

Hypomagnesemia in Patients with Type 2 Diabetes

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ABSTRACT

Background: Decreased magnesium levels are found with increasing frequency among patients with type 2 diabetes mellitus as compared with their counterparts without diabetes. There are several studies which show a link between type 2 diabetes and decreased magnesium levels. Awareness of this seems to be very poor among physicians. This article reviews the literature, incidence of hypomagnesemia in patients with type 2 diabetes, implicated contributing factors.

Aim: To assess the frequency of hypomagnesemia among patients of Type 2 diabetes mellitus and to see the relationship between decreased magnesium levels and various diabetic complications.

Methods: One hundred type 2 diabetes mellitus patients, who reported to out patient department of Gujranwala Medical College Gujranwala with uncontrolled hyperglycemia and/or various diabetic complications were studied. Serum magnesium was assessed at admission and rechecked in those found to be deficient.

Results: Hypomagnesemia (Se magnesium <1.6mg/dl) was documented in 22(22%) with diabetes mellitus. Mean HbA1c was 10.5% in the hypomagnesemic patients compared with 9.5% in controls ($P = 0.0016$). Nephropathy, retinopathy, neuropathy and foot ulcers were present in 42.2%, 61.5%, 56.5% and 18.5% respectively, of the patients with hypomagnesemia as compared with 33.6% ($P = 0.118$), 40.5% ($P = 0.704$), ($P = 0.566$), 46.5% ($P = 0.011$) and 10.5% ($P = 0.976$) without hypomagnesemia. Coronary artery disease was less common in the hypomagnesemia group (18.6% vs 38%)

Conclusion: Hypomagnesemia in diabetes was associated with poorer glycemic control, retinopathy, nephropathy, and foot ulcers.

Keywords: Diabetic complications, glycemic control, hypomagnesemia, type 2 diabetes

INTRODUCTION

Type 2 diabetes is responsible for 90 to 95% total cases of diabetes¹. With its associated complications, diabetes is 6th cause of death recorded on death certificates (of USA in 2000¹. In particular, although hypomagnesemia has been reported to occur with increased frequency among patients with type 2 diabetes, it is frequently overlooked and under treated. Magnesium is the fourth most important, vital and abundant cation in the human body and the second most abundant intracellular cation. It is an important enzyme activator involved in several vital functions of human body like neuromuscular excitability, cell permeability, cell proliferation and apoptosis etc. There are several other key roles of magnesium in different cell processes which are still unclear and need intensive research.

Several researches have shown that magnesium levels are low in diabetics as compare to non diabetics^{2,3,4,5,6,7}. The study was conducted to see magnesium levels in diabetic patients and its relationship with glycemic control and different complications of diabetes in diabetic patients of Gujranwala.

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MATERIALS AND METHOD

This was a cross sectional study conducted over 6 months from December 2013 to June 2014. One hundred patients of type 2 diabetes mellitus (63 male and 37 female) coming to out patient department for glycemic control or various complications belonging to all age groups in Gujranwala DHQ hospital were included in the study. The reference range of magnesium was taken between 1.6 and 2.2 mg/dl. The patients with hypomagnesemia were taken as cases and the patients with normal magnesium levels were taken as controls. Patients on drugs known to affect magnesium levels, (aminoglycosides, amphotericin, cyclosporin, digoxin and diuretics etc) with a Se creatinine >1.5mg/dl, with acute or chronic diarrheal/ malabsorption states, with thyroid or adrenal dysfunction, h/o alcohol intake, h/o vitamin or mineral supplements in the recent past, recent metabolic acidosis, pregnancy, lactation, or sepsis were excluded from the study.

SPSS 19 (IBM) was used for analysis of data. All parametric variables were expressed as mean +/- SD. The comparison between groups was made by unpaired *t*-test and *P* values < 0.05 were considered significant.

RESULT

Twenty two out of 100 subjects (22%) had hypomagnesemia (Se magnesium <1.6mg/dl) where as 78(78%) were found to have normal levels of magnesium. The mean duration of diabetes in the patients with hypomagnesemia was 8.4years. All the patients assessed came to out patient department DHQ Hospital Gujranwala. The various causes for presentation were, uncontrolled blood sugar levels, numbness of feet, pain in feet, decreased vision, and feet ulcers respectively. Patients with hypomagnesemia were found to have blood sugar level of 350+-90.55mg/dl whereas patients with normal magnesium levels were having blood sugar level of 280+-88.22mg/dl. Out of 100 patients 10 presented with decreased vision, which were confirmed to have varying grades of diabetic retinopathy confirmed by direct and indirect ophthalmoscopy. 4(40%) were having normal magnesium levels. 6(60%) were having low magnesium levels. 5 presented with pain in feet, which was ischemic in nature confirmed by feeble pulses and other signs of limb ischemia. out of these 5 two (40%) were having normal magnesium levels. Three (60%) out of five were having low magnesium levels. Four patients out of 100 presented with various grades of feet ulcer. One out of 4 (25%) was having normal magnesium levels. While 3(75%) out of 4 were having low magnesium levels. Seven out of 100 patients presented with numbness of feet and peripheral neuropathy. 5(71.42%) were having low magnesium levels. Whereas 2 (28.57%) were having normal magnesium. 74% patients presented for control of high blood sugar levels. 53(71.62%)out of these were having blood sugar levels of 350+-90.55mg/dl. While 21(28.37%) were having normal magnesium.

DISCUSSION

The most common endocrine and metabolic disorder in our country is diabetes mellitus^{9,10}. Many studies have proven that magnesium levels are lower in patients of diabetes as compared to healthy non diabetic subjects There are several causes of decreased magnesium including diet low in magnesium¹¹ mainly decreased use of whole grains and more use of meat and meat products, osmotic diuresis of magnesium resulting in increased magnesium excretion hence, causing loss of extracellular magnesium¹² and due to insulin resistance decreased tubular reabsorption of

magnesium¹³. In the present study hypomagnesemia was found in 22% of diabetics. Studies have reported incidence rates of low magnesium in 13.5-47.7% in diabetic subjects.

Intracellular magnesium plays a vital role in insulin mediated glucose uptake. Decreased magnesium levels lead to insulin resistance, defective tyrosine kinase activity which in turn leads to post receptorial defect in insulin actions. Intracellular magnesium is an important cofactor which is somehow or other involved in glucose transport and glucose oxidation and insulin release¹⁴. Chronic magnesium deficiency has also been associated with elevated concentrations of TNF-alpha, and this may also contribute to postreceptor insulin resistance¹⁵.

We found statistically poorer glycemic control in the hypomagnesemia patients as compared with the normomagnesemia patients. Meta-analysis of 13 prospective cohort studies involving 536,318 participants and 24,516 cases detected a significant inverse association between magnesium intake and risk of type 2 diabetes (relative risk [RR] 0.78 [95% CI 0.73–0.84]). This association was not substantially modified by geographic region, follow-up length, sex, or family history of type 2 diabetes. This meta-analysis provides further evidence supporting that magnesium intake is significantly inversely associated with risk of type 2 diabetes in a dose-response manner¹⁶. In our study 60% patients with diabetic retinopathy were having low magnesium levels as compared to 40% patients of retinopathy with normal magnesium levels. Dipanker Kundu et al conducted a study, which had population comprising of 30 type 2 diabetic patients without retinopathy taken as group 2, 30 type 2 diabetic patients with retinopathy as Group 3 in the age group 45-75 years as cases and 60 age and sex matched healthy individuals as controls (Group 1). All the diabetic patients enrolled in the study were screened for the presence of retinopathy by direct and indirect ophthalmoscopy and fundus photography who attended the outpatient and inpatient department of Medical College. Mean values of serum magnesium was found to be lower in cases, 1.38±0.39 mg/dl with diabetic retinopathy (Group 3) compared with both the diabetic cases without retinopathy (Group 2), 2.02±0.29mg/dl and healthy controls (Group 1), 2.62±0.36mg/dl and was statistically significant¹⁷. Mirza Sharif Ahmed Baig et al conducted a study showing that serum magnesium levels is not only lower in patients of diabetic retinopathy but its low

levels also predict about severity of retinopathy¹⁸. A study from Brazil with type 1 and type 2 diabetics, however, did not demonstrate a significant correlation between the severity of retinopathy and Mg concentration in the plasma¹⁹.

The existence of a close relationship between impaired magnesium balance and retinopathy was also established by Fuji *et al.*, who found a marked depletion in plasma and erythrocyte magnesium levels in diabetic patients with advanced retinopathy²⁰.

Neuropathy was 71.42% in patients with low magnesium levels as compared to 28.42% patients with normal magnesium levels. Studies have found that intracellular magnesium levels are lower in patients with diabetic peripheral neuropathy²¹ with improvement in the nerve conduction following supplementation²².

The incidence of foot ulcer was significantly more in the hypomagnesemia group (vs%). Sakir Ozker et al conducted a study of 147 patients divided in 3 groups, showing that serum magnesium was low in patients with feet ulcer. than patients of diabetes without feet ulcers²³.

CONCLUSION

Hypomagnesemia was found to be associated with poor glycemic control and increased incidence of retinopathy, neuropathy, and foot ulcers. Thus it is prudent to monitor magnesium levels in all type 2 diabetic patients regularly. Further studies on the role of magnesium supplementation in T2DM in our population are recommended.

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