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HUMAN NUTRITION

RESEARCH NOTES

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Mineral Considerations in Diabetes Mellitus

The incidence of diabetes mellitus in the United States and throughout the world is ever growing. Recent estimates have indicated that about 18 million people in the USA are afflicted by this metabolic disorder. It is the fourth leading cause of death by disease in the USA, and it is a major cause of blindness and kidney disease. The cost of diabetes in the USA is in excess of $100 billion per year, and on the rise. Nutritional management, along with exercise are central to the management of the diabetic patient. The nutritional emphasis of traditional medical management of diabetes has revolved around macronutrient intake. In fact, a quick glance at recent medical and nutritional texts on the subject show that established medical opinion is that the diabetic has the same micronutrient needs as the non-diabetic. This opinion lives on, despite the strong evidence that diabetics have an abnormal metabolism of several micronutrients.

In reviewing clinical studies published on this topic over the last few years, it becomes apparent that several minerals are of great importance and have potential impact on the typical diabetic individual. In certain instances, the findings are in favor of what some would call pharmacological mineral supplementation in the diabetic. The minerals found to be subjects of concern in the diabetic most commonly are: magnesium, zinc, chromium, and manganese. In addition, vanadium has been studied, as a possible benefit to diabetics, but most speak of it in terms of a pharmacotherapy. Other minerals that have received mention in research surrounding the treatment of diabetes or the palliation of the most frequent complications seen in diabetics (cardiovascular disease, nephropathy, neuropathy, and retinopathy), include copper and selenium.

The rationale for the range of minerals that have come under research scrutiny in the attempt to control the complex metabolic defects surrounding diabetes mellitus is as multifaceted as the disease itself. In some cases, the need for mineral supplementation intervention may be simply the result of excess loss of that mineral due to the polyuria often found in this disorder. In others, it may be that the mineral in question has been ingested in less than needed amounts, which for some minerals can lead to inefficient function of insulin action for the transfer of glucose from the blood stream into the cell. Research has also shown that zinc maybe malabsorbed and hyperexcreted in diabetics. Additionally, it may be that the mineral has been shown to fight against insulin resistance, one of the leading factors in Type 2 diabetes.

One last consideration is that certain minerals have been shown to be keys to fighting against the oxidative stress of diabetes. The oxidative stress seen in diabetes

Classification of Diabetes Mellitus

Type 1 diabetes is characterized by pancreatic beta-cell destruction usually leading to complete insulin deficiency. Its etiology is likely due to a combination of genetic and environment factors.

Type 2 diabetes is characterized by insulin resistance and an insulin secretory defect. It is the most prevalent type of diabetes, and represents up to 90% of the population diagnosed with diabetes. It has both a genetic and an environment component. Type 2 diabetes ranges from cases with predominantly insulin resistance and relative insulin deficiency to cases with predominantly secretory defects and some degree of insulin resistance.

Note: There are other specific types of diabetes, including gestational diabetes, however, Type 1 and Type 2 are the ones of most general interest.

mellitus has been shown to be one of the leading causes of the destructive metabolic forces associated with this disease.

It is interesting to note that according to a U.S. Dietary survey (CSFII), the average magnesium intake for women (aged 20-49 years) was 207mg (RDA 400 mg), with 90% of the women in this group having a magnesium intake of 310mg or less per day. The same survey showed that the average intake of zinc for this same group of women was 50% of the RDA, with the vast majority receiving less than the RDA. This survey did not monitor manganese, chromium or selenium. However, it should be noted that 90% of these women took in less than the RDA for copper. With these data in mind, and knowing what trouble minerals are for diabetics, it is surprising that the medical establishment does not currently monitor the mineral intake in patients suffering with the condition of diabetes mellitus. It is unfortunate that the vast majority of effort to address this issue has come through self supplementation by the patients themselves, an effort that is often addressed in a dismissive fashion by their medical practitioner.

Zinc and Diabetes

There is a complex relationship between diabetes, insulin and zinc. In Type 1 diabetes, there is an obvious lack of insulin production, and in Type 2 diabetes, resistance to the effects of insulin is predominant. In both forms of diabetes, zinc homeostasis is affected. Diabetes can affect the balance of zinc in several ways, although it is most likely that hyperglycemia, rather than any primary lesion related to diabetes, causes the increased urinary loss and subsequent decreases in total body zinc[1]. In addition, a review of the literature has shown that in addition to the zincuria, there is evidence that Type 1 and Type 2 diabetics can cause zinc malabsorption. Some researchers have indicated that diabetics may lose zinc by excreting more zinc into the intestine during the digestive processes[2]. Zinc plays a key role in the synthesis, storage and secretion of insulin, and it accounts for the conformational integrity of insulin in its hexameric crystalline form. The addition of zinc to the insulin structure will increase the insulin's ability to bind to its receptor. A decrease in zinc affects the ability of the islet cells to produce and secrete insulin, which could compound the problems of Type 2 diabetics in particular. In addition to the findings that zinc levels are often low in diabetics, it is also felt that zinc (in concert with other micronutrients) may participate as an integral component of antioxidant enzymes or as a cofactor in a variety of enzymatic processes of importance in glucose and lipid metabolism. The complications of diabetes are a direct result of the prolonged exposure of tissues to high glucose concentrations and its associated oxygen free radical activity. The consequences of both (high glucose concentration and low zinc levels) is an increase in the oxygen free radicals known to directly cause the neuropathy, nephropathy, and retinopathy seen in diabetes. A recently published study[3] suggests that the supplementation of zinc may produce beneficial antioxidant affects in individuals with Type 2 diabetes. Given the deleterious consequences mentioned from oxidative stress seen in diabetes, the findings of this study could have particularly vital implications. An earlier study[4] in France found that zinc deficiency in insulin-dependent diabetic patients could be corrected by zinc supplementation, and that moreover this supplementation decreased lipid peroxidation and had a significant impact on patients with retinopathy. Zinc was seen to be linked to a protective effect via increasing the Se-GPx activity (glutathione peroxidase).

Given the incidence of low zinc found in diabetes, the link between zinc, insulin, and glucose metabolism, along with the potential antioxidant benefits (specific to the complications seen in diabetes), it would seem that the recommendation for zinc to be a mineral to supplement in the diabetic is obvious.

Magnesium is Another Key for the Diabetic

There is an almost absolute relationship between the presence of diabetes mellitus (Type 1 or Type 2) and magnesium deficiency. According to Hua and Rude[5], there is strong evidence that magnesium depletion may contribute to the complications of diabetes mellitus, like vascular problems and osteoporosis. They feel that the intracellular depletion of magnesium results from osmotically induced renal loss. However, they add

that the impaired ability of insulin to increase intracellular magnesium during insulin deficiency or insulin resistance may play a role here, as well. In a more recent study[6], it was clearly shown that by increasing plasma glucose from 5 to 12 mmol/L, the renal excretion of magnesium was more than doubled. Other factors in the study gave further evidence to the hypothesis that hyperglycemia is a far greater influence in the etiology of hypermagnesuria than other possible causes like hyperinsulinism. Magnesium deficiency, per se, has been reported to lead to insulin resistance. In the Hua and Rude study[5] on Type 2 diabetics (non-insulin dependent), the accumulated data suggest that insulin resistance and magnesium depletion may result in a vicious cycle of worsening insulin resistance and the decrease in intracellular magnesium, cutting off the effect of magnesium in many vital cellular processes. Research in Type 1 diabetes mellitus[7] found a magnesium deficit to be directly related to the development of cardiovascular disease. In this study, 80% of the diabetics reviewed ingested less than 90% of the RDA for magnesium. The repletion of magnesium in these Type 1 diabetics resulted in a decrease in the atherogenic lipid fractions (specifically decreasing total serum cholesterol, LDL, and apolipoprotein B). Further support for the idea of supplementing magnesium in diabetics was seen in a clinical trial on magnesium depleted Type 1 diabetics[8]. The supplementation of magnesium was observed to improve nerve conduction in younger diabetics with early signs of neurological complications. It should be noted that other research[9] has indicated that intracellular magnesium depletion in Type 1 diabetes has been correlated to increased urinary loss of magnesium.

In looking at the dietary habits of Type 2 diabetics[10, 11], it has been concluded that low dietary intake of magnesium does not confer the risk of Type 2 diabetes. However, Kao WH, et al11 found that compartmentalization and renal handling of magnesium were factors in the relationship between low serum magnesium and the risk of Type 2 diabetes. Lima ML, et al[12] examined the effects of magnesium supplementation on the control of Type 2 diabetics. In this double-blind placebo controlled trial, it was observed that magnesium depletion was a common finding for 128 Type 2 diabetics at the commencement of the study, especially for those with who were showing signs of neuropathy or coronary disease. The improvement in magnesium status was directly related to the dose of magnesium and there was a significant improvement in at least one major indicator of diabetes control. Hypomagnesemia is associated with the development of neuropathy and abnormal platelet activity, both of which are risk factors for the progression of ulcers on the feet. A study[13] on a group of patients with Type 2 diabetes divided into groups (with or without foot ulcers) found that there was a very strong relationship between serum magnesium depletion and the presence of foot ulcers.

More research has to be done to determine what magnesium dosages are recommended for diabetics. There can be no question that the use of magnesium by patients suffering from diabetes can provide important health benefits.

Chromium and Diabetes Control

In a recent review by RA Anderson[14], he stated that chromium increases insulin binding to cells, insulin receptor number, and to activate insulin receptor kinase leading to an increase in insulin sensitivity. Suboptimal intake of chromium is associated with increased risk factors associated with diabetes and cardiovascular diseases. Over the past few years, chromium has been shown to improve glucose and related variables in subjects with glucose intolerance and Type 1, Type 2, gestational and steroid-induced diabetes. The vast majority of published, peer-reviewed research have verified the importance of chromium in the metabolism of glucose, insulin and blood lipids. The observation that chromium (III) serves as a nutrient and not as a therapeutic agent has been summarized by John Vincent[15]:

"If sufficient chromium is maintained in pools, where it is available to be mobilized in response to insulin and subsequently to enter insulin-sensitive cells and sufficiently load apoLMWCr to appropriately stimulate insulin receptor kinase activity, increasing the body's content of chromium should have little if any positive effect".

In other words, individuals who are chromium sufficient should not

see any benefit from the intake of additional chromium. One of the big problems with the whole area of chromium and its use in diabetes has been finding a way to determine the chromium status of an individual. Studies on steroid-induced diabetes mellitus have helped show the benefits in patients with compromised chromium status. Ravina, A, et al[16] studied patients who were on corticosteroids and developed diabetes. They noted that urinary loss of chromium following corticosteroid treatment increased by about 60%. They treated these patients with 600 mcg of organically bound chromium per day. The chromium treatments lead to much improved blood glucose values. Hypoglycemic drugs were also reduced by 50% in all patients on supplemental chromium. The researchers concluded that chromium supplementation can reverse steroid-induced diabetes. It should also be noted that in another recent study[17], it was clearly shown that the chromium lost and excreted in the human body increases with aging, and is related to the development of diabetes. This study recommends the supplementation of a certain amount of chromium to elderly diabetics according to their nutritional level. RA Anderson, et al[18] demonstrated that chromium requirement increases as glucose intolerance and diabetes increases. In their study, individuals with Type 2 diabetes were randomly divided into three groups (placebo, 200 mcg chromium per day, and 1,000 mcg chromium per day). The greatest benefits were seen in the individuals receiving the highest dose of chromium. There were modest benefits seen in the lower dosed group and no benefit in the placebo group. The data in the study indicated that the supplemental groups showed beneficial effects on HbA1c, glucose, insulin, and cholesterol variables for the Type 2 diabetics, with the greatest benefits coming at doses well above the upper limit of the Estimated Safe and Adequate Daily Dietary Intake.

Much needs to be further elucidated in the area of chromium and diabetes. Is there a pharmacological effect that is seen at higher doses? How does one know that someone is chromium deficient? One recent study[19] has shown hopeful results for the use of urinary chromium loss, in response to glucose load, as an indicator of chromium status. One thing remains certain, chromium is an element that is essential to glucose tolerance and should be a strong consideration for all forms of diabetes mellitus.

Manganese Possibilities[20]

Although manganese has received a paucity of attention in diabetes research, defects in carbohydrate metabolism have been associated with manganese deficiency. Animal studies have shown that manganese deficiency results in severe pancreatic abnormalities, leading to aplasia and hypoplasia of all pancreatic cell components. Glucose challenge to manganese deficient animals have been followed by a diabetic-type glucose tolerance curve. Manganese supplementation completely reverses the abnormalities in pancreas and glucose tolerance seen in these animals. Additional animal research has shown that manganese deficiency results in depressed pancreatic insulin synthesis, enhanced intracellular insulin degradation, as well as a depression in the insulin secretory process. Manganese production of MnSOD may protect pancreatic Beta-cells from destruction by high concentrations of superoxide radicals. Manganese deficiency has also been linked to a reduction in the number of glucose transporters in adipose tissue.

Other Mineral Considerations

There have been other minerals which have received their share

MINERALS AND DIABETES MELLITUS

Lost due to polyuria	Magnesium Zinc
Often of low intake	Magnesium Chromium Zinc Manganese
Poorly absorbed	Zinc
Hyperexcreted	Zinc
Linked to insulin resistance	Magnesium Zinc Manganese Chromium
Fights oxidative stress	Copper Zinc Chromium Selenium Manganese

of mention in connection with the control of diabetes. The ones that we have mentioned earlier are those which have been shown to have definite nutritional links to diabetes. Vanadium is another mineral that has been researched in connection to diabetes. At present there is only circumstantial evidence that vanadium is essential for humans. However, vanadium has shown therapeutic potential in clinical studies[21] with patients of both insulin-dependent and noninsulin-dependent diabetes mellitus. Initially, some thought that vanadium had its own insulin-mimetic actions. However, most recent studies have found that vanadium's glucose lowering effects depend on the presence of endogenous insulin. It is felt that vanadium's effects on carbohydrate and lipid metabolism is not global, and that it acts selectively by enhancing rather than mimicking the effects of insulin[22].

Some research has pointed to caution concerning copper status and diabetes. Specifically, they have observed that copper appears to be lost when diabetics remain out of control, and this can open the door to lowering the diabetic's ability to fight against the potential harmful effects that can accrue from free radical damage. The copper loss leads to a lessening of the ability for the body to form Cu/Zn SOD, leading to a weakening of that line of bodily defense.

As time and research goes on, much more will come to light concerning the importance of minerals in the growing health hazard of diabetes mellitus.

A Matter of Choice

Diabetic nutritional formulations can have a mineral component that is a blend of magnesium, zinc, and chromium. Additional rationale can bring the addition of manganese, copper, and for some even vanadium. One of the chief considerations in the selection of the mineral form for such products has to be bioavailability. It would seem that this should be coupled with safety. A third consideration besides bioavailability and safety which is critical to compliance would be the tolerability of the mineral form. In all three of these important aspects, the Albion mineral amino acid chelate form of that mineral has been shown to be the best choice. On the issue of safety, Albion's mineral amino acid chelates have been shown to have lower toxicity than to any of the other inorganic mineral forms. This could be especially crucial for the ultra trace elements of chromium and vanadium, where the margin between a useful and toxic dose could be very narrow. Over the years, we have listed in this publication results of studies that have clearly shown that Albion's magnesium, zinc, chromium, copper, and manganese (as well as all of our other chelates) are by far more bioavailable that other mineral forms. Importantly, these data have also shown that the more an individual needs a particular mineral, the higher the relative absorption advantage is for the Albion mineral amino acid chelate form.

It has been observed that typical doses of magnesium salt forms can cause diarrhea. This low bowel tolerance to other magnesium forms is often critical to the compliance of people who need to take magnesium in higher does for extended periods. The problem of laxation from magnesium will more often than not cause the patient to stop taking their supplement. Albion's Magnesium Chelazome® does not cause diarrhea, as a high dose of magnesium can be taken without the discomfort and inconvenience of that laxative effect. Zinc salts commonly cause nausea, in the short term, and gastric erosion in the long run, when taken at needed doses for extended periods. This too can cause the patient to not take their supplements. Albion's Zinc Chelazome® is a very well tolerated form of zinc, without those nasty side effects.

When thinking about Diabetic Nutritional Formulas, the right choice for mineral form comes down to one - Albion Mineral Amino Acid Chelates.

* Better Absorption
* Greater Safety
* Much Better Tolerance

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