magnesium, manganese, selenium, vanadium and zinc.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Rosyid FN. Micronutrient deficiency in type 1 and 2 diabetes mellitus: diagnosis and therapy. Int J Res Med Sci 2022;10:973-9.