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THIAMINE SUPPLEMENTATION IN DIABETES MELLITUS: A POTENTIAL THERAPEUTIC STRATEGY

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ABSTRACT

Thiamine, often known as vitamin B1, plays a crucial role in energy metabolism and the proper functioning of cells that rely on insulin. The presence of thiamine deficiency has been seen in individuals with diabetes mellitus, potentially leading to the worsening of comorbidities and metabolic abnormalities. A comprehensive examination was undertaken to evaluate the influence of thiamine levels on metabolic parameters in individuals diagnosed with diabetes based on current studies. This study investigated the correlation between plasma thiamine concentration, renal thiamine clearance, lipid profiles, glucose control, and diabetes complications. The findings of the review are as follows: Patients diagnosed with diabetes, including both Type 1 and Type 2, have a notable decrease in plasma thiamine concentrations when compared to individuals without diabetes. This decline cannot be attributed to inadequate food intake but rather to an elevated excretion of thiamine through the kidneys. Significant associations were seen between diminished thiamine concentrations and unfavorable lipid profiles, heightened glucose levels, and high blood creatinine levels. The possible mitigating effects of thiamine supplementation on these abnormalities have been demonstrated by a reduction in resting energy expenditure and enhancements in clinical indicators. In conclusion, it can be inferred that the available data indicates that adding thiamine supplementation may be a beneficial supplementary treatment in managing diabetes, as it can enhance metabolic results and decrease the likelihood of complications. Nevertheless, it is essential to do more studies to develop definitive protocols about the most effective dosage and long-term advantages of thiamine supplementation in individuals with diabetes.

KEYWORDS: Thiamine, Diabetes Mellitus, Micronutrient Deficiency, Metabolic Regulation, Diabetic Complications, Thiamine Supplementation.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose levels resulting from defects in insulin secretion. Diabetes mellitus (DM) is a complex metabolic condition characterized by impaired metabolism and elevated blood glucose levels. From an etiological perspective, the development of DM and hyperglycemia can be attributed to many reasons, including diminished insulin secretion, hereditary or acquired insulin insufficiency, insulin ineffectiveness, and impaired glucose utilization coupled with heightened glucose generation. There are several categories of diabetes mellitus (DM) that are attributed to hereditary or environmental causes as well as individual lifestyle decisions. Different forms of DM are characterized based on the pathogenic process. There are two significant classifications of DM, namely type 1 and type 2. Type 1 diabetes mellitus (DM), also referred to as juvenile diabetes, is characterized by a condition known as insulin-dependent diabetes mellitus (IDDM). This form of diabetes arises when the pancreas cannot generate insulin due to the death of beta cells caused by an autoimmune response. Diabetes is a very prevalent medical condition affecting a substantial portion of the global population, and its incidence has exhibited an upward trend over the last twenty years on a worldwide scale.

Diabetes mellitus (DM) is a highly significant health issue characterized by a rapid increase in prevalence across various age groups. Diabetes can manifest through two primary mechanisms: autoimmune and metabolic processes. Malabsorption, obesity, physical inactivity, and hormonal imbalance are recognized as prominent risk factors for the development of diabetes mellitus. Diabetes mellitus is associated with complications such as insulin shock, renal failure, atherosclerosis, and stroke. The most effective strategies for preventing the onset of diabetes mellitus, particularly type II diabetes mellitus, encompass regular physical activity and adherence to a nutritious dietary regimen. The relationship between diabetes and inadequate thiamine storage in the body has been identified since thiamine plays a direct role in regulating glucose metabolism.[6] The disease of diabetes mellitus (DM) presents a significant public health issue due to its associated mortality, morbidity, and financial cost.[2]

Type 2 Diabetes Mellitus is a multifaceted condition frequently associated with energy metabolism, mainly regulating glucose and fat inside the body. Type 2 diabetes is the prevailing form of diabetes, including around 5 to 10% of the total cases of this medical condition. The presence of obesity, insulin resistance, and inadequate insulin production commonly distinguishes type 2 diabetes. Diabetes mellitus, a naturally occurring metabolic disorder resulting from insufficient insulin action (either absolute or relative), is characterized by varying levels of chronic hyperglycemia and often occurs alongside specific microvascular complications such as nephropathy, retinopathy, and neuropathy.[3]

Thiamine is classified as a water-soluble vitamin, serving as a crucial co-enzyme in the metabolic pathways responsible for regulating glucose homeostasis and facilitating energy generation. Emerging studies indicate that thiamin has the potential to modulate specific mechanisms underlying hyperglycemic outcomes. Consequently, the administration of thiamine has been associated with several benefits in individuals with hyperglycemia. Previous studies have demonstrated that the administration of high-dose thiamine supplements leads to a reduction in fasting plasma glucose levels among individuals with type 2 diabetes (T2D), as well as an improvement in glucose tolerance in those with hyperglycemia. It is plausible that the impact of thiamine on blood glucose levels might potentially coincide with alterations in energy metabolism, considering the association above between hyperglycemia and energy metabolism. Thiamine is a cofactor for many enzyme complexes, namely pyruvate dehydrogenase (PDH), pyruvate transketolase (Tk), and α-ketoglutarate dehydrogenase. These enzyme complexes play a crucial role in intracellular glucose metabolism by enhancing the activity of the Krebs cycle.[11] Risk factors associated with thiamine deficiency, including gastrointestinal dysfunction, such as chronic vomiting (e.g., hyperemesis gravidarum) or malabsorption, inadequate nutritional status, diuretic use, and hemodialysis.[14]

Thiamine, often known as vitamin B1, plays a pivotal role as a cofactor for many enzymes involved in glucose metabolism. Published research suggests that individuals with diabetes exhibit decreased thiamine metabolism.[12]

The existing body of research has extensively examined the relationship between thiamine and diabetes mellitus (DM). A notable proportion of individuals without pre-existing health conditions (ranging from 36% to 47%) exhibited a deficiency in thiamine when experiencing hyperglycemia, which can occur in several circumstances, such as pregnancy, diabetes, or a

diet heavy in carbohydrates. The study revealed that individuals diagnosed with type 1 diabetes exhibited reduced amounts of thiamine in their plasma. A reduction in thiamine reserve was seen in untreated litters of diabetic rats. Lactic acidosis, hyperglycemia, and diabetic ketoacidosis (DKA) manifest as clinical manifestations of acute thiamine deficiency in pediatric patients.[11]

Previous clinical studies with limited sample numbers and varying durations have seen higher levels of thiamine and its derivatives without any subsequent enhancement in renal function. Individuals diagnosed with type 2 diabetes mellitus (DMT2) may potentially experience favorable outcomes by undergoing a thiamine intervention lasting six months. This intervention aims to elevate lipid and creatinine levels while addressing any existing thiamine shortage. Extensive documentation exists about the frequency of thiamine deficiency among outpatients with diabetes. The animal models demonstrate that a deficiency in insulin hinders the absorption of thiamine via the gastrointestinal tract and diminishes the reuptake of thiamine in the renal proximal tubule. Severe thiamine deficiency can induce acute lactic acidosis. Thiamine functions as a cofactor in the process of mitochondrial oxidative decarboxylation, enabling pyruvate and α-ketoglutarate in the citric acid (Krebs) cycle. The entry of pyruvate into the Krebs cycle is contingent upon the presence of thiamine, as its absence results in the conversion of pyruvate to lactic acid. A recent study has revealed that the prevalence of lactic acidosis in diabetic ketoacidosis (DKA) may reach up to 68%, thereby contributing to the growing recognition of this illness.[13]

Previous studies have demonstrated the enhanced levels of thiamine and its derivatives resulting from oral supplementation. These studies were conducted using small sample sizes and varying durations but showed no subsequent improvement in renal function. The administration of thiamine supplements over six months has the potential to provide advantages for those diagnosed with type 2 diabetes mellitus (DMT2). These benefits include the correction of thiamine deficiency, as well as improvements in lipid profiles and creatinine levels. Studies have demonstrated that individuals diagnosed with diabetes exhibit a slight deficiency in thiamine or reduced levels of thiamine in their plasma.[12]

Furthermore, it has been shown that alterations in the activity of erythrocyte transketolase indicate a potential deficiency of thiamine in individuals with type 2 diabetes. However, there is variation in the level of erythrocyte transketolase activity seen between persons with diabetes and those who are considered healthy. Conflicting findings on the amounts of

thiamine and its derivatives were seen when assessing blood, serum, and plasma samples, with some studies reporting decreased or low levels while others said normal levels. Our study examines the relationship between blood thiamine and its phosphate esters status in individuals diagnosed with DMT.[1]

Literature review

Thiamine has been seen to inhibit the progression of retinopathy and nephropathy, as well as mitigate the microvascular impairments induced by hyperglycemia in diabetic mice. The occurrence of renal damage in individuals with diabetes is attributed to the diminished availability of thiamine. The presence of two single-nucleotide polymorphisms in the SLC19A3 gene, responsible for encoding thiamine transporter2, is associated with the lack of diabetic retinopathy and nephropathy in individuals with long-term type 1 diabetes.[1]

A wide range requires the enzyme cofactor thiamine (vitamin B1) of organisms throughout different stages of both anabolic and catabolic intermediate metabolism. Nevertheless, there exists a dearth of knowledge regarding the mechanisms via which thiamine exerts its therapeutic effects on individuals who have type 1 diabetes, also known as diabetes mellitus type 1 (DMT1). The objective of this study was to evaluate the biochemical changes resulting from thiamine deficiency in adult patients with DMT1 in Saudi Arabia. It was hypothesized that individuals exhibiting symptoms of DMT1 may potentially have an elevated prevalence of metabolic syndrome as a result of a deficiency in blood thiamine levels.[2]

The initial association between thiamine and diabetes was documented during the 1940s. In subsequent years, it was shown that the presence of thiamine deficiency plays a role in the development of diabetic neuropathy. Consequently, several preliminary experiments were conducted to evaluate the possible impact of thiamine supplementation. The potential impact of thiamine on retinopathy's formation or progression remains unexplored despite several promising proofs of concept. Several preliminary studies on human subjects have demonstrated the potential positive impact of thiamine supplementation on diabetic nephropathy.[3]

The present review article investigates the correlation between several vitamins and the development of type 2 diabetes. Managing oxidative stress resulting from glucose metabolic irregularities necessitates the presence of lower quantities of antioxidant vitamins, including vitamins A, C, and E. Nevertheless, metformin is considered the optimal therapeutic approach

for managing type 2 diabetes, a condition that is associated with many complications such as cardiovascular disease and diminished levels of vitamin D. Individuals who engage in prolonged metformin usage may potentially derive advantages from the administration of supplementary folic acid and vitamin B12.[4]

The relationship between diabetes and low thiamine reserves in the body has been established due to thiamine's direct influence on glucose metabolism. Elevated renal clearance of thiamine has been seen in persons diagnosed with both type 1 and type 2 diabetes. Research findings have indicated that administering large doses of thiamine might yield positive outcomes in treating early-stage diabetic nephropathy. Based on the results of the study, it was observed that individuals diagnosed with both type 1 and type 2 diabetes had notably elevated levels of fasting blood sugar (FBS), random blood sugar (RBS), glycated hemoglobin (HbA1c), triglycerides, and total cholesterol in comparison to the control group.[5]

Diabetes, particularly type 2, exerts a significant impact on a substantial population worldwide. The subsequent stages of this study focused on examining thiamine's identification, purification, characterization, and influence on the levels of marker proteins in individuals with type 2 diabetes. The discussion also encompassed protein biomarkers that can be utilized for the early diagnosis of pathological conditions such as diabetes mellitus. The use of thiamine in animal experiments has been seen to mitigate the lipid irregularities linked to diabetic nephropathy. The results of this investigation will also facilitate the identification of protein markers associated with type 2 diabetes mellitus, enabling the development of innovative diagnostic methodologies for the timely diagnosis of this condition among those at risk within our community. The present study findings have the potential to contribute to the development of preventative and efficacious treatment approaches for individuals with diabetes through the identification of protein biomarkers and the utilization of high dosages of thiamine.[6]

Thiamine is a cofactor for transketolase (Tk) and the pyruvate dehydrogenase and α-ketoglutarate dehydrogenase complexes. These enzymes are of significant importance in the intracellular glucose metabolism process. The existing research has documented the association between thiamine and diabetes mellitus (DM). The levels of thiamine and the activity of thiamine-dependent enzymes are reduced in individuals with diabetes mellitus. Thiamine has a significant role in the pathogenesis of several diabetic endothelium vascular

disorders, including microangiopathy and macroangiopathy. Additionally, thiamine has been found to impact lipid profiles, retinopathy, nephropathy, cardiopathy, and neuropathy in individuals with diabetes.[7]

Hyperglycemia is widely believed to be a significant contributing factor to the synthesis of advanced glycated end products (AGEs). The inhibition of this pathway has the potential to mitigate diabetes-related complications significantly. The objective of this study is to examine the anti-diabetic characteristics of thiamine in both in vivo and in vitro settings. The ability of thiamine to inhibit glycation was assessed by employing human serum albumin (HSA) as a representative protein model.[8]

The available findings indicate that only raising plasma levels may not be the optimal approach, as intracellular TDP levels are not solely determined by the levels of its precursor in the plasma. Before obtaining a conclusive answer, it is essential to conduct experimental investigations that delve into the molecular mechanisms of thiamine deficiency in individuals with diabetes.[9] The objective of this study is to assess the thiamine status in individuals with type 1 and type 2 diabetes by examining plasma, erythrocytes, and urine samples and establish any potential associations with indications of vascular dysfunction. Individuals diagnosed with type 1 and type 2 diabetes often have decreased levels of thiamine in their plasma, which is associated with an elevated rate of thiamine elimination from the body. The conventional assessment of thiamine status was hindered by the increased presence of thiamine transporters in erythrocytes.[10]

The exploration and identification of novel therapy targets is crucial to comprehend the molecular etiology of chronic micro-, macro-, and avascular complications resulting from hyperglycemia. Thiamine (vitamin B1) is an essential cofactor for several enzymes involved in glucose metabolism. Existing literature suggests that individuals with diabetes have irregularities in thiamine metabolism. The objective of this study is to elucidate the physiological role of thiamine in the metabolic processes of amino acids and glucose, to present a comprehensive overview of thiamine metabolism, and to examine the consequences of thiamine shortage.[11]

About the correction of thiamine status and the improvement of cholesterol and creatinine levels, administering 100 mg of thiamine supplementation over six months may confer benefits to those diagnosed with type 2 diabetes mellitus (DMT2).[12] Thiamine plays a vital

role in the process of aerobic metabolism, and a shortage of thiamine can result in the development of lactic acidosis. While there have been observations of a rising incidence of thiamine deficiency among diabetic outpatients, the relationship between this disease and diabetic ketoacidosis (DKA) has not yet been investigated. The present study postulates a potential association between elevated lactate levels in individuals diagnosed with diabetic ketoacidosis (DKA) and a shortage in thiamine. The occurrence of thiamine deficiency was observed to be widespread among individuals diagnosed with diabetic ketoacidosis (DKA). There was an observed negative correlation between lactate levels and thiamine levels in individuals with diabetic ketoacidosis (DKA). Further investigation is required about the use of thiamine as a supplement in cases of diabetic ketoacidosis (DKA).[13]

The etiology of lactic acidosis (LA) is commonly attributed to factors such as contracted intravascular volume, metabolic abnormalities, and thiamine deficiency. Thiamine deficiency warrants a reduction in the clinical threshold for thiamine infusion in patients with severe illness, exhibiting alterations in mental state or nonspecific neurological symptoms, or experiencing malnutrition.[14] The objective of this study is to assess the impact of thiamine supplementation on the resting energy expenditure (REE) of individuals with hyperglycemia. The study employed a double-blind, randomized design and included 12 individuals diagnosed with hyperglycemia. The participants were administered a dosage of thiamine at a rate of 300 mg per day, along with a placebo carefully selected to match the thiamine, for six weeks. This administration was carried out in a cross-over manner. The administration of high doses of thiamine has the potential to reduce resting energy expenditure (REE) in individuals who have inadequate glucose regulation. The findings of our study suggest that improved glycemic control may contribute to the observed impact of thiamine on resting energy expenditure (REE).[15]

RESULTS

Thiamine, often known as vitamin B1, plays a crucial role in energy metabolism and is taken up by the body by particular transporters, namely THTR1 and THTR2, or by passive diffusion at elevated concentrations. Thiamine insufficiency has been associated with the development of severe systemic disorders, including thiamine-responsive megaloblastic anemia (TRMA), which manifests with symptoms such as diabetes, anemia, and deafness.

Recent research findings indicate that persons diagnosed with Type 1 and Type 2 diabetes mellitus (T1DM and T2DM) demonstrate notably diminished levels of thiamine in their

plasma when compared to individuals without diabetes. Specifically, T1DM patients exhibit a reduction of 76% in plasma thiamine concentrations, while T2DM patients display a drop of 75%. The absence of an evident clinical shortage, as demonstrated by the absence of enhanced transketolase (TKT) activity in red blood cells (RBCs), suggests that the shortfall in question is likely associated with diabetes itself rather than a dietary insufficiency of thiamine. The observed reduction in plasma thiamine concentrations is associated with an elevated renal clearance rate of thiamine, indicating a potentially dysfunctional excretion mechanism in individuals with diabetes. Moreover, there is a high prevalence of diabetic patients, namely those diagnosed with Type 2 Diabetes Mellitus (T2DM), in several countries, including the Kingdom of Saudi Arabia. These individuals face significant problems, one of which is diabetic retinopathy. A notable negative association exists between thiamine levels and several measures, such as serum HDL, glucose levels, urine thiamine, and serum creatinine. Elevated levels of THTR2 protein were seen in human microvascular endothelial cells (HMECs) when exposed to high glucose concentrations, suggesting a potential adaptive mechanism to sustain thiamine transportation during periods of hyperglycemic stress.

An association has been shown between thiamine deficiency and elevated lactate levels, indicating a potential connection with lactic acidosis. This condition can pose a problem in individuals with diabetes, particularly in the presence of diabetic ketoacidosis (DKA). The administration of thiamine as a supplement has demonstrated a notable reduction in resting energy expenditure (REE) after six weeks in comparison to the initial measurement, suggesting a possible beneficial effect on metabolism. The available research indicates that using thiamine supplementation might yield diverse metabolic advantages for individuals with diabetes, encompassing enhancements in lipid profiles and glucose regulation. Additionally, it can potentially decrease the likelihood of vascular problems through its impact on the functioning of endothelial cells. The potential association between thiamine and lactate levels might significantly affect managing problems such as lactic acidosis and diabetic ketoacidosis (DKA).

DISCUSSION

The discourse around the administration of thiamine supplements to individuals with diabetes is contextualized by the increasing body of research that highlights its metabolic importance and potential for therapeutic use. The observation of reduced plasma thiamine levels in

persons with both type 1 and type 2 diabetes mellitus is significant, as these levels are much lower in comparison to those found in those without diabetes. This implies that the metabolic abnormalities in diabetes may be attributed to thiamine losses resulting from increased renal clearance rather than a direct shortage induced by inadequate food intake. The negative associations between thiamine levels and indicators such as serum HDL, glucose, urinary thiamine excretion, and serum creatinine highlight the possible diverse impact of thiamine in influencing risk variables linked to diabetes complications. The upregulation of THTR2 in endothelial cells during hyperglycemia may indicate a compensatory response to mitigate thiamine deficit, emphasizing the body's effort to maintain thiamine homeostasis in the dysregulation caused by diabetes. In addition, the association between a shortage in thiamine and elevated lactate levels may provide valuable insights into the treatment and prevention of problems connected to diabetes, such as lactic acidosis and diabetic ketoacidosis (DKA). The administration of thiamine has demonstrated potential in mitigating resting energy expenditure (REE), which might have consequences for regulating energy equilibrium and weight control in the context of diabetes therapy. Considering these findings is crucial within diabetes care since the emphasis on macronutrient consumption and glucose control typically overshadows the focus on micronutrient status. The potential efficacy of thiamine supplementation in enhancing clinical outcomes holds considerable promise. However, its implementation necessitates a meticulous evaluation of the specific requirements of each patient, possible drug interactions, and a comprehensive assessment of the trade-off between advantages and potential drawbacks.

CONCLUSIONS

The use of thiamine supplements has demonstrated potential advantages in regulating specific biochemical indicators linked to diabetes. This discovery has the potential to facilitate the development of novel treatment approaches targeting the consequences of thiamine shortage, ultimately leading to enhanced clinical outcomes for individuals with diabetes. It is advisable to do more research to investigate the therapeutic possibilities of thiamine supplementation, determine the most effective dosage, and assess the long-term consequences of diabetes problems.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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