Ameliorative Effects of Magnesium and Copper Sulphates on Blood glucose and Serum Electrolytes Levels in Fructose-induced Diabetic Wistar Rats

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INTRODUCTION

Fructose, a natural sugar found in many fruits, is consumed in significant amounts in Western diets (Miller and Adeli, 2008). In equal amounts, it is sweeter than glucose or sucrose and is therefore commonly used as a bulk sweetener (Salwa, 2010). Diabetes mellitus is a leading cause of morbidity and mortality worldwide, with an estimated 346 million adults being affected in year 2011. The prevalence is expected to double between years 2005-2030, with the greatest increases expected in low- and middle-income developing countries of the African, Asian, and South American regions (Wild et al., 2004). Type II diabetes accounts for 90-95% of those diagnosed with diabetes mellitus. People with type II diabetes mellitus often exhibit high blood glucose and normal, slightly elevated, or slightly decreased insulin secretion. Unlike type I diabetes mellitus, type II diabetes mellitus is not an autoimmune condition, but rather a disease with contributions from diet, stress and sedentary lifestyle.

Type II diabetes mellitus also often presents with insulin resistance. In insulin resistance, the pancreas is able to secrete insulin, but the cells don’t respond to it efficiently; this process inhibits the cell from absorbing glucose, which in turn, keeps blood glucose levels high. Diabetes mellitus is one of the chronic diseases most frequently associated with magnesium deficiency (Walter et al., 1991). Serum magnesium concentrations have been found to be significantly lower in patients with diabetes mellitus than in healthy controls and poor control of diabetes mellitus is often associated with low serum magnesium (hypomagnesemia) (Vanroelen et al., 1985). Magnesium, the second most abundant intracellular cation involved in a number of important biochemical reactions, including all ATP-transfer reactions. Possibly because of its relevance to all protein kinases, magnesium appears to mediate hormonal as well as other aspects of cellular glucose utilization (Reinhart, 1988). There was significant decreased level of magnesium found in diabetic patients in the present study as described by various previous workers. Magnesium depletion is a common feature of diabetes mellitus, apparently related to glycemic control (Djurhuus et al., 2000).

The aim of this study is to evaluate the effects of magnesium and copper sulphates on blood glucose and serum electrolytes levels in fructose-induced diabetic Wistar rats. Diabetes was induced by administration of 20% (20g/100ml) of fructose dissolved in distilled water and administered to the animals for a period of six (6). After which the animals were randomly assigned into 4 groups of 6 rats each. Group I served as diabetic control and were administered distilled water, Group II were administered Magnesium sulphate (250 mg/kg b w), Group III were administered Copper sulphate (250 mg/kg b w) and Group IV administered Metformin (250 mg/kg b w). All treatments were given orally for a period of seven days. The results obtained showed a statistically significant decrease (p<0.05) in the blood glucose levels in groups administered with 250 mg/kg b w of magnesium and copper sulphate after day 3 and 7 when compared to diabetic control group. The results also showed that magnesium and copper sulphates at doses tested i.e 250 mg/kg b w, produced a significantly decreased (p<0.05). With regard to serum levels of sodium, potassium and bicarbonate ions when compared to diabetic untreated control group. However, there was no significant difference in the levels of serum chloride in the groups treated with 250mg/kg b w of magnesium and copper sulphate when compared to diabetic control group.
The magnesium deficiency that has been demonstrated in insulin-resistance such as hypertension and type II diabetes mellitus may thus contribute to suppress glucose metabolism and insulin action (Resnick, 1999; Paolilso and Barbagallo, 1997; Syed et al., 2005). Electrolytes play an important role in many body processes, such as controlling fluid levels, acid-base balance (pH), nerve conduction, blood clotting and muscle contraction. Electrolyte imbalance resulting from kidney failure, dehydration, fever and vomiting has been suggested as one of the contributing factors toward complications observed in diabetes and other endocrine disorders (Rao, 1992).

Electrolyte imbalance secondary to compromise in kidney function in prolonged and uncontrolled hyperglycemia of diabetes mellitus has long been established. Usually, glycosuria, a prominent diagnostic feature of diabetes mellitus imposes dehydration via glucose osmotic diuresis, which is usually accompanied with severe loss of electrolytes including sodium, potassium, calcium, chloride and phosphates (Item et al., 2009). Therefore, this research study was aimed at evaluating the effects of magnesium and copper sulphates on blood glucose level and some biochemical parameters in fructose-induced diabetic wistar rats.

MATERIALS AND METHODS

Drugs and Chemicals

All drugs and chemicals used were of analytical grades.

Animals

Twenty four (24) healthy albino Wistar rats of both sexes weighed between 150g-200g were purchased from the Department of Pharmacology and Therapeutics Animal House Ahmadu Bello University Zaria.

The animals were harboured in stainless steel cages under standard laboratory condition of 12 hours light /dark cycle and fed on commercial feed (grower mash) and drinking water ad libitum. They were acclimatized to laboratory environment for a period of two weeks before the commencement of the study.

Experimental induction of diabetes mellitus

D-Fructose (BDH, Poole, England) with a molecular weight of 180.16g was used for the study. Each rat, regardless of their weight was made diabetic by feeding them with 20% (20g/100ml) of fructose dissolved in distilled water for a period of six (6) weeks (Comte, et al, 2004).

Diabetes mellitus was confirmed by collecting fasting blood samples from the tail vein of the rats by using glucose oxidase method (Beach and Turner, 1958) using a digital glucometer (Accu-Chek Advantage, Roche Diagnostic, Germany). Rats having fasting blood glucose level greater than 130 mg/dl were considered as diabetic.

Experimental design

Group I: Served as diabetic control and received 1 ml/kg distilled water. Group II: Received Magnesium sulphate 250 mg/kg b w. Group III: Received Copper sulphate 250 mg/kg b w., Group IV: Received Metformin 250 mg/kg b w. All treatment were given orally for a period of seven days.

Serum samples preparation

After the last day of administration the animals were euthanized and blood samples were drawn from the heart of each by cardiac puncture into plain tubes and were allowed to clot and the serum separated by centrifugation using Denley BS400 centrifuge (England) at 3000 r p m for 15minutes and the serum collected and then subjected to biochemical assays.

Determination of blood glucose levels

Fasting blood samples were collected from the tail vein of the rats at intervals of 0, 1, 3, 5 and 7 days respectively. Blood glucose levels were determined by using glucose oxidase method (Beach and Turner, 1958) using a digital glucometer (Accu-Chek Advantage, Roche Diagnostic, Germany). Results were expressed in the unit of mg/dl (Rheney and Kirk).

Estimation serum electrolytes

Serum sodium and potassium ions were measured by the flame photometry method of Vogel (1960) and bicarbonate ion was determined using the titration method of Segal (1955), Chloride ion was analysed using the method of Schales and Schales (1941).

Statistical analysis

Data obtained were expressed as mean ± SEM. The data were analysed using one-way analysis of variance (ANOVA) and Turkey’s post hoc test was used to determine the level of significance between control and the experimental groups. The value of P<0.05 were considered significant.

RESULTS AND DISCUSSION

Results

Effect of magnesium and copper sulphates on blood glucose levels in fructose-induced diabetic wistar rats.

Table 1 shows the mean blood glucose values of control and experimental groups of magnesium and copper sulphate treated animals of fructose-induced diabetic rats. Data generated revealed that the blood glucose levels was not significantly different (p>0.05) in groups that received magnesium and copper sulphate 250mg/kg b w after 1day of treatment when compared to diabetic control group respectively. However, a statistically significantly decreased (p<0.05) blood glucose level was recorded in groups administered with 250mg/kg b w of magnesium and copper sulphate after day 3 and 7 when compared to diabetic control group.
Effect of magnesium and copper sulphates on serum electrolyte levels in fructose-induced diabetic Wistar rats

Table 2 shows the mean serum electrolytes values of control and experimental groups administered with magnesium and copper sulphates in fructose-induced diabetic wistar rats. Results obtained showed that magnesium and copper sulphates at dose concentration of 250mg/kg b w produced a significantly decreased (p<0.05) serum levels of sodium, potassium and biocarbonate ions in the treated groups when compared to diabetic control group. However, there was no statistical significant change (p>0.05) in the groups treated with 250mg/kg b w of magnesium and copper sulphates when compared to diabetic control group.

DISCUSSION

Diabetes is characterized by increased volume and metabolites excretions via the kidneys, usually in excess of normal thresholds. These usually give rise to derangements in homeostatic balance with respect to electrolytes (Item et al., 2009). It is however a known fact that kidney function is compromised in uncontrolled diabetes mellitus. Glycosuria, which is a pertinent diagnostic feature of diabetes, causes dehydration via glucose osmotic diuresis. This dehydration is accompanied with severe loss of electrolytes including sodium, potassium, calcium, chloride and phosphates (Eteng et al., 2008).

Magnesium is also a co-factor for a number of enzyme systems utilizing glucose oxidation as well as facilitating the transport of glucose through cellular membranes (Moordian 1994). These observations prompted investigators to review magnesium’s role in, for example, insulin sensitivity and metabolic control among individuals with type II diabetes. In a placebo-controlled study, 65 individuals with type II diabetes on glibenclamide (Glyburide®) were randomized to receive 2.5 grams of magnesium chloride or placebo daily for 16 weeks. After four months of therapy and in contrast to placebo, those utilizing the supplement had significantly lower homeostasis model assessment of insulin resistance (HOMA-IR) scores (3.8 vs 5), fasting glucose levels (8 vrs 10.3 mmol/L), and HbA1c scores (8 vs 10.1%) (Rodriguez-Moran, 2003). Micronutrients are vitamins and minerals that our bodies require in small quantities for specific functions. They most commonly function as essential coenzymes and cofactors for metabolic reactions and thus help support basic cellular reactions (i.e., glycolysis, the citric acid cycle, lipid and amino acid metabolism) required to maintain energy production. Magnesium supplementation has many in vivo and in vitro beneficial effects on insulin sensitivity, lipid profiles, platelet aggregation and blood pressure (Paolillo, 1997). The results obtained from the study showed the levels of serum electrolytes levels (Na+, K+, HCO3− and Cl−) there was a reduction in Na+ concentration after the administration of magnesium with control value of Na+ of 150.4±7.80mmol/L to 116.0±4.80mmol/L after administration of magnesium. Also K+ concentration decreased also in administration of magnesium from 4.2±0.14 in normal healthy control to 11.6±0.48 in magnesium subacute administration (P<0.05). The HCO3− concentration of magnesium in the diabetic rats was significantly reduced (P<0.05). This electrolytes imbalance might also occur due to inhibition of the rennin angiotensin aldosterone system, which plays a key role in the regulation of fluid and electrolyte balance.

CONCLUSION

The copper and magnesium sulphates show significant decrease in the serum level of HCO3−, Na+, K+. The copper and magnesium sulphates show significant decrease in the serum glucose level. It can be concluded that impaired trace-element metabolism may have a role in the pathogenesis and progression of type-2 diabetes mellitus. Electrolytes imbalance characterized with depletion in sodium and potassium ions accompanied with non significant change in chloride ion compared with diabetic control group.

REFERENCES


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