The possible treatment of Diabetes Mellitus by the element Vanadium: A literature review

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Abstract

Objective:

To provide a thorough background of the two main types of Diabetes Mellitus and the negative effects of hyperglycemia has on the body. To provide a concise explanation of vanadium, and its relationship to the treatment of diabetes.

Background: Diabetes Mellitus, a disease that is on the increase in this country and the world, affects how the body deals with the glucose ingested during eating. Diabetes is a group of diseases characterized by increased blood glucose levels resulting from decreased insulin. insulin action or both.

Methods:

There were 17 sources cited from various journals and articles obtained through searches conducted over the Internet on Medline and Mantis search engines. Various textbooks describing diabetes were consulted as well.

Results:

The positive results from the studies on the insulin-like properties of vanadium in vitro and in clinical trials demonstrate the effectiveness the mineral vanadium can play in the treatment of diabetes mellitus.

Conclusion: The number of cases of diabetes has risen significantly over the vears. An estimated 5.5 million Americans have been diagnosed already with this condition. Patients with diabetes mellitus need to control their blood sugar to decrease the risks of complications such as, retinopathy, neuropathy and nephropathy. Vanadium can play a part in the control of blood sugar levels and the Chiropractor needs to fully understand this condition and inform a willing patient the benefits of achieving euglycemia.

Key Words: Vanadyl Sulfate, Vanadium, Glucose, Hyperglycemia, Diabetes, IDDM, and NIDDM

Introduction

Diabetes mellitus is a disease that afflicted 15.7 million people or 5.9% of the population in 1996. This disease affects how the body handles sugar ingested by daily eating, and is caused by a problem with insulin production or action. (1). The individual due to this problem, will accumulate glucose in the blood which is both toxic to the body but is also the primary energy supply. The high blood glucose if left unchecked in the body will lead to serious side effects due to the toxicity, and these side effects in conjunction with the disease itself cost society in 1996 a total of \$98 billion dollars. The 98 billion dollars is divided into direct medical costs of \$44 billion and indirect cost due to disability, work loss and premature mortality of \$54 billion dollars (1). In addition, to all the costs and complications of diabetes it was the seventh leading cause of death, a total of 193,140 people (2). Diabetes has come a long way from when a diagnosis was considered a death sentence, with the introduction of insulin, and a special diet to help the diabetic to live with this disease. Research has shown that the serious side effects of diabetes can be reduced significantly with the strict control of blood glucose levels, this control can lead to a decreased risk of eye, kidney and nerve disease (3). The research has never stopped in the search of a better treatment and has lead to many substances making claims as to their effectiveness, vanadium is one such substance. The treatment and effects of vanadium on the treatment of diabetes will be the focus of this article. This information was found in various journals, articles and texts and is presented to the chiropractor to better inform them of the benefits of alternative approaches to the treatment of diabetes mellitus.

Background

Diabetes is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action or both. The resulting chronic high blood sugar levels, if they remain unchecked for a prolonged period, can and will lead to complications; such complications are heart, cardiovascular, kidney, eye, and nervous system diseases. A diabetes

control and complications trial performed from 1983 to 1993 showed that keeping blood sugar levels as close to normal as possible slows the onset and progression of the complications of diabetes (3). Specifically the study showed that intensive therapy reduced the risk for developing retinopathy by 76%, kidney disease by 50%, nerve disease by 60% and cardiovascular disease by 35% reduced risk (3). Diabetes is divided up into four distinct groups, type 1, insulin dependent (IDDM), type 2, non-insulin dependent (NIDDM), gestational and other.

Type 1 (IDDM) was formerly called juvenile onset diabetes due to the fact that this condition afflicts mostly people aged 20 and under. This classification has changed due to the fact this disease also afflict young adults. Type 1 diabetics accounts for 5% – 10% of all diagnosed cases in this country and has increased risk for complications due to prolonged elevated glucose levels over a lifetime. Type 1 diabetics don't produce insulin due to an destruction of the pancreases beta cells which is believe to be cause by a variety of factors such as autoimmune, genetic and environmental causes. The daily injection of insulin is used to treat the resulting hyperglycemia but mostly to prevent ketosis, a condition that occurs when the body starts using fats as a source of energy. This can lead to death due to the build up of the ketones and the resulting ketoacidosis.

Type 2 diabetes (NIDDM) is the most common and accounts for 90% to 95% of all diagnosed cases of diabetes. This classification of diabetics produce insulin but the cells in their bodies are "insulin resistant", which means that the cells don't respond properly to the hormone, so therefore glucose accumulates in their blood. Insulin resistance increases as weight increases and physical activity decreases. Most people who develop this condition are older sedentary people who are obese (weigh at least 20 percent more than what's recommended for their height and build).

Gestational diabetes develops in 2% to 5% of all pregnancies in this country but disappears when the pregnancy is over. Women who get this condition have no previous history of diabetes, but 40% of women who get gestational diabetes go on to develop type 2 diabetes within 15 years. Hormones that are produced during the pregnancy that are essential to the baby's growth may also make the mother insulin resistant. All pregnant women have some degree of insulin resistance but if a woman is to develop full-blown resistance it usually appears around the 24th week of pregnancy. This is why all pregnant women should be screened for gestational diabetes around this time.

Other specific types of diabetes result from many specific genetic syndromes, surgery, drugs, malnutrition, infections, and other illnesses. Such types of diabetes may account for 1% to 2% of all diagnosed cases of diabetes.

Vanadium (V) is a transitional element and is the 21st most abundant element of the earth's crust. A Swedish scientist Sefstrom discovered vanadium in 1831, but it wasn't until 1980 when research into this element first showed its insulin-mimicking abilities. This research produced exciting results in the studies of rodents and, in a limited number of, human studies. As a transitional metal in the periodic table, vanadium is positioned with known essential minerals suck as chromium, molybdenum, manganese and iron, which have been shown to have insulin-mimicking properties. Vanadium exists in five different forms with the most biologically significant being either vanadyl or vanadate, the two most widely research forms. The two main forms of vanadium, from the few controlled studies or therapeutic trials, have demonstrated the most common side effect as mild gastrointestinal intolerance. This has lead to the development of an organic from of vanadium, bis(maltolato)oxovanadium (BMOV), which is 2 or 3 times more potent and which has in research to this date shown less toxic side effects (4).

Vanadium has a total body concentration in man at about 20-25mg, and during our daily diet we ingest about 2mg per day. Vanadium is widely distributed across the food supply with rich sources in pepper, dill, radishes, eggs, and oats (5). It appears that food refining and processing increases the vanadium content of foods. Although vanadium has been found to have insulinomimetic properties in experimental animals, isolated tissues and cell preparations, the metabolic processes regulating vanadium remains incomplete. It appears that the exact cellular mechanism of action involves a combination of several post-receptor events in the insulin-signaling cascade (4).

Research

There are a growing number of experimental and clinical researches into the benefits of the mineral vanadium. The research is supported by the hypothesis that vanadium has the ability to exert potent insulin-mimetic effects in vitro and in vivo when used in high doses. The effect of vanadium has been used extensively on streptoxotocin (STZ) diabetic rats with significant clinical outcomes. The very first reported study demonstrating vanadium's insulinmimetic effects was conducted by Heylinger on STZ rats which were fed sodium orthovanadate at a level of 100mg/kg per day. This treatment was found to normalize hyperglycemia and improve cardiac function independent of changes in plasma insulin levels (6). These results led to a long-term study in which vanadyl sulfate was given in various concentrations to both non-diabetic rats and STZ diabetic rats. In the non-diabetic rats it was noted that there was a significant decrease in body weight gain and plasma insulin levels, but no significant alteration in the fluid and food intake, the plasma levels of glucose, triglycerides or cholesterol. The vanadyl sulfate treatment on the STZ diabetic rats significantly alleviated or prevented the occurrence of hyperglycemia, hypoinsulinanemia, hyperphagia, polydipsia, hyperlipidemia, or cataract formation. An added finding was the continuation of the benefits of the vanadyl sulfate treatment, which continued for sixteen-week post withdrawal (7).

The positive studies on the insulin-like properties of vanadium in vitro and in animal studies have allowed for clinical studies to begin. In a recent trail conducted by Goldfine et al, two group of diabetic patients were administered small doses, at levels 100 fold lower than in animal studies, of vanadyl sulfate or sodium metavanadate. Clinical benefits were found in type 1 diabeties in the form of a significant (14%) decrease in the amount of insulin needed on a daily basis. and in 2 of the 5 patients there was a improved glucose utilization. There were more dramatic improvements seen in the type 2 diabetics consisting of increased insulin sensitivity, which is attributed to a greater inhibition of hepatic glucose production by insulin and an enhancement of non-oxidative glucose disposal rates. The main side effects observed in this trial were gastrointestinal in nature. This positive result in the type 2 diabetic was repeated in a study conducted by Cohen et al, in which six patients were give 100mg/day of vanadyl sulfate. This treatment resulted in a reduction in fasting plasma glucose without changes in plasma insulin levels. These clinical studies still leave it uncertain whether the persistent beneficial effect result from a long-lasting action of vanadium or from the alleviation of glucose toxicity brought about by the treatment. These results however are encouraging and call for further evaluation of the long-term effectiveness and safety of vanadium.

Toxicity

The positive effects of vanadium can often be an overriding factor in the promotion of the mineral, but the research has shown some negative effects that can not be overlooked. Toxic effects of the vanadate form of vanadium used on animals have shown elevated blood pressure, reduction of coenzyme q10 & coenzyme A levels, stimulation of amine oxidase inhibitors and interference with cellular energy production. Dr. Sreedhara, a noted Ohio State researcher, has in his studies on the use of vanadium shown more disturbing effects including

damage to DNA, blocking of protein synthesis as well as oxidation of lipids (8,9). However, the above toxicity studies have used vanadate, not vanadyl or the new organic BMOV, and humans subjects appear to tolerate vanadium better than other species. The two most common side effect observed in the clinical trials of vanadium have been mild gastrointestinal intolerance and a slower body weight gain. This slower body weight gain can be regarded as an adverse reaction in a type 1 diabetic, and possibly a positive side effect in the type 2 diabetic (4). In the research being performed right now on the organic versions of vanadium, the preliminary data suggest a decrease in toxic side effects and an increased in absorption rate, which is promising but still lacking the further long term clinical trials.

Discussion

The number of people in this country and the world afflicted with diabetes mellitus is on the rise with projections of doubling the current diabetics in 30 years. This leads to serious problems caring for these people due to the serious complications and the resulting rising cost. This serious problem leads to the question of what can we do, considering the current treatment of daily injections or medication, diet and exercise have not reduced the serious side effects and the resulting death from this disease. Diabetic are living longer today then ever because of the introduction of insulin and the development of a specific diet, but this hopefully was just a stepping stone to the possible future advancements. Vanadium has the potential to be one of these advancements, based on the past research and the current clinical trials. Vanadium has been shown to cause marked sustained decreases in plasma glucose, triglyceride and cholesterol levels, it also has been shown to ameliorate secondary complications of diabetes including cardiomyopathy, vascular hyperactivity and cataract formation. It has been well researched by the clinical diabetes and complication trial that strict control of the associated hyperglycemia will decrease the risk of serious side effect and death, and from the research, vanadium does just that. The

unanswered questions of toxic side effects of long term supplementation of vanadium in humans still remains unanswered, but given the seriousness and finality of the present side effects the question needs to be answered by the patient themselves. The use of vanadium as an adjunctive therapy for the treatment of diabetes can be incorporated into their lifestyles along with the necessary monitoring by a doctor. This can be and effective means of treating diabetes mellitus along with the associated hyperglycemia.

Bibliography

- 1. American Diabetes Association. Economic consequences of diabetes mellitus in the U.S. in 1997. Diabetes Care 1998; 21(2): 296-309
- 2. National Diabetes Data Group, National Institutes of Health. Diabetes in America, 2nd Edition. Bethesda, MD: National Institutes of Health, 1995. NIH Publication No. 95-1468
- 3. Nathan et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulindependent diabetes mellitus. The New England Journal of Medicine, Sept 30, 1993. 329(14) pp977-985
- Verma S, et al. Nutritional factors that can favorably influence the glucose/insulin system: vanadium.
 J Am Coll Nutr. 1998 Feb; 17(1): 11-8. Review.
 - 5. French, J, Role of Vanadium in Nutrition: Metabolism, essentiality & dietary considerations. Life Sciences, Vol. 52, pp. 339-346
 - 6. Bricherd SM, et al, The insulin-like properties of vanadium: a curiosity or a perspective for the treatment of diabetes?
 Diabete Metab. 1991 Sep-Oct; 17(5): 435-40. Review.
 - 7. Cros GH, et al. Long-term antidiabetic activity of vanadyl after treatment withdrawal: restoration of insulin secretion?

 Mol Cell Biochem. 1995 Dec 6-20; 153(1-2): 191-5. Review.
 - 8. A. Sreedhara et al: Biochem & Biophys Res. Comm.; 224, 115-120; 1996
 - 9. A. Sreedhara et al: Inorg. Chimica Acta; 263, 189-194; 1997
 - 10. Pederson RA, et al. Long-term effects of vanadyl treatment on streptozocin-induced diabetes in rats.
 Diabetes. 1989 Nov; 38(11): 1390-5.
 - 11. BOULEY, J Diabetes: Best Defense--Reducing Blood Glucose Staves off Complications of Diabetes. DO. 1995 MAR. 36(3). Pp. 56-60.
 - 12. Hamel FG, et al, Alteration of tissue vanadium content in diabetes. Metabolism. 1993 Dec; 42(12): 1503-5.
 - 13. Poucheret et al. Vanadium and diabetes. Mol Cell Biochem 1998 Nov;188 (1-2): 73-80.

- 14. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S Adults. Diabetes Care 1998; 21(4): 518-524.
- 15. Hamel et al. Alteration of Tissue Banadium Content in Diabetes Alteration of Tissue Vanadium Content in Diabetes. Metabolism, Dec 1993. Vol. 42(12) 1502-1505
- 15. Goldfine et al. Metabolic effects of sodium metavanadate in humans with insulin-dependent and non-insulin-dependent diabetes mellitus in Vivo and in Vitro Studies. JCE & M 1995; 80(11): pp. 3311-3319.
- 16. Bricherd SM, et al, The role of vanadium in the management of diabetes. Trends Pharmacol Sci. 1995 Aug; 16(8): 265-70. Review.