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Research Article

Preliminary study of serum magnesium in diabetes mellitus

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ABSTRACT

Background: Diabetes mellitus is not a single disease entity but rather a group of metabolic disorders sharing the common underlying feature of hyperglycemia. Hyperglycemia in diabetes results from defects in insulin secretion, insulin action, or, most commonly, both. Magnesium (Mg) is one of the most abundant ions present in living cells and its plasma concentration is remarkably constant in healthy subjects. Plasma and intracellular Mg concentrations are tightly regulated by several factors. Among them, insulin seems to be one of the most important. A poor intracellular Mg concentration, as found in noninsulin-dependent diabetes mellitus (NIDDM), may result in a defective tyrosine-kinase activity at the insulin receptor level and exaggerated intracellular calcium concentration. Both events are responsible for the impairment in insulin action and a worsening of insulin resistance in noninsulin-dependent diabetic.
Methods: This study was undertaken to evaluate role of serum magnesium in type 2 diabetes mellitus.
Results: In this cross sectional study Parameters analysed were serum magnesium and calcium in 2 groups, one: Normal healthy age matched controls not suffering from diabetes mellitus (n=50) and other: Patients of Type 2 diabetes mellitus with or without complications (n=50). Biochemical data analysed using Unpaired Students t test. Results demonstrated that serum magnesium levels were lower in type 2 diabetic patients when compared to controls.
Conclusions: Magnesium and calcium deficiency may have profound ill effects on human health and should be supplemented to prevent complications.

Keywords: Type2 diabetes mellitus, Magnesium, Calcium

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.[1] The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.

Diabetes is one of the most challenging health problems of the 21st century.[2] Type 2 DM is a significant cause of premature mortality and morbidity related to cardiovascular disease, macrovascular complications, and microvascular complications in older adults.[3-5] The global prevalence of diabetes mellitus is expected to increase from 4% in 1995 to 5.4% by the year 2025.[6] According to the International Diabetes Federation (IDF), prevalence of diabetes in India is expected to increase from 61.3 million people in 2011 to 101.2 million by

2030. IDF data reveals that India has more diabetics than the United States and ranks second in the world in diabetes prevalence, just behind China.[7] Diabetes is a major cause of mortality, but several studies indicate that diabetes is likely underreported as a cause of death. A recent estimate suggested that diabetes was the fifth leading cause of death worldwide and was responsible for almost 4 million deaths in 2010 (6.8% of deaths were attributed to diabetes worldwide).[1]

Several vitamins and minerals act as coenzymes and cofactors in the enzyme reactions which are regulated by insulin. Deficiencies of certain vitamins and minerals such as vitamin E, potassium, magnesium, zinc and chromium may aggravate carbohydrate intolerance.[8,9]

Magnesium (Mg) has wide spread distribution being particularly concentrated in the bone, muscle and heart. It is a cofactor for over 300 enzymes particularly those concerned with ATP production.[10] Magnesium is also required for normal DNA function, cell permeability regulation and neuromuscular excitability. Magnesium is necessary for both the release and function of the parathyroid hormone and formation of 25-OH D3. Hypomagnesemia occurs frequently in diabetic patients, especially those with poor glycemic control.[11] Magnesium is a necessary cofactor for several enzymes that play an important role in glucose metabolism. Animal studies have shown that magnesium deficiency has a negative effect on the post-receptor signaling of insulin. Magnesium is involved in insulin secretion, binding and activity. Cellular magnesium deficiency can alter the membrane bound sodium-potassium-adenosine triphosphatase which is involved in the maintenance of gradients of sodium and potassium and in glucose transport.[12]

In diabetics there is a direct relationship between serum magnesium level and cellular glucose disposal that is independent of insulin secretion. This change in glucose disposal has been shown to be related to increased sensitivity of the tissues to insulin in the presence of adequate magnesium levels.[13] Increased magnesium intake may improve insulin secretion and action,[14,15] dyslipidaemia,[16,17] and endothelial dysfunction,[18] and decrease thrombotic tendency[19] and vascular contractility.[14,19,20]. Hypomagnesemia has been related as a cause of insulin resistance, also being a consequence of hyperglycemia, and when it is chronic leads to the installation of macro and microvascular complications of diabetes, worsening the deficiency of Mg.[11,21]

In elderly type 2 diabetics, Paolisso et al demonstrated that oral magnesium supplements given for 4 weeks resulted in lower fasting plasma glucose levels, increased plasma and erythrocyte magnesium levels and a slight but statistically significant increase in B-cell response to glucose and arginine.[22]

Hypomagnesemia in diabetes is usually observed in patients with deficient metabolic control, or associated to the DM chronic complications, according to Tosiello L et al, Ma J, Folsonm AR et al clinical and epidemiological studies.[11,23] Although diabetes can induce hypomagnesemia, magnesium deficiency has also been proposed as a risk factor for type 2 diabetes.[9]

Clinically, hypomagnesemia may be defined as a serum Mg concentration $\leq$ 1.6 mg/dl or $\geq$ 2 SD below the mean of the general population.[24,25] However, because Mg is mostly an intracellular cation, it has been questioned whether one can use measurements of serum Mg concentrations to study the impact of Mg on various physiologic conditions. Some investigators, instead, have used measurements of intracellular Mg concentrations. Clinically, it has been suggested that in a patient with suspected Mg deficiency, a low serum Mg concentration is sufficient to confirm the diagnosis.[26]

Despite the growing realization of the importance of magnesium in human health and disease, measurement of magnesium status remains problematic. Serum magnesium concentrations can be normal despite depletion of intracellular magnesium (Resnick et al., 1993).[27]

METHODS

The study was conducted at the Department of Biochemistry, in a tertiary care centre hospital, after being approved by the Institutional Ethics committee.

An informed consent was signed by all the participating cases and controls. 50 age matched healthy controls and 50 diagnosed cases of type 2 diabetes mellitus were considered for the study.

Inclusion criteria:

Normal healthy age matched subjects (For group A).

Type 2 diabetes mellitus patients with or without any complications (For group B).

Exclusion criteria:

Pregnant and lactating women.

Individuals on calcium and magnesium supplementations.

Individuals having any past medical history of various vascular complications before the diagnosis of diabetes mellitus such as ischemic heart disease, cerebral and peripheral vascular diseases, congestive heart failure and renal failure.

2ml of blood sample was collected by venipuncture, with all aseptic precautions in plain vacutainer. Blood was allowed to clot. Serum was separated by centrifuging at 3000 rpm for 10 min. Immediate analysis was carried out for following parameters.

Parameter	Method
Serum magnesium	Calmagite-EGTA.Colorimetric
Serum calcium	O-cresophthalein complexone method

Comparison was done for the above parameters between the 2 groups.

Statistical analysis:

For each parameter studied, mean and standard deviation was calculated to estimate the significance. The difference between the groups was measured by Unpaired Students t test. P Value less than 0.05 considered as statistically significant. The calculations were performed using the statistical program SPSS for Windows Version 13, with a p value of < 0.05 considered significant.

RESULTS

Table 1: Age distribution.

Age in Years	Group A		Group B	
	Number	%	Number	%
41-50	15	30	41-50	15
51-60	25	50	51-60	25
61-70	06	12	61-70	06
>70	04	08	>70	04
Total	50	100	50	100
Mean ± SD	54.22 ± 9.63		54.96 ± 7.28	

As evident from table 1, the mean age of the subjects in group A was 54.22 ± 9.63 years, group B was 54.96 ± 7.28 years. The maximum numbers of subjects were in the age group of 51-60 i.e.50-60 %.

Table 2: Sex distribution.

Sex	Group A		Group B	
	Number	%	Number	%
Male	31	62	30	60
Female	19	38	20	40
Total	50	100	50	100

Table 2 highlights the sex distribution of the study groups. In our study, 60 – 70 % were males (group A - 62%, group B - 60%) and 30-40 % were females (group A - 38%, group B - 40%).

Table 3 highlights comparison of serum magnesium and calcium in Group A and Group B. As seen from this table there is statistically highly significant difference in serum magnesium in both groups ($p<0.05$). Mean serum magnesium in control group was 2.06 ± 0.16 mg/dl while in group B of type 2 diabetics was lower when compared to controls i.e., 1.92 ± 0.22 mg/dl but within normal range (1.7-2.4 mg/dl).

- Results are expressed as mean ± SD (Standard Deviation)
- Group A: Normal healthy controls not suffering from diabetes mellitus.
- Group B: Patients of Type 2 diabetes mellitus
- S – Statistically Significant, HS – Statistically Highly Significant, NS – Statistically Not Significant.

Table 3: Comparison of serum magnesium and calcium in Group A and Group B.

Parameters (mg/dl)	Group A	Group B	P value	Statistical Significance
Serum Magnesium	2.06 ± 0.16	1.92 ± 0.22	0.0004	HS
Serum Calcium	9.14 ± 0.34	9.06 ± 0.37	0.263	NS

DISCUSSION

Our study revealed that the mean serum magnesium in group B of type 2 diabetics (1.92 ± 0.22 mg/dl) was lower when compared to control group (2.06 ± 0.16 mg/dl) but within normal range (1.7-2.4 mg/dl).These results are in accordance with the study by Nazar S. Haddad, Salah Zuhair et al on serum magnesium and severity of diabetic retinopathy published in the medical journal of Basrah university showing that Diabetic patients had lower mean plasma magnesium concentration than non-diabetic control subject[28] also it is evident from the table that the trend for serum calcium showed no statistically significant change. Normal serum calcium being 8.4-10.4 mg/dl.

However our results are not in accordance with Ma J, Folsom AR, Melnick SL who showed that hypomagnesemia is a common feature in patients with type 2 diabetes.[23]

The reasons for Mg deficiency in diabetes are not clear, but they may include lower dietary intake of Mg, lower intestinal Mg absorption, increased losses of urinary Mg (along with glucosuria) or decreased Mg uptake into the cells compared to healthy individuals. It has been suggested that low dietary intake may contribute to low Mg status in diabetics (Durlach & Rayssiguier, 1983; Sheehan, 1991; White & Campbell, 1993).[29,30]

Several authors have suggested that impaired intestinal absorption might contribute to low Mg status in diabetics (Durlach & Rayssiguier, 1983; Nadler et al., 1993; Tosiello, 1996).[11,31]

Lower serum magnesium concentration is a consistent finding in diabetics and thus maintenance of serum magnesium levels in such patients can help to reduce the morbidity, duration, severity and complications in diabetics.

CONCLUSION

From the above study, following conclusions could be drawn.

1. Serum magnesium levels were lower in type 2 diabetic patients when compared to controls. Since 99 % of total body Mg is intracellular, determination of intracellular Mg might be a better indicator of Mg status. Because erythrocytes are easily accessible, measurement of erythrocyte Mg has been proposed for the estimation of intracellular Mg.
2. For these patients' magnesium supplementation is recommended to avoid risk of diabetes mellitus and its complications.

Limitations of our study:

a) Small sample size.
b) Intracellular magnesium was not estimated.
c) Atomic absorption spectrometry, a greater precise and accurate method for magnesium measurements could be used instead of photometric methods.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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