Vanadium: Nutritional Supplementation as a Treatment for Diabetes Mellitus

Sr. Research Project
A literature review

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Abstract

Objective: The goal of this paper is to provide a background of the two main types of diabetes mellitus and the negative effects of hyperglycemia on the body, provide a concise explanation of vanadium and to explain the relationship of vanadium in the treatment of diabetes.

Background: Diabetes mellitus is a disease that is progressively on the rise worldwide. Diabetes mellitus affects how the body deals with the glucose ingested. Diabetes is a group of diseases characterized by increased blood glucose levels resulting from decreased insulin, insulin action or both.

Data Sources: There were 25 sources cited from various journals and articles obtained through searches conducted over the internet on Medline and Mantis and Pubmed. Various textbooks were also consulted.

Results: The positive results from the studies on the insulin-like properties of vanadium in vitro, in vivo, and in clinical trials demonstrate the effectiveness that vanadium has on the treatment of Diabetes mellitus. The studies reviewed showed that the benefits strongly out weigh the negative affects.

Conclusion: The number of cases of diabetes has risen significantly over the years. An estimated 5.5 Million Americans have been diagnosed 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 significant part in the control of blood sugar levels.

Key Words: Vanadium, Vanadyl Sulfate, 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. 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 dollars 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. The introduction of insulin and a special diet have helped the diabetic patient 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. The focus of this paper will be the treatment and effects of vanadium on the treatment of diabetes. The information used was found in various journals, articles and texts.

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 levels, if remained uncheck for a long period of time, 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% (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 afflicts young adults. Type 1 diabetes 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 do not produce insulin due to a destruction of the pancreatic beta cells, which is believed to be caused by a variety of factors such as autoimmune, genetic and environmental causes. A 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 fat 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 diabetic patients produce insulin but the cells in their bodies are “insulin resistant”, which means that the cells do not respond properly to the hormone, therefore glucose accumulates in the 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 is 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 develop this condition have no previous history of diabetes, but 40% of women who acquire gestational diabetes go on to develop type 2 diabetes within 15 years. Hormones that are produced during the pregnancy 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 should 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 it’s 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 such 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 vanadyl and vanadate, the two most widely researched 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 form 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 of gastrointestinal intolerance (4). The research performed by Badmaev et al demonstrated that the organic forms of vanadium as opposed to the inorganic sulfate salt of vanadium, are recognized as safer, more absorbable, and able to deliver a therapeutic effect up to 50% greater than the inorganic forms. The goal is to provide vanadium with better gastrointestinal absorption, and in a form that is best able to produce the desired biological effects. As a result, numerous organic complexes of vanadium have developed including bis(maltolato)oxovanadium (BMOV), bis(cysteinate N-octyl)oxovanadium known as Naglivan, bis(pyrididine-N-carbodithioato)oxovanadium, vanadyl-cysteine methyl ester, and bis-glycinato oxovanadiumm (BGOV) (5).

Vanadium has a total body concentration in man at about 20-25 mg, and during our daily diet we ingest about 2 mg per day. Vanadium is widely distributed across the food supply with rich sources in pepper, dill, radishes, eggs, oats, skim milk, lobster, vegetable oils, grains and cereals (5,6). It appears that food refining and processing increases the vanadium content of foods although not a significant amount to be considered therapeutic. One study demonstrated that wine storage conditions might increase vanadium content (7). Although vanadium has been 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 effects of vanadium have been used extensively on streptozotocin (STZ) diabetic rats with clinical outcomes. The very first reported study demonstrating vanadium’s insulin mimicking effects was conducted by Heylinger on STZ rats which were fed sodium orthovanadate at a level of 100 mg/kg per day. This treatment was found to normalize hyperglycemia and improve cardiac function independent of changes in plasma insulin levels (8). These results led to a long-term study in which vanadyl sulfate was given in various concentrations to both non-diabetic rats and STZ rats. In the non-diabetic rats it was noted that there was significant decrease in body weight gain and plasma insulin levels, but no significant alteration in the fluid 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, hypoinsulinemia, hyperphagia, polydipsia, hyperlipidemia, or cataract formation. An added finding was the continuation of the benefits if the vanadyl sulfate treatment, which continued for sixteen-week post withdrawal (9).

A study of newly acquired diabetes was conducted studying the influence of vanadium and food restriction. A group of STZ diabetic rats were untreated; one group had vanadyl sulfate added to their drinking water at one week prior to and for five weeks following the administration of STZ. An additional group was pair-fed with the equal amounts of food as that consumed by the treated group. Shortly after the induction of STZ the untreated group had a significant rise in plasma insulin to levels that initially exceeded that of the control group. This was followed by a steady reduction over several weeks, suggesting a gradual depletion of functional beta-cells. Both the vanadium treated rats and the pair-fed rats
eliminated the insulin hypersecretion following the STZ administration. Glucose lowering was enhanced in the treated rats when administered higher concentrations of vanadium, despite no further reduction in food intake, and all the treated rats were normoglycemic within five weeks. Mean pancreatic insulin content in the treated rats was improved fourfold and was associated with a greater number of granulated beta-cells. Conversely, food restriction only modestly improved glycemia and the pancreatic insulin store and, unlike the Treated rats, the pair-fed rats remained glucose-intolerant. At five weeks of diabetes, fed circulating glucose and insulin levels were strongly correlated in the untreated and pair-fed groups, supporting the notion that glucose lowering with food restriction is dependent on improved plasma insulin levels. A separate correlation was observed in the treated rats within a lower range of plasma insulin, suggesting that vanadium, unlike food restriction, reduced plasma glucose by enhancing insulin sensitivity. Thus, vanadium preserves beta-cells in STZ-diabetes at least partially by abolishing the insulin hypersecretion and the eventual exhaustion of residual insulin stores following a moderate dose of STZ (10).

The effects of a one year combined vanadium and insulin treatment on blood glucose levels of insulin dependent diabetic rats were studied. For two months the rats were injected with low doses of insulin to keep them from going into hyperglycemic shock. In the first group of rats, hyperglycemia improved during one year by increasing the daily dose of insulin. In the second group of rats, vanadyl oxide sulfate pentahydrate was orally administered in place of the insulin. The results of the study indicated that the one year vanadium treatment regenerated new beta-cells, and relieved diabetes both during treatment and after withdrawal. The one year insulin treated rats showed no trophic effects on the destroyed beta-cells, therefore no improvement in the glycemic status of the rats was seen after withdrawal. It appears that long term vanadium treatment regenerated beta-cells and possibly improved their secretory function (11).

A study of organic forms of vanadium as compared to vanadyl sulfate showed greater efficacy of the organic forms, especially vanadyl acetylacetonate. Activities and mRNA levels of key glycolytic enzymes (glucokinase and L-type pyruvate kinase) which are suppressed by the diabetic liver, were restored by vanadium treatment. The data suggests that differences in potency between compounds are due to differences I
their insulin-like properties. There was no marked toxicity observed on hepatic or renal functions. However, diarrhea occurred in 50% of the rats chronically treated with vanadyl sulfate, but not in those receiving the organic compound (12). Another study showed that peroxovanadate administered orally at 1 mg/kg could significantly reduce the plasma glucose levels over four weeks treatment, whereas the same dose of single sodium vanadate did not have hypoglycemic effects (13).

One study that should be mentioned was performed by Brand and Hamel demonstrating that a series of peroxovanadium compounds that are more potent at lowering blood glucose levels than sodium metavanadate, sodium orthovanadate and vanadyl sulfate have been synthesized. These compounds probably will not be orally active so transdermal administrations are a potential option. The compound’s insulin mimetic properties administered transdermally were evident within 60 min of current initiation. Blood glucose levels were reduced to 74 +/- 14% of the original level after 16 hours of passive treatment. The compound was ineffective when fed to animals (14). This study, although incorporating synthetic compounds, does provide us with a convenient form of administering vanadium into the body’s system.

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 trial conducted by Goldfine et al, two groups of diabetic patients were administrated small doses, at levels 100 fold lower than in animal studies of vanadyl sulfate or sodium metavanadate. Clinical benefits were found in type 1 diabetes of a significant (14%) decrease in the amount of insulin needed on a daily basis, and in 2 of the 5 patients there was an improved glucose utilization. There were more dramatic improvements seen in the type 2 diabetes consisting of increased sensitivity, which is attributed to a greater inhibition of hepatic 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 given 100 mg/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 of 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 of vanadium (15).

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 used on animals have shown elevated blood pressure, reduction of coenzyme Q10 and coenzyme A levels stimulation of amine oxidase inhibitors and interference with cellular energy production. Dr Sreedhara, a noted Ohio State University 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 (16,17). However, the above toxicity studies have used vanadate, not vanadyl or the new organic BMOV, and humans subject appear to tolerate vanadium better than other species. The two most common side effects 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 date a suggest a decrease in toxic side effects and an increase in absorption rate, which is promising but still lacking the further long term clinical trials.

Discussion

The number of people in this country and in 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 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 patients are living longer today than ever before
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 trails.
Vanadium has been shown to cause marked sustained decrease 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 trail that
strict control of the associated hyperglycemia will decrease the risk of
serious side effects and death, and from the research, vanadium does just
that. The toxic side effects of long term supplementation of vanadium in
humans still remain unanswered although look very promising. Given the
seriousness and finality of the present side effects, the question needs to
be answered by the patients 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 the doctor. This
can be an effective means of treating diabetes mellitus along with the
associated hyperglycemia. Vanadium and its derivatives appear to be an
alternative to insulin in the near future, due to its low cost, low toxicity
and ready availability.
Bibliography


