ORIGINAL ARTICLE

Diabetes Type 2; Correlation of Magnesium Levels in managing the patients - A cohort study at Khawaja Safdar Medical College, Sialkot.

MUHAMMAD SHOAIB[1], MUHAMMAD QASIM ZIA[2], ANSAR LATIF[3], ANILA ANSAR[4], IBRAHIM LIAQAT[5]
[1]*Associate Professor, Department of Physiology, Khawaja Safdar Medical College, Sialkot*
[2]*Assistant Professor, Department of Gastroenterology, Khawaja Muhammad Safdar Medical College, Sialkot.*
[3]*Professor & Head of Surgery Department, Khawaja Safdar Medical College, Sialkot*
[4]*Professor & Head of Gynae Department, Khawaja Safdar Medical College, Sialkot.*
[5]*Senior Demonstrator, Department of Physiology, Khawaja Muhammad Safdar Medical College, Sialkot,*
Correspondence to Dr Muhammad Shoaib, Email: drshoaib11@yahoo.com Cell 03004734180

ABSTRACT

Aim: To evaluate and monitor Magnesium levels in the management of patients with Diabetes type 2 at Khawaja Muhammad Safdar Medical College, Sialkot
Study Design: Prospective Study
Place and Duration of Study: Departments of Physiology and Medicine, Khawaja Muhammad Safdar Medical College, Sialkot from June 2016 to May June 2020.
Methodology: The diabetic (type 2) were patients included in this study were managed at treated and followed in Department of Physiology and Department of Medicine, Khawaja Muhammad Safdar Medical college. Sialkot. Written consent was taken from the patients before including them in the study conducted. All patients reporting to medical OPD 2000 type-II diabetes during the study duration were included. These patients were divided into three groups according to their HbA1c levels. First group (Group I) included 1100 subjects who had borderline HBA1c (5.7-6.4%) with good control of diabetes on oral hypoglycemic agents, (Group II) 500 subjects had moderately high HBA1c (6.5%-7.4%) and poorly controlled diabetes with oral hypoglycemic agents while (Group III) 400 subjects had very high HBA1c (≥7.5%) levels and very poor control of diabetes and these patients were also admitted in the hospital to control hyperglycemia.
Results: Total 2234 patients were enrolled in this study. 234 lost to follow up and they were excluded from the study. 2000 subjects included in the study. Age range of subjects was 17-89years with mean age of 46±9.7(S.D) years. Male to females (622:1378) ratio was 1:2.21. Total duration of diabetes diagnosis in these patients ranged from 1-15 years with mean age 9±4.5(S.D) years. Total 7883 blood complete picture and 7883 serum magnesium tests were performed. Total 3451 fasting plasma glucose tests and 3900 glycosylated hemoglobin (HbA1c)% tests were carried out. Follow up duration was ranged from 3 months to 15 months with mean duration of 5±3.11(S.D) months. Subjects were divided into three groups according to their fasting glucose and HbA1c levels. Group I (n=1100) had diabetes with good control, Group II (n=500) included diabetics with poor control while Group III (n=400) were uncontrolled diabetics.
Conclusion: Low Magnesium levels have a strong relation in poor glycaemic control in patients with Type 2 Diabetes. The laboratory investigations including Serum Mg levels can guide better in management of such patients.
Keywords: Aging, Endothelium Hypertension, Inflammation, Insulin resistance, Magnesium, Metabolic syndrome

INTRODUCTION

Magnesium is an important electrolyte, an intracellular cation along with potassium in our body. The importance of magnesium can be explained by its vital role in about three hundred chemical reactions as well as essential phenomenon in our body. It is involved in contraction of muscles, nerve function, blood pressure regulation, synthesis of proteins and nucleic acids, excitability of the heart, binding of a hormone to its receptor and calcium channel gating. It is also directs flux of ions through cell membrane and aids in the production of important source of energy in our body known as ATP. It acts as a coenzyme in the conversion of serotonin from tryptophan.

Increased use of prepackaged food is reducing the daily-required intake of magnesium leading to its deficiency. Absorption of magnesium in gastrointestinal tract is reduced in individuals suffering from vitamin D deficiency. Nearly 40% of the magnesium taken in our daily diet is lost in the urine. Diseases like Celiac and Crohn's disease contribute to dissipation of magnesium from the gastrointestinal tract as well as conditions like severe vomiting, diarrhea and steatorrhea. In Diabetes Mellitus, it is lost as a result of increased urinary output due to higher glucose concentrations. Alcoholism and excessive sweating are also contributing factors. The requirement of magnesium is increased in pregnancy and growth stage. Severe bronchospasm is observed in patients suffering from asthma as result of magnesium deficiency. Intravenous administration of magnesium sulfate improves gasping of breath in severe acute exacerbation of asthma according to numerous studies[7,8]. Magnesium is required for converting vitamin D into its active form. Sufficient levels of vitamin D increase magnesium absorption by 300%. Vitamin D-resistant rickets respond to magnesium supplementation instead of vitamin D. Excessive doses of vitamin D leads to reduced retention of magnesium as it enhances letters excretion. In postmenopausal women and young males, bone turnover is decreased by magnesium

Received on 17-10-2020
Accepted on 09-01-2021

supplementation. Administration of magnesium hydroxide has been found to result in fewer fractures in increased bone density according to a study. Results of some recent reviews have shown the benefit of magnesium supplementation in muscle cramps especially in pregnancy but it does not aide if the problem is due to another nutrient. Its oral supplementation has found to be effective in reducing the risk of preterm births, LBW infants and SGA newborns before 25th week of gestation.

Improvement of glycemic control in patients of Diabetes Mellitus as well as increased sensitivity of insulin in individuals who are in pre-diabetic stage has been improved by magnesium indicated by recent trials. Magnesium intake increases HDL and decreases waist circumference, body fat, and BMI. It also improves neuropathy in Type 1 Diabetes Mellitus. It can also be used as a natural antidepressant and for cessation of smoking as it antagonizes NMDA receptor. It can also be used as a therapy for dementia and insomnia.

Magnesium supplementation in elderly diabetic patients improves vascular and endothelial function. According to a review, magnesium decreases the incidence of sudden cardiac death and reduces blood pressure by acting as it blocks calcium ion channels. It is also effective in cases of torsades de pointes and digoxin toxicity. Patients who undergo CABG or cardiac bypass surgeries are given magnesium to prevent atrial fibrillation. Atrial fibrillation in some cases too rapidly resolves with the depletion of magnesium. It also improves symptoms related to congestive cardiac failure and mitral valve prolapse. Vascular supplementation is reduced in chronic kidney disease by magnesium. Magnesium pyrrolidone carboxylic acid results in diminished pain and fewer mood changes in premenstrual syndrome. Magnesium oxide reduces hot flushes, fatigue, and sweating in women undergoing breast cancer therapy[15, 16, and 17]. Progression of cataracts in magnesium deficient patients is also prevented. Risk of glaucoma is also eliminated. It is also used as infusion to reduce the release of adrenaline in autonomic dysfunction. Magnesium also improves physical performance and increases life expectancy by preventing the shortening of telomeres.

The deficiency of hypomagnesemia is encountered in cases of metabolic conditions like type 2 diabetes especially when it is not controlled. Magnesium deficits of both ICF and ECF are found in patients of Diabetes Mellitus type 2. The regulation of magnesium metabolism is related to glucose level and insulin; even the intracellular actions of insulin are dependent upon magnesium e.g. insulin-mediated glucose uptake. The deficiency or depletion of magnesium occurs due to less intake or its urinary loss in type 2 diabetes. Dietary intake deficiency may lead to type 2 diabetes as well as metabolic syndrome. There are shreds of evidence of benefits on the metabolic profiles of patients with Diabetes Mellitus. Deficiency of magnesium is frequently seen in this disease. There are no accurate tests for clinical status of magnesium. When the serum magnesium concentrations ≤0.61mmol/L or 1.5 magnesium/dL, it is considered as hypomagnesemia. Preclinical hypomagnesemia is when the magnesium concentrations are ≤0.75mmol/L or 1.8 magnesium/dL. Hypomagnesemia can occur with or without the deficiency of magnesium. Nevertheless, it indicates about the systemic deficit of magnesium. Diabetic older patients are more susceptible to hypomagnesemia. It is closely associated with metabolic control as measured by glycated hemoglobin. The most important causes of magnesium deficiency in diabetes mellitus type 2 patients are reduction in dietary intake and increased loss of urine, while the absorption and retention of magnesium is maintained. Urinary magnesium excretion is increased in both cases of hyperglycemia as it prevents its tubular reabsorption and hyperinsulinemia. Good metabolic control is associated with a reduction of urinary magnesium wasting. The regulation of insulin signaling, phosphorylation of insulin receptor kinase, post-receptor action of insulin, and insulin-mediated cellular glucose uptake is carried out by magnesium.

SUBJECTS AND METHODOLOGY

The diabetic (type 2) were patients included in this study were managed at treated and followed in Department of Physiology and Department of Medicine, Khawaja Muhammad Safdar Medical college. Sialkot. Written consent was taken from the patients before including them in the study conducted. All patients reporting to medical OPD 2000 type-II diabetes during the study duration were included. These patients were divided into three groups according to their HbA1c levels. First group (Group I) included 1100 subjects who had borderline HBA1c (5.7-6.4%) with good control of diabetes on oral hypoglycemic agents, (GroupII) 500 subjects had moderately high HBA1c (6.5%-7.4%) and (Group III) poorly controlled diabetes with oral hypoglycemic agents while 400 subjects had very high HBA1c (≥7.5%) levels and very poor control of diabetes and these patients were also admitted in the hospital to control hyperglycemia.

The objectives and methods were explained to the subjects and written consent was obtained. Five milliliters of venous blood were taken from each subject after 12 hours of fasting. Two milliliters of blood were taken in fluoride and EDTA containing test tubes for fasting glucose and glycated hemoglobin estimations. Three milliliters blood was allowed to clot and then centrifuged to extract serum. Serum was stored in plastic aliquots at 25 ^{0}C for other tests. Serum magnesium was measured using Calmagite by colorimetric method (Randox). Plasma glucose was measured using GOD-PAP enzymatic colorimetric method (Boehingir Mannheim). The estimation of glycated hemoglobin was measured by Ion exchange method (Human). The patients' investigations carried out were recorded and the frequency of Magnesium levels were carried out regularly every 2 months. The data was entered on a proforma which consisted of history, examination, investigations which included metabolic profile and blood glucose monitoring, diagnosis and treatment record. Other comorbidities alongside Diabetes were also noted and managed concomitantly with the assistance of Department of Medicine. The patients who refused to give consent or not completed their 3 month follow up were excluded from the data. Data was entered and analyzed using SPSS v 22.0.

RESULTS

Table I: General demographic findings of the study.

Total patients enrolled	2234	
Lost to follow up	234	
Study sample	2000	
Age	17- 89	Mean 46± 9.7 years (SD)
M:f	622:1378	1: 2.21
Duration of diagnosed disease	1-15 years	9± 4.5 years
Blood complete picture	7883	
Serum magnesium	7883	
Fasting plasma glucose	3451	
Glycosylated hemoglobin (HbA1c) %	3900	
Follow up	3- 15 moths	5± 3.11 (duration + SD)
Diabetics with good control	1100	(n=1100)(100%)
Diabetics with poor control	500	(n=500) (100%)
Uncontrolled diabetics	400	**(n=400) (100%)**

Table II: Differential statistics

	Group I		**Group II**		**Group III**	
	Normal range values	**lower levels**	**Normal range values**	**lower levels**	**Normal range values**	**lower levels**
Serum Magnesium (mmol/L)	978(88.90%)	122(11.09%)	412(82.40%)	88(17.60%)	131(32.75%)	269(67.25%)
Fasting plasma glucose (mmol/l)	1034(94%)	66(6%)	390(78%)	110(22%)	108(27%)	292(73%)

DISCUSSION

In our study , Age range of subjects was 17-89 years with mean age of 46±9.7(S.D) years. Male to females (622:1378) ratio was 1:2.21. Follow- up duration was ranged from 3 months to 15 months with mean duration of 5±3.11(S.D) months. Total 978 (94%) subjects in Group I were found to have normal levels of serum magnesium while 122(11.09%) subjects had slightly lower values. In Group II 412(82.40%) subjects had normal range values of serum magnesium and 88(17.60%) had lower serum magnesium values while group III had only 131(32.75%) subjects with normal range values for serum magnesium and 269(67.25%) subjects were found to have very low values. Out of 1100 subjects in Group I, 1034(94%) subjects had normal range fasting blood glucose. In group II, 412(82.40%) out of 500 had normal range fasting blood glucose while only 108(27%) subjects out of 400 in Group III had normal range fasting blood glucose.

Our study proves that low levels of magnesium are present in poorly controlled diabetes mellitus. These findings are consistent with those presented in studies carried by Ramadass S et al[21], Barbagallo M et al[22], Wang J et al[23], Hruby A et al[24], Veronese N et al[25], Simental-Mendía LE et al[26] and Barbagallo M et al[27].

Supplementation of magnesium helps improve control of diabetes in chronic cases. Magnesium is not freely available, as the physicians are not very much aware of its utility in uncontrolled diabetes. Management can be improved by giving supplemental magnesium or consistently adding diets rich in magnesium like green vegetables, nuts, seeds, dry beans and whole grains. Low magnesium levels and diabetes are interlinked to use of refined flour and quick fix foods. Preclinical and clinical departments can join hands to improve patients' management by providing them with adequate dietary balance.

As hypomagnesaemia has been observed in patients with type 2 diabetes mellitus especially in uncontrolled patients; it is recommended that the effects of magnesium supplementation in patients of type 2 diabetes be studied.

Mechanism of hypomagnesaemia in patients of diabetes mellitus needs investigations at cellular level**.** The importance of magnesium can be explained by its vital role in about three hundred chemical reactions as well as essential phenomenon in our body. It is involved in contraction of muscles, nerve function, blood pressure regulation, synthesis of proteins and nucleic acids, excitability of the heart, binding of a hormone to its receptor and calcium channel gating. It is also directs flux of ions through cell membrane and aids in the production of important source of energy in our body known as ATP. It acts as a coenzyme in the conversion of serotonin from tryptophan.

CONCLUSION

Low Magnesium levels have a strong relation in poor glycemic control in patients with Type 2 Diabetes. The laboratory investigations including Serum Mg levels can guide better in management of such patients.

REFERENCES

1. Van Laecke S, Nagler EV, Verbeke F, Van Biesen W, Vanholder R. Hypomagnesemia and the risk of death and GFR decline in chronic kidney disease. Am J Med. 2013;126:825–831. [PubMed] [Google Scholar]
2. Tin A, Grams ME, Maruthur NM, Astor BC, Couper D, Mosley TH, Selvin E, Coresh J, Kao WH. Results from the Atherosclerosis Risk in Communities study suggest that low serum magnesium is associated with incident kidney disease. Kidney Int. 2015;87:820–827. [PMC free article] [PubMed] [Google Scholar]

3. Ruel G, Shi Z, Zhen S, Zuo H, Kröger E, Sirois C, Lévesque JF, Taylor AW. Association between nutrition and the evolution of multimorbidity: the importance of fruits and vegetables and whole grain products. Clin Nutr. 2014;33:513–520. [PubMed] [Google Scholar]
4. Campbell S. C., Stockmann C., Balch A., et al. Intrapartum magnesium sulfate and the potential for cardiopulmonary drug-drug interactions. Therapeutic Drug Monitoring. 2014;36(4):544–548. doi: 10.1097/FTD.0000000000000050. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
5. Samsel A., Seneff S. Glyphosate, pathways to modern diseases III: manganese, neurological diseases, and associated pathologies. Surgical Neurology International. 2015;6, article 45 doi: 10.4103/2152-7806.153876. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Kotlinska-Hasiec E., Makara-Studzinska M., Czajkowski M., et al. Plasma magnesium concentration in patients undergoing coronary artery bypass grafting. Annals of Agricultural and Environmental Medicine. 2017;24(2):181–184. doi: 10.5604/12321966.1232767. [PubMed] [CrossRef] [Google Scholar]
7. Hermes Sales C., Azevedo Nascimento D., Queiroz Medeiros A. C., Costa Lima K., Campos Pedrosa LF., Colli C. There is chronic latent magnesium deficiency in apparently healthy university students. Nutricion Hospitalaria. 2014;30(1):200–204. doi: 10.3305/nh.2014.30.1.7510. [PubMed] [CrossRef] [Google Scholar]
8. Colice G. L. Comparative effectiveness of intravenous and inhaled magnesium in acute asthma. Journal of Comparative Effectiveness Research. 2013;2(5):437–441. doi: 10.2217/cer.13.55. [PubMed] [CrossRef] [Google Scholar]
9. Goodacre S., Cohen J., Bradburn M., et al. The 3Mg trial: a randomised controlled trial of intravenous or nebulised magnesium sulphate versus placebo in adults with acute severe asthma. Health Technology Assessment. 2014;18(22):1–168. doi: 10.3310/hta18220. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Castiglioni S., Cazzaniga A., Albisetti W., Maier J. A. M. Magnesium and osteoporosis: current state of knowledge and future research directions. Nutrients. 2013;5(8):3022–3033. doi: 10.3390/nu5083022. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
11. Nieves J. W. Skeletal effects of nutrients and nutraceuticals, beyond calcium and vitamin D. Osteoporosis International. 2013;24(3):771–786. doi: 10.1007/s00198-012-2214-4. [PubMed] [CrossRef] [Google Scholar]
12. Derom M.-L., Sayón-Orea C., Martínez-Ortega J. M., Martínez-González M. A. Magnesium and depression: a systematic review. Nutritional Neuroscience. 2013;16(5):191–206. doi: 10.1179/1476830512y.0000000044. [PubMed] [CrossRef] [Google Scholar]
13. Murck H. Ketamine, magnesium and major depression—from pharmacology to pathophysiology and back. Journal of Psychiatric Research. 2013;47(7):955–965. doi: 10.1016/j.jpsychires.2013.02.015. [PubMed] [CrossRef] [Google Scholar]
14. Chiuve S. E., Sun Q., Curhan G. C., et al. Dietary and plasma magnesium and risk of coronary heart disease among women. Journal of the American Heart Association. 2013;2(2) doi: 10.1161/JAHA.113.000114.e000114 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
15. Khan A. M., Lubitz S. A., Sullivan L. M., et al. Low serum magnesium and the development of atrial fibrillation in the community: the framingham heart study. Circulation. 2013;127(1):33–38. doi: 10.1161/CIRCULATIONAHA.111.082511. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
16. Massy Z. A., Nistor I., Apetrii M., et al. Magnesium-based interventions for normal kidney function and chronic kidney disease. Magnesium Research. 2016;29(4):126–140. doi: 10.1684/mrh.2016.0412. [PubMed] [CrossRef] [Google Scholar]
17. Yu L., Li H., Wang S. Serum magnesium and mortality in maintenance hemodialysis patients. Blood Purification. 2017;43(1-3):31–36. doi: 10.1159/000451052. [PubMed] [CrossRef] [Google Scholar]
18. Agarwal R., Iezhitsa I. N., Agarwal P., Spasov A. A. Mechanisms of cataractogenesis in the presence of magnesium deficiency. Magnesium Research. 2013;26(1):2–8. doi: 10.1684/mrh.2013.0336. [PubMed] [CrossRef] [Google Scholar]
19. Ekici F., Korkmaz Ş., Karaca E. E., et al. The role of magnesium in the pathogenesis and treatment of glaucoma. International Scholarly Research Notices. 2014;2014:7. doi: 10.1155/2014/745439.745439 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
20. Veronese N., Berton L., Carraro S., et al. Effect of oral magnesium supplementation on physical performance in healthy elderly women involved in a weekly exercise program: A randomized controlled trial. American Journal of Clinical Nutrition. 2014;100(3):974–981. doi: 10.3945/ajcn.113.080168. [PubMed] [CrossRef] [Google Scholar]
21. Ramadass S, Basu S, Srinivasan AR. Serum magnesium levels as an indicator of status of Diabetes Mellitus type 2. Diabetes Metab Syndr. 2015;9:42–45. [PubMed] [Google Scholar]
22. Barbagallo M, Di Bella G, Brucato V, D'Angelo D, Damiani P, Monteverde A, Belvedere M, Dominguez LJ. Serum ionized magnesium in diabetic older persons. Metabolism. 2014;63:502–509. [PubMed] [Google Scholar]
23. Wang J., Persuitte G., Olendzki B. C., et al. Dietary magnesium intake improves insulin resistance among non-diabetic individuals with metabolic syndrome participating in a dietary trial. Nutrients. 2013;5(10):3910–3919. doi: 10.3390/nu5103910. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
24. Hruby A., Ngwa J. S., Renstrom F., et al. Higher magnesium intake is associated with lower fasting glucose and insulin, with no evidence of interaction with select genetic loci, in a meta-analysis of 15 charge consortium studies. The Journal of Nutrition. 2013;143(3):345–353. doi: 10.3945/jn.112.172049. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
25. Veronese N., Watutantrige-Fernando S., Luchini C., et al. Effect of magnesium supplementation on glucose metabolism in people with or at risk of diabetes: a systematic review and meta-analysis of double-blind randomized controlled trials. European Journal of Clinical Nutrition. 2016;70(12, article 1463) doi: 10.1038/ejcn.2016.209. [PubMed] [CrossRef] [Google Scholar]
26. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. Oral magnesium supplementation decreases C-reactive protein levels in subjects with prediabetes and hypomagnesemia: a clinical randomized double-blind placebo-controlled trial. Arch Med Res. 2014;45:325–330. [PubMed] [Google Scholar]
27. Barbagallo M., Di Bella G., Brucato V., et al. Serum ionized magnesium in diabetic older persons. Metabolism: Clinical and Experimental. 2014;63(4):502–509. doi: 10.1016/j.metabol.2013.12.003. [PubMed] [CrossRef] [Google Scholar]