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Research Article

A STUDY OF SERUM MAGNESIUM LEVEL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

INTRODUCTION: Magnesium is present in higher concentration within the cell and it is the second most abundant cation next to potassium. It plays an important role in manipulating important biological pyrophosphate compounds. The disturbance in magnesium level i.e., hypomagnesemia has been reported to occur in diabetic patients. Although diabetes can induce hypomagnesemia, magnesium deficiency has also been proposed as a risk factor for diabetes. Animal studies have shown that magnesium deficiency has a negative effect on post receptor signalling of insulin. Some short term metabolic studies suggested that magnesium supplementation has a beneficial effect on insulin action and glucose metabolism. Persistent hypomagnesemia leads to raised glucose level, insulin resistance and the degree of magnesium depletion positively correlates with serum glucose concentration and degree of glycosuria. The cause of hypomagnesemia was attributed to (1).Osmotic renal loss from glycosuria, (2). Decreased intestinal absorption of magnesium. Recently a specific tubular magnesium defect in patients with diabetes has been postulated. Hypermagnesuria results specifically from reduction in tubular absorption of magnesium.

MATERIALS AND METHODS: This was a case control study conducted in 100 diabetic patients and 100 non- diabetic healthy controls who attended General Medicine OPD at Government Rajaji Hospital, Madurai during a period of 6 months (April 2014 to September 2014) .Patients aged between 30 to 70 years with positive history of diabetes were included in the study. Those patients with history of hypertension, gastrointestinal disorders, impaired renal function, alcoholic pancreatitis, therapy with diuretics, aminoglycosides, endocrine disorders, heart disease and those who were not willing to give consent were excluded from the study.100 diabetic patients and 100 non diabetic healthy controls in the age group of 31 to 70 years attending General Medicine OPD were included.A detailed history with detailed clinical examination was done. Blood samples were taken from each of the study groups and magnesium levels were assessed and compared between the case and control groups. Blood pressure was recorded. Cardiovascular disease was ruled out by history and ECG. Urine was examined for proteinuria.FBS valueswere assessed after 8 hours of fasting. PPBS values, Blood urea and serum creatinine values were measured. Serum magnesium was determined by using photometric method. Calmagite – a metallochromatic indicator when binds with magnesium in alkaline medium, it forms red colour complex and it is measured at 530 to 550 nm. To prevent interference by calcium, specific calcium chelating agent EDTA was added. To avoid the heavy metal complex formation, KCN was added. Polyvinylpyrrolidone and surfactant were also included to reduce the interference from lipemia and protein. Intensity of colour formed was directly proportional to the amount of magnesium present in the sample.

RESULTS: In the present study, the mean age group of cases and controls were 50.39 ± 9.76 and 50.01 ± 10.15 respectively. The minimum age was 31 years and maximum age was 70 years. Maximum number of patients were in the age group of 41 to 50 i.e., 42%.Out of 100 cases, 70% were males and 30% were females. The mean FBS level among cases and control were 102.42mg/dl and 91.93 mg/dl respectively. The mean PPBS level among cases and control were 187.02 mg/dl and 123.83 mg/dl respectively

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INTRODUCTION

Magnesium is present in higher concentration within the cell and it is the second most abundant cation next to potassium. It plays an important role in manipulating important biological pyrophosphate compounds. The disturbance in magnesium level i.e., hypomagnesemia has been reported to occur in diabetic patients.

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renal loss from glycosuria, (Rude and Singer, 1981). Decreased intestinal absorption of magnesium. Recently a specific tubular magnesium defect in patients with diabetes has been postulated. Hypermagnesuria results specifically from reduction in tubular absorption of magnesium.

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RESULTS

In the present study, the mean age group of cases and controls were 50.39 ± 9.76 and 50.01 ± 10.15 respectively. The minimum age was 31 years and maximum age was 70 years. Maximum number of patients were in the age group of 41 to 50 i.e., 42%.Out of 100 cases, 70% were males and 30% were females. The mean FBS level among cases and control were 102.42mg/dl and 91.93 mg/dl respectively.

Table 1. Comparison of Serum Magnesium Level Between Cases And Controls

Serum magnesium	Mean	Sd	'p' value
Cases	1.29	0.42	
Controls	1.96	0.25	<0.001

Table 2. Comparison Of Serum Magnesium Level Between Controlled And Uncontrolled Diabetes

Hba1c	Cases	Serum magnesium level(< 1.3 meq/l)	'p' value
< 7	61	25	
≥ 7	39	39	0.01

The mean PPBS level among cases and control were 187.02 mg/dl and 123.83 mg/dl respectively. There was significant difference (<0.001) between levels of serum magnesium levels among cases and controls based on student T test. The mean serum magnesium level in cases and controls were 1.29 mEq/L and 1.96 mEq/L respectively. Out of 61 cases with controlled diabetes, 25 cases had low serum magnesium level. Out of 39 cases with uncontrolled diabetics, 39 cases had low serum magnesium level. Based on chi-square test, serum magnesium was significantly (p=0.01) lower in uncontrolled than that of controlled diabetics.

DICUSSION

Magnesium is a trace element needed for the body.Ninety nine percent of total body magnesium is present in muscles, bone and non muscular soft tissues 1. Fifty to sixty percent of magnesium resides as the hydroxyapatite mineral component of bone.One-third of skeletal magnesium is exchangeable and serves as the reservoir to maintain physiological extracellular magnesium. Intracellular magnesium concentrations range from 5 to 20mmol/L, of which 1 to 5 percent is in ionised form and the remainder is bound to proteins, adenosine triphosphate (ATP) and negatively charged molecules.

Extra cellular magnesium is about 1% of total body magnesium and it is found mainly in serum and red blood cells (RBCs).Extra cellular magnesium exist in three fractions – ionised/free, protein bound and complexed with anions like phosphate, bicarbonate and sulphate or citrate 2. Out of these three fractions, ionised magnesium has the greatest biological activity. Magnesium acts as a cofactor in more than 300 enzyme regulated reactions, particularly reactions forming and using ATP. There is a direct effect on sodium (Na+), potassium (K+) and calcium (Ca2+) channels. Magnesium acts as an essential cofactor for enzymes concerned with cell respiration and glycolysis. Activity of Sodium-Potassium ATP-asedepends on magnesium.

Magnesium can affect enzyme activity by binding in the active site and causing conformational changes during catalytic process and also by promoting aggregation of multi enzyme complexes. Magnesium also affects permeability characteristics and electrical properties of cell membrane. Reduced extracellular magnesium concentration increases membrane excitability in tissues. Magnesium also acts to maintain a low resting concentration of intracellular calcium. Magnesium competes with calcium for membrane binding sites and stimulates calcium sequestration by sarcoplasmicreticulum. ATP metabolism, normal neurological function, muscle contraction and relaxation and release of neurotransmitters are magnesium dependent. Magnesium also regulates vascular tone, bone formation and heart rhythm. Magnesium has a role in insulin secretion. Magnesium is considered as a natural 'calcium antagonist '. Magnesium inhibits calcium induced cell death and antagonizes calcium overload triggered apoptosis. Humans have to consume magnesium regularly to prevent its deficiency. Recommendations in literature suggests lower daily minimum magnesium intake of 350mg for men, 280 to 300mg for women, 355mg during pregnancy and lactation.It is present in green leafy vegetables, chlorophyll, cocoa derivatives, nuts, wheat, seafood and meat. Legumes, fish and fruits have intermediate magnesium concentration.

Dairy products have low magnesium concentrations. Magnesium is absorbed in the small intestine and gets stored in the bone and excess of it gets excreted in urine and faeces.Serum magnesium is measured by various techniques like titration, precipitation, photometry, fluorometry and flame emission spectroscopy. Today most commonly used technique in many laboratories is photometric method 3. Reference interval for serum magnesium is 0.70 to 0.99 mmol/L (1.3 to 2.5 mEq/L). Hypomagnesemia is common in ICU settings, diabetics, ondiuretics, etc.

In presence of hypomagnesemia, renal excretion of magnesium is decreased. Hypomagnesemia also occurs in gastrointestinal and renal losses. It is often associated with hypokalemia, hypocalcemia and metabolic acidosis.clinicalfeatures include weakness, tremors, positivetrousseau's sign and chvostekssign, seizures, arrhythmias, prolonged QT. Treatment is by Mg supplementation. Magnesium ion has an important fundamental role in metabolism of carbohydrate and particularly in the action of insulin 4. Magnesium acts as a cofactor of various enzymes involved in carbohydrate oxidation. Magnesium is involved in multiple steps in insulin secretion, insulin binding and activity. It is a cofactor for adenylatecyclase and ATPase. Recently it has been proposed that magnesium plays a novel factor in pathogenesis of complications in diabetes. Relation between magnesium and carbohydrate intolerance, insulin resistance, accelerated atherosclerosis, hypertension, dyslipidemia has been observed.It is important to recognize the symptoms and signs of diabetes associated magnesium deficiency because its deficiency occurs long before its reflection in serum values. It has been suggested that there is prevalence of 25 to 39% of magnesium deficiency associated with diabetes mellitus. Hypomagnesemia in diabetes indicates secondary magnesium deficiency. Mechanism for magnesium deficiency in diabetes mellitus is not exactly known.

It has been proposed that osmotic diuresis is responsible for magnesium loss. Glycosuria, which accompanies thediabetic state, impairs the magnesium reabsorption from renal tubules. Magnesium is principally reabsorbed in proximal tubule (30%), ascending loop of Henle (65%) with minimal (1 to 5%) reabsorption in distal convoluted tubule. Glucose is a crucial part in maintaining cellular ion homeostasis, increasing intracellular calcium level and decreasing intracellular magnesium level. Influence of magnesium on ATPaseactivity in cell membrane and consequently on sodium, potassium and calcium metabolism play a role in diabetic complications. Sodium potassium ATPase which is necessary to maintain intracellular potassium is a magnesium dependent enzyme. Impaired enzymatic activity plays a role in pathogenesis of diabetic polyneuropathy.

Possible causes of hypomagnesemia in diabetes

- Reduced renal reabsorption
- Enhanced filtered load
- Enhanced gastrointestinal loss
- Decreased intake

Diabetes is a state of increased free radical activity5 . It is associated with increased prevalence of atherosclerotic disease and cardiovascular morbidity and mortality.Magnesium acts as a cofactor for enzymatic reaction of glutathione synthesis.Magnesium has some relationship with pathogenesis of atherosclerosis and hypertension and diabetes. Several studies have shown that there is magnesium deficiency in hypertensive animals and there is inverse relationship between diastolic blood pressure and intracellular magnesium ion. Magnesium deficiency is also associated with hyperlipidemia 6. Thus Magnesium deficiency in diabetes gains importance as it increases the complications of diabetes and other associated systemic illnesses.

Conclusion

- Serum magnesium levels were lower in type 2 diabetes patients when compared to healthy non-diabetic controls.
- Levels of serum magnesium in uncontrolled type 2 diabetes were further lower when compared to controlled diabetic patients.

Hypomagnesemia is one of the factors in type 2 diabetes which leads to various complications. Hence it is worthwhile to estimate serum magnesium level in type 2 diabetic patients and hypomagnesemia should be corrected to prevent insulin resistance and for better glycemic control.

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