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A cross sectional study of fasting serum magnesium in patients with type-2 diabetes mellitus

Bandana Singh[1], Hemant Kumar Sharma[2], Ila Pahwa[3*]
[1] Junior Resident, Department of Medicine, Muzaffarnagar Medical College Muzaffarnagar, Uttar Pradesh, India
[2] Professor, Department of Medicine, Muzaffarnagar Medical College Muzaffarnagar, Uttar Pradesh, India
[3] Professor and Head, Department of Medicine, Muzaffarnagar Medical College Muzaffarnagar, Uttar Pradesh, India

Abstract
Aim: To evaluate fasting serum magnesium in patients with Type-2 diabetes mellitus.
Material and Method: This cross-sectional study consisted of patients with type 2 diabetes (n=200) visiting out-patient and in-patient department of medicine at Muzaffarnagar Medical College and Hospital, Muzaffarnagar. A detailed history was taken and clinical examination was done in all patients. Blood investigations and urine examination was carried out. All patients with type 2 diabetes mellitus who meet the inclusion criteria were evaluated, detailed history including age, gender, duration of diabetes, mode of diabetic treatment, duration of diabetes, symptoms suggestive of diabetic retinopathy, diabetic nephropathy and ischemic heart disease and current use of medication, including anti diabetic drugs and antihypertensive drugs, was obtained by a standard interview questionnaire. Clinically, hypomagnesemia may be defined as a serum magnesium level <1.5mg/dl. Magnesium levels were measured by photometric methods.
Results: Patients with diabetes of more than 10 years duration had significantly lower serum magnesium levels. Non-proliferative and proliferative diabetic retinopathy was significantly seen in patients with low serum magnesium. Median nerve sensory conduction velocity correlated significantly with serum magnesium.
Conclusion: The results of the present study suggest that, and inverse relationship exists between serum magnesium and poor glycemic control, albuminuria, retinopathy and risk of coronary artery disease, respectively.

Keywords: diabetes, hypomagnesemia, retinopathy, neuropathy

Introduction

Diabetes is a group of metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels [1].

Magnesium is the second most abundant intercellular cation after potassium present in living cells. Of the 21-28 gram of magnesium present in adult human body, 99% is distributed in the intercellular compartment, and only 1% in the extracellular fluid. Serum concentration of magnesium ranges from 1.9to 2.6mg/dl [2]. The plasma concentration in healthy adults remains remarkably constant, whereas 25-39% of diabetics have low concentrations of serum magnesium [3, 5]. Studies have reported incidence rate of hypomagnesemia of around 13.5%-47.7% in diabetic subjects [6].

Low magnesium status has repeatedly been demonstrated in patients with type 2 diabetes, which appear to have a negative impact on glucose homeostasis and insulin sensitivity in patient with type 2 diabetes as well as on the evaluation of complications such as retinopathy, nephropathy, neuropathy, hypertension and ischemic heart disease [7, 9].

The present study is undertaken with an aim to estimate prevalence of hypomagnesemia in patients with type 2 diabetes mellitus and to correlate the serum magnesium concentrations with complications of diabetes i.e. retinopathy, nephropathy, neuropathy and ischemic heart disease as the prevalence of diabetes is more in India.

Materials and Methods

This cross-sectional study consisted of patients with type 2 diabetes (n=200) visiting out-patient and in-patient department of medicine at Muzaffarnagar Medical College and Hospital, Muzaffarnagar. Patients profile were collected in details including their age, gender, duration of diabetes, mode of diabetic treatment, glycemic control, presence or absence of comorbidities (ischemic heart disease and hypertension) and presence or absence of diabetic complications (diabetic retinopathy, diabetic neuropathy and diabetic nephropathy). A detailed history was taken and clinical examination was done in all patients. Blood investigations and urine examination was carried out.

Inclusion criteria: All diagnosed cases of type 2 diabetes mellitus as per ADA criteria.

Exclusion Criteria: Patients with chronic renal failure, Acute myocardial infarction in last 6 months, Patients on medicines which cause alteration in serum magnesium level e.g. Aminoglycosides, Amphotericin B, Cyclosporine, Digoxin, Diuretics (loop, thiazides, osmotic), Patients receiving magnesium supplements or magnesium containing antacids and pregnant women.

Methodology: All patients with type 2 diabetes mellitus who meet the inclusion criteria were evaluated, detailed history including age, gender, duration of diabetes, mode of diabetic treatment, duration of diabetes, symptoms suggestive of diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, associated disease such as hypertension and ischemic heart disease and current use of medication,

including anti diabetic drugs and antihypertensive drugs, was obtained by a standard interview questionnaire, followed by

a. Physical and neurological examination
b. Twelve lead electrocardiography
c. Detailed fundus examination of both eyes done by direct ophthalmoscopy examination to confirm diabetic retinopathy.
d. Monofilament testing or Nerve conduction study done to confirm the presence of diabetic neuropathy

Hypomagnesemia

Clinically, hypomagnesemia may be defined as a serum magnesium level <1.5mg/dl. Magnesium levels were measured by photometric methods. Plasma magnesium was graded as follows:

Diabetic Retinopathy was diagnosed if it was documented by either the ophthalmologist or the treating physician in the medical records, or if the patient had received laser treatment. Patients with diabetic retinopathy were further classified as those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative diabetic retinopathy (PDR).

Diabetic Neuropathy was diagnosed if there was any of the following symptoms (numbness, tingling or pain in toes, feet, legs, hands, arm and fingers) in the patient's records or if the patient had done Nerve conduction Study (NCS) which proves the presence of diabetic neuropathy or if the patient was receiving treatment for the above condition and was confirmed by monofilament testing or Nerve Conduction Study (NCS).

Statistical methods

Statistical analysis was performed using IBM, SPSS Statistics version 25 (IBM Corp., New York, NY). Descriptive data was expressed as mean ± standard deviation unless otherwise stated. Chi-square tests were used for proportions. Continuous variables were compared with t- test. A P value less than 0.05 was considered statistically significant. A correlation analysis was performed to study the relationship between serum magnesium (dependent variable) and independent variables like HbA1c (marker of diabetic control), serum homocysteine (marker for risk of cardiac disease), urine albumin (marker for diabetic nephropathy), and nerve conduction velocity (marker od diabetic peripheral neuropathy).

Results

The mean age of patients was 51.9±10.9 (range, 32-80 years). There were 116(58%) males and 84(42%) females respectively. Patients with diabetes of more than 10 years duration had significantly lower serum magnesium levels (Chi-square tests, P<0.001) as shown in table 1.

Non-proliferative and proliferative diabetic retinopathy was significantly seen in patients with low serum magnesium (Chi-square tests, P<0.001) as shown in table 2.

Median nerve sensory conduction velocity correlated (Graph 1) significantly with serum magnesium (Pearson's correlation coefficient, r=0.461, P<0.001).

Table 1: Prevalence of hypomagnesemia according to duration of diabetes, diabetic retinopathy and ischemic heart disease patients

Duration of Diabetes (years)	N	%
Less than 5	106	53%
6-10	62	31%
11-15	22	11%
More than 15.1	10	5%
Retinopathy		
No Retinopathy	157	78.5%
NPDR	35	17.5%
PDR	8	4%
Ischemic Heart Disease		
Present	44	22%%
Absent	156	78%
Total	200	100%

Table 2: Association of Serum Magnesium with type of retinopathy and duration of diabetes

Serum Magnesium (mg/dl)	Type of Retinopathy			Total
	No retinopathy	NPDR	PDR	
Less than 1.89	26	18	8	52
1.9-2.6	127	17	0	144
More than 2.6	4	0	0	4
Total	157	35	8	200
Serum Magnesium (mg/dl)	Duration of Diabetes			Total
	Less than 10	10.1-15	More than 15.1	
Less than 1.89	3	12	37	52
1.9-2.6	132	8	4	144
More than 2.6	4	0	0	4
Total	139	20	41	200

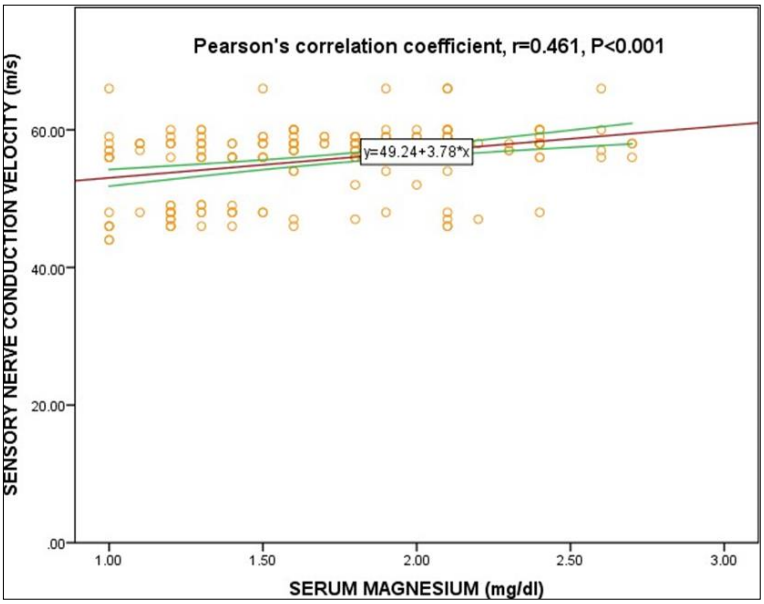

Fig 1: Correlation between sensory nerve conduction velocity and serum magnesium. The correlation was statistically significant (P<0.001).

Discussion

The prevalence of hypomagnesemia in the present study was 55%. There occurs a wide variability in prevalence of hypomagnesemia ranging from 14 to 48% across studies worldwide in patients with type 2 diabetes. This wide range in prevalence could probably be due to differences in study population, differences in technique to measure serum magnesium levels and the criteria of defining serum levels of magnesium [10, 12]. It is now widely accepted that intracellular magnesium facilitates the action of insulin by increasing glucose uptake and maintaining vascular tone. Hypomagnesemia impairs activity of the enzyme tyrosine-kinase and leads to resistance to the actions of insulin on insulin receptors [13, 14].

Diabetic retinopathy is one of the leading causes of blindness in the world. Hypomagnesemia has been reported to occur at an increased frequency among patients with type 2 diabetes compared to non-diabetes. In the present study, we found that serum magnesium was significantly lower (Chi-square tests, P<0.001) in patients with retinopathy (non-proliferative and proliferative) as compared to those without retinopathy. In a case control study, Kundu *et al* found that serum magnesium was significantly lower in patients with and without retinopathy in comparison to controls. Moreover, serum magnesium correlated significantly and inversely with HbA1c (Pearson's correlation coefficient, r= -0.480). We found more stronger association between the two variables (r=-0.791). The authors suggested that hypomagnesemia alone or in conjunction with albuminuria an indicator for impaired glucose tolerance and may be considered as marker for the risk of diabetic retinopathy [15].

Lu *et al* found that patients with albuminuria and/or retinopathy had lower levels of serum magnesium than patients without diabetes complications (P < 0.001). The prevalence of albuminuria, retinopathy, and combined albuminuria+retinopathy decreased as the concentration of serum magnesium increased. On multiple logistic regression, the odds ratio for albuminuria, retinopathy, and concomitant albuminuria and retinopathy decreased by 20% for every 0.1 mmol/L increase in serum magnesium concentration. Serum magnesium levels were negatively associated with the risk of diabetic microvascular complications. A similar observation was observed in our study on correlation analysis [16].

Chu *et al* revealed that the serum magnesium levels were significantly lower in patients with abnormal conduction velocity than in those with normal conduction velocity (0.87 [0.82, 0.92] vs. 0.88 [0.83, 0.93] mmol/L, P = 0.048). After adjusting for all potential confounders, hypomagnesemia was associated with lower composite z score of amplitude (β = 0.095, P = 0.014). The authors concluded that lower serum magnesium might affect peripheral nerve function through axonal degeneration [17].

Zhang *et al* reported that serum magnesium levels were significantly lower (P<0.01) in patients with diabetic peripheral neuropathy. In the present study, serum magnesium correlated significantly with nerve conduction velocity (r=0.461, P<0,001) [18].

Liao *et al* findings suggest that low magnesium concentration may contribute to the pathogenesis of coronary artery disease. In the present study, there was a significant and inverse correlation (r= -0.455, P<0.001) between hypomagnesemia and elevated homocysteine levels indicating increased risk of coronary artery disease [19].

The limitation of the present study was the absence of a control group to compare results. There was no blinding and follow up of patients in the study. Clinical trials with large sample size are needed to determine whether the correction of Mg deficiency could be effective to reduce the incidence of micro and macro-vascular complications of diabetes.

Conclusion

The results of the present study suggest that, and inverse relationship exists between serum magnesium and poor glycemic control, albuminuria, retinopathy and risk of coronary artery disease, respectively. A direct correlation occurs between serum magnesium and sensory nerve conduction velocity. As available data suggest that adverse outcomes are associated with hypomagnesemia in diabetics, it is prudent that routine surveillance for hypomagnesemia be done and the condition be treated whenever possible.

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