RESEARCH ARTICLE

A STUDY OF MAGNESIUM SUPPLEMENTATION ON GLYCEMIC CONTROL IN PATIENTS OF TYPE-2 DIABETES MELLITUS

Yogendra Raj Singh[1], Shilpi Verma[2], Dushyant Agrawal[3,*], Brijendra Singh[4], Ashutosh Bhardwaj[5], Gitika Arya Agrawal[6]

[1]Department of Physiology, [2]Department of Anesthesiology, [3,4]Department of Anatomy,
All India Institute of Medical Sciences (AIIMS), Jodhpur, India
[5]Department of Physiology, S.N.Medical College, Agra, India
[6]Dr. Sarvepali Radhakrishnan Rajasthan Ayurved University, Jodhpur, India

*Corresponding Author:
E-mail: dushyantanatomy@gmail.com

ABSTRACT

Aim: *To study the effect of magnesium supplementation on glycemic control in diabetic patients.*

Material and Methods: *Total of 120 patients of diabetes mellitus type-2 (Group I- 60 patients with oral Magnesium & Group II- 60 without Magnesium supplementation) were investigated for Fasting Blood Sugar, Serum Magnesium, at various visits to OPD. Measured data was analyzed statistically.*

Observations & Result: *Mean Baseline value for fasting blood glucose was 144.32±0.94 and after treatment values at 16 weeks 128.93±0.75 was observed in Group I patients. In Group II; fasting blood glucose was 145.20±1.12 and after treatment values at 16 weeks 134.18±0.94.*

Conclusion: *This difference between before and after treatment was considered highly significant in group I patients than Group II patients. This suggested magnesium supplementation helps in glycemic control.*

Key Words: *Diabetes Mellitus, Glycemic Control, Metformin, Magnesium*

INTRODUCTION

India is only second to china in world for the number of people suffering from diabetes. The number of people with diabetes in India is currently around 40.9 million in 2015 and is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken. Diabetes is the leading known cause of neuropathy in the world. Neuropathy is the most common complication and greatest source of morbidity and mortality in diabetes patients. It is estimated that the prevalence of neuropathy in diabetes patients is approximately 20%. The main risk factor for Diabetic Neuropathy is hyperglycemia. It is important to note that people with diabetes are more likely to develop symptoms relating to peripheral neuropathy as the excess glucose in the blood results in a condition known as glucogasinogen. This condition is affiliated with erectile dysfunction and epigastric tenderness which in turn results in lack of blood flow to the peripheral intrapectine nerves which govern the movement of the arms and legs.

Diabetes is commonly thought to have no cure. It is progressive and often fatal, and while the patient lives, the mass of medical complications it sets off can attack every major organ. This medical review of diabetic neuropathy introduces a much needed medical intervention for the prevention and treatment of diabetes and the many complications that come from it. Though safe effective treatments are desperately needed there is something strange in the medical establishments approach to diabetic care. Magnesium is the fourth most abundant mineral in the body and is essential to good health. Approximately 50% of its total in the body is found in bone. The other half is found predominantly inside cells of body tissues and organs. It is needed for more than 300 biochemical reactions in the body. It also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis. There is an increased interest in its role in preventing and managing disorders such as hypertension, cardiovascular disease, and diabetes. Dietary magnesium is absorbed in the small intestines. It is excreted through the kidneys.

Magnesium plays an important role in carbohydrate metabolism. It may influence the release and activity of insulin. Individuals with poorly-controlled diabetes may benefit from its supplements because of increased loss of magnesium in urine associated with hyperglycemia. Low serum and intracellular magnesium concentrations are associated with insulin resistance, impaired glucose tolerance, and decreased insulin secretion [1]. There is a strong relationship between magnesium and insulin action and it is important for the effectiveness of insulin. Magnesium deficiency is the most evident disturbance of metal metabolism in diabetes mellitus. Hypomagnesaemia has been linked both to the acute metabolic and late chronic complication of diabetes [2]. Without insulin magnesium doesn't get transported from our blood into our cells where it is most needed. A study observed that the plasma magnesium level has been shown to be inversely related to insulin sensitivity [3]. Insulin-mediated glucose disposal is decreased in normal subjects with relatively low plasma magnesium concentrations [4]. Oral magnesium supplementation improves both insulin sensitivity and metabolic control in type 2 diabetic subjects with decreased serum magnesium levels [5]. Higher intake of magnesium has been shown to improve glucose and also insulin homeostasis [6]. So it would be prudent for physicians who treat diabetic patients to consider magnesium deficiency as a contributing factor in many diabetic complications and as a main factor in exacerbation of the disease itself [7]. Few studies [8] emphasize the role of magnesium in diabetes but not much work has been done in India. So we conducted this study to strengthen the role of magnesium supplementation in diabetes mellitus.

MATERIAL AND METHODS

Total of 120 patients from out door of Medicine division were taken and examined and investigated. For evaluating the level of improvements in fasting blood glucose levels, the type II Diabetic patients who were attending O.P.D of diabetic clinic were divided into two groups:

Group-I (Case): Patient of diabetes mellitus type-2 receiving magnesium supplementation (Magnesium Chloride sustained release tablet 300 mg/day) and Metformin (750 mg BD) + Gabapentin (400 mg TDS) therapy (n=60).

Group-II (Control): Patient of diabetes mellitus type-2 receiving only Metformin (750 mg BD) + Gabapentin (400 mg TDS) therapy (n=60)

All Patients were subjected to a Detailed History and thorough Clinical Examination. They were thoroughly examined and investigated for Fasting Blood Sugar, S.Magnesium, at first visit (0 weeks) and subsequently these tests were repeated at 4, 8, 16 weeks respectively

Inclusion Criteria:

1. A known case of diabetes mellitus.
2. Patient with clinical sign/symptom suggestive of diabetes mellitus after being investigated for blood sugar.

Exclusion Criteria:

1. Patients of diabetes mellitus with altered sensorium or disturbed mental state.
2. Patients with diabetes mellitus having very high blood sugar level and is on insulin therapy.
3. Patients showing abnormal levels of blood urea, serum creatinine, and abnormal liver function tests.

Serum magnesium level is measured by flame spectrophotometry. Each parameter measured was analyzed statistically. Data before and after administration of Magnesium supplementation were compared for statistical analysis. Student "t" test was performed and t and p value were obtained for knowing the significance between different variables.

Observations:

Serum magnesium (mg/dl) level observed before and after treatment-

In Group I: Mean baseline value for serum magnesium is 1.49±0.0174 and after treatment values at 4 weeks is 1.54±0.0179, 8 weeks 1.62±0.0180, at 16 weeks 1.72+0.0181 respectively. In this group we observed that serum magnesium values before and after 16 weeks of magnesium supplementation was highly significant (Table-1).

Table No. 1: S. Magnesium *(mg/dl)* before and after treatment

	GROUP I (n=60)				GROUP II (n=60)			
	Before treatment	After Treatment			Before treatment	After Treatment		
		4 weeks	8 weeks	16 weeks		4 weeks	8 weeks	16 weeks
Mean	1.49	1.54	1.62	1.72	1.55	1.522	1.492	1.45
S.D	0.135	0.139	0.137	0.14	0.1928	0.187	0.178	0.173
S.E.M	0.0174	0.0179	0.0177	0.0181	0.024	0.024	0.023	0.022
% Change Over Baseline				15.51				-5.87
p Value				P<0.001 (H.S)				P<0.05 (S)

In Group II: Mean baseline value for serum magnesium is 1.55±0.024 and after treatment values at 4 weeks is 1.52±0.024, 8 weeks 1.49+0.023, at 16 weeks 1.45±0.022 respectively. In this group there was negatively less significant difference in serum magnesium between before and after 16 weeks of treatment (Table-1).

Fasting Blood Glucose (mg/dl) level observed before and after treatment -

In Group I: Mean Baseline value for fasting blood glucose is 144.32±0.94 and after treatment values at 4 weeks is 140.70+0.87, 8 weeks 134.81±0.84, at 16 weeks 128.93±0.75 respectively. This difference between before and after treatment was considered highly significant (Table-2).

Table No 2: Fasting Blood Glucose *(Mg/Dl)* Before and After Treatment

	GROUP I (n=60)				GROUP II (n=60)			
	Before treatment	After Treatment			Before treatment	After Treatment		
		4 weeks	8 weeks	16 weeks		4 weeks	8 weeks	16 weeks
Mean	144.32	140.70	134.81	128.93	145.20	142.23	138.40	134.18
S.D	7.28	6.79	6.51	5.82	8.68	8.14	7.87	7.30
S.E.M	0.94	0.87	0.84	0.75	1.12	1.05	1.01	0.94
% Change Over Baseline				-10.66				-7.58
p Value				P<0.001 (H.S)				P<0.001 (H.S)

In Group II; Mean Baseline value for fasting blood glucose is 145.20±1.12 and after treatment values at 4 weeks is 142.23±1.05, 8 weeks 138.40±1.01, at 16 weeks 134.18±0.94 respectively. This difference was also significant (Table-2).

DISCUSSION

In present study mean serum magnesium level in group I before treatment (first visit) was 1.49±0.0174 mg/dl as compared to after treatment values (16 weeks) 1.72±0.0181 mg/dl in group I patients. This difference was considered statistically highly significant (p<0.0O1).

In group II before treatment (first visit) values of mean serum magnesium level

was 1.55±0.024 mg/dl as compared to after treatment (after 16 weeks) 1.45+0.022 mg/dl values of serum magnesium. This difference was statistically less significant between before and after treatment values of mean serum magnesium ($p<0.05$).

Phoung - Chi T. Pham et al (2007) observed hypomagnesaemia in patients with type 2 Diabetes. They observed that serum magnesium was decreased in Diabetes mellitus type 2 patients.

Martha Rodrfguez-Moran et al (2003) conducted a study to determine whether oral magnesium supplementation (as magnesium chloride solution) improves both insulin sensitivity and metabolic control in type 2 diabetic subjects with decreased serum magnesium levels.

At the end of the study, subjects who received magnesium supplementation showed significant higher serum magnesium concentration (0.74 ± 0.10 vs. 0.65 ± 0.07 mmol/1, p =0.02) and lower HOMA-IR index (3.8 ± 1.1 vs. 5.0 ± 1.3, p = 0.005).

Fasting Blood Glucose levels in different groups:

In present study values for mean fasting blood glucose level in group I before treatment (first visit) was 144.32±0.94 mg/dl as compared to 128.93±0.75 mg/dl values of after treatment. This difference was considered extremely significant between before and after treatment values for fasting blood glucose levels ($p<0.001$).

In group II values for mean fasting blood glucose level before treatment (first visit) was 145.20±1.12 mg/dl as compared to 134.18±0.94 mg/dl values of fasting blood glucose after treatment. This Difference was considered significant ($p<0.05$).

Song Y. *et al.* (2006) studied the effect of oral magnesium supplementation on glycemic control in Type 2 diabetes: a meta-analysis of randomized double-blind controlled trials. They concluded that oral magnesium supplementation for 4-16 weeks may be effective in reducing plasma fasting glucose levels and raising HDL cholesterol in patients with

Type 2 diabetes mellitus, although the long-term benefits and safety of magnesium treatment on glycemic control remain to be determined.

Yiqing Song *et al.* (2004) observed that higher intake of magnesium appears to improve glucose and insulin homeostasis. There was a significant inverse association between magnesium intake and risk of type 2 diabetes, independent of age and BMI (p = 0.007 for trend).

Martha Rodriguez-Moran *et al.* (2003) conducted a study to determine whether oral magnesium supplementation (as magnesium chloride solution) improves both insulin sensitivity and metabolic control in type 2 diabetic subjects with decreased serum magnesium levels.

At the end of the study, subjects who received magnesium supplementation showed significant higher fasting blood glucose levels (8.0 ± 2.4 vs. 10.3 ± 2.1 mmol/1, p = 0.01), and HbA1c (8.0 ± 2.4 vs. 10.1 + 3.3%, p = 0.04) than control subjects.

No potential conflict of interest relevant to this article was reported

REFERENCES:

1. Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG and Metcalf PA: Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid wall thickness: the ARIC study. J Clin Epidemiol 1985, 48: 927-940
2. Elamin A, Tuvemo T. Magnesium and insulin-dependent diabetes mellitus. Diabetes Res Clin Pract. 1990; 10(3): 203-9.
3. De Valk HW. Magnesium in diabetes mellitus. Neth J Med. 1999; 54(4): 139-46.
4. Rosolova H., O. Mayer, Jr, and G.M. Reaven. Insulin mediated glucose disposal is decreased in normal subjects with relatively low plasma magnesium concentrations. Metabolism Volume 49, Issue 3, March 2000, 418-420.

5. Luis E Simental-Mendfa, Martha Rodriguez-Moran, Fernando Guerrero- Romero. Failure of β-cell function for compensate variation in insulin sensitivity in hypomagnesemic subjects. Magnesium Research. 2009; 22 (3),151-156
6. Yiqing Song, Jo Ann E. Manson, Julie E. Buring, Simin Liu. Dietary Magnesium Intake
7. in Relation to Plasma Insulin Levels and Risk of Type 2 Diabetes in Women Dietary Magnesium Intake in Relation to Plasma Insulin Levels and Risk of Type 2 Diabetes in Women Diabetes Care, 2004 27:59-65.
8. Hasanein P. et al. Oral magnesium administration prevents thermal hyperalgesia induced by diabetes in rats. Department of Biology, Bu-Ali Sina University, Hamadan, Iran. Diabetes Res Clin Pract. 2006; 14.
9. Sales CH, Pedrosa Lde F. Sales CH, Pedrosa Lde F. Relation between magnesium and diabetes. Clin Nutr. 2006; 25(4):554-62.
10. Phuong-Chi T. Pham, Phuong-Mai T. Pham, Son V. Pham, Jeffrey M. Miller, and Phuong-Thu T. Pham. Hypomagnesaemia in Patients with Type 2 Diabetes. Clin J Am Soc Nephrol 2: 366-373, 2007
11. Martha Rodriguez-Moran and Fernando Guerrero-Romero. Oral Magnesium Supplementation improves Insulin sensitivity and metabolic control in type-2 diabetic subject's .Diabetes Care 26:1147–1152, 2003
12. Song Y, He K, Levitan EB, Manson JE, Liu S. Effects of oral magnesium supplementation on glycemic control in Type 2 diabetes: a meta-analysis of randomized double-blind controlled trials. Diabet Med. 2006 Oct; 23(10):1050-6.
13. Yiqing Song, JoAnn E. Manson, Julie E. Buring, Simin Liu. Dietary Magnesium Intake in Relation to Plasma Insulin Levels and Risk of Type 2 Diabetes in Women Dietary Magnesium Intake in Relation to Plasma Insulin Levels and Risk of Type 2 Diabetes in Women Diabetes Care January 1, 2004 27:59-65.