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ASSOCIATION OF SERUM MAGNESIUM WITH BLOOD PRESSURE IN PATIENTS WITH DIABETES MELLITUS: A CROSS SECTIONAL STUDY

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ABSTRACT

The role of magnesium supplement on blood pressure has been studied among hypertensive; however, there is lack of studies exploring the role of magnesium with blood pressure in Type 2 diabetic patients. The primary objective of this study was to evaluate the relationship between serum magnesium and blood pressure in Type 2 diabetic patients. The patients were

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included if they were eighteen years of age or older and a documented magnesium level on their electronic medical record. The primary outcome of the study was the correlation between supplemented magnesium, and blood pressure in patients with Type 2 diabetes. Three hundred and fifty patients were included in the study. The primary outcome result showed that serum magnesium was negatively correlated with systolic (SBP) blood pressure (r = -0.47, p = 0.01), and diastolic (DBP) blood pressure (r= -0.32, p=0.05). This study found a significant negative association between magnesium and systolic blood pressure, and diastolic blood pressure. This negative association of serum magnesium with SBP and DBP was maintained after adjusting for covariates. This study's findings suggest a potential role of magnesium in blood pressure among Type 2 diabetic patients.

KEYWORDS: magnesium; blood pressure; Type 2 diabetic patients.

ASOCIACIÓN ENTRE EL MAGNESIO SÉRICO Y LA PRESIÓN ARTERIAL EN PACIENTES CON DIABETES MELLITUS: UN ESTUDIO TRANSVERSAL

RESUMEN

Se ha estudiado el papel de los suplementos de magnesio en la presión arterial de pacientes hipertensos; sin embargo, existe una falta de estudios que exploren la relación entre el magnesio y la presión arterial en pacientes con diabetes tipo 2. El objetivo principal de este estudio fue evaluar la relación entre el magnesio sérico y la presión arterial en pacientes con

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diabetes tipo 2. Se incluyó a pacientes mayores de dieciocho años que contaban con un registro documentado de sus niveles de magnesio en su historia clínica electrónica. La variable principal del estudio fue la correlación entre el magnesio (administrado como suplemento) y la presión arterial en pacientes con diabetes tipo 2. En el estudio participaron trescientos cincuenta pacientes. Los resultados mostraron una correlación negativa entre el magnesio sérico y la presión arterial sistólica (PAS) (r = -0,47; p = 0,01), así como con la presión arterial diastólica (PAD) (r = -0,32; p = 0,05). El estudio halló una asociación negativa significativa entre el magnesio y tanto la presión arterial sistólica como la diastólica. Dicha asociación negativa del magnesio sérico con la PAS y la PAD se mantuvo tras ajustar por covariables. Los hallazgos de este estudio sugieren que el magnesio podría desempeñar un papel relevante en la presión arterial de los pacientes con diabetes tipo 2.

PALABRAS CLAVE: magnesio; presión arterial; pacientes con diabetes tipo 2.

INTRODUCTION

Diabetes mellitus, is a serious chronic metabolic disorder that develops when the body either generates insufficient or no insulin, or uses it in an inefficient manner. An important hormone generated by the pancreas is insulin. It enables circulatory glucose to enter the body's cells, where it can be stored or transformed into energy. Additionally, the metabolism of fat and protein depends on insulin. Hyperglycemia, the clinical sign of diabetes, is caused by high blood glucose levels (hyperglycemia), which occur when there is insufficient

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insulin or when cells are unable to respond to it (1). India had the highest rate of diabetes mellitus in the world in 2000. With over 62 million people in India already living with diabetes, the disease is quickly assuming the position of a possible epidemic. The prevalence of diabetes is expected to double globally from 171 million in 2000 to 366 million in 2030, with India experiencing the greatest growth. It is estimated that up to 79.4 million people in India could have diabetes mellitus by 2030. (2). In India, diabetes is thought to have directly contributed to 1.6 million mortality as of 2017. (2). The biggest number of cases of diabetes have been reported in South India's Kerala and Tamilnadu, followed by Karnataka and Andhra Pradesh. Magnesium is a physiologically significant electrolyte in the body. It is the second common cellular ion in cells after potassium and the fourth cation in the human body, (3). Alteration in magnesium level is frequently present in type 2 diabetes mellitus patients. Magnesium deficiencies are more common in DM2 patients, particularly in those with poorly managed glycemic profiles. Important metabolic regulators of magnesium include insulin and glucose (4). Intracellular magnesium is significantly influenced by insulin action, insulin-mediated glucose absorption, and vascular tone. Diabetes patients show higher insulin resistance and impaired insulin action as a result of decreased intracellular Mg concentrations. The two most significant factors that may favour magnesium depletion in type 2 diabetic individuals are a low magnesium intake and an increased magnesium loss in urine (5). Low dietary

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magnesium intake has been related to the development of type 2 diabetes and metabolic syndrome. Larger prospective studies are required to support the potential role of dietary magnesium supplementation as a potential public health strategy in reducing diabetes risk. Very few clinical studies have shown benefits of magnesium supplementation on metabolic profiles in diabetic patients, but still further exploration is required.

The vasoconstriction brought on by hypomagnesaemia results in hypertension in DM2 patients. But there is no study available on the effect of magnesium on blood pressure in diabetes mellitus. The aim of this study is to find the relationship between serum magnesium and blood pressure in type 2 diabetes patients.

Material & Methods

Study design

It is a cross sectional comparative study conducted following 'Strengthening the Reporting of Observational Studies in Epidemiology'' (STROBE) guidelines. Institutional ethical clearance also obtained (ethical number:) from the host institution.

Study population

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Patients with diabetic attending General Medicine OPD and Endocrinology Clinic of the host institute were recruited for the study based on convenience sampling technique. Three hundred and thirty-three patients were included in the study of both the gender and between the age group of 20 to 50 years. Smokers, alcoholic, Type 1 Diabetes Mellitus, Coronary Heart Disease, patients on diuretic drugs and antacids were excluded from the study.

Outcome measurement

For each patient, 10 ml of blood from peripheral vein was collected after 8 to 12 h of fasting in the morning. Standard operating procedures regarding blood-sample collection, processing, and storage were followed. The primary predictor was serum magnesium concentration, which was measured in mmol/L by the xylidyl-blue colorimetric method. Fasting and post prandial glucose was measured with the glucose oxidase-phenol aminophenazone method. Using a standard mercury manometer blood pressure was determined for each patient after 15 minutes of rest. The blood pressure measurement was repeated after 15 minutes and the mean value of two measurements was considered as the patient blood pressure value.

Statistical analysis

Statistical analyses were performed using R software version 4.2.0. A p-value of less than 0.05 was considered statistically significant in the two-tailed test. Descriptive statistical analysis was performed on

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demographic characteristics. Measures of central tendency were obtained for continuous measures and frequency distribution for categorical measures. Simple linear regression was conducted to assess the correlation (r) between serum magnesium in relation to blood pressure (SBP and DBP).

Results

The details of the baseline demographics are presented in Table 1. The majority of patients were male (70%) and the average age of patients in the study was 46.7 years. Around 42% of patients had hypertension and the average BMI was 30.6 kg/m^2. The primary outcome result is presented in Table 2, and this reveals that serum magnesium was negatively with SBP correlated (r = -0.43, p-value = 0.01) and DBP (r=-0.38, p-value=0.05). Table 3 assessed the relationship with serum magnesium and both SBP and DBP with adjusting for covariates. The results show that as serum magnesium increased by 1 mg/dL, SBP decreased 5.46 mmHg after adjusting for covariates in the model (p-value = 0.04). Similarly, significant association was found with serum magnesium and DBP after adjusting for covariates and found that serum magnesium increased by 1 mg/dL, DBP decreased 2.89 mmHg in the model.

Table: 1. Baseline demographical details of the patients included in the study

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Demographic Variables	Details
Age (Mean ± SD years)	46.7± 11.28
Sex, n (%)	Male: 245(70%) Female: 135 (30%)
Hypertensive, n (%)	150 (42%)
Use of Proton Pump Inhibitors, n (%)	217 (62%)
Serum Magnesium at Crises (Mean ± SD mg/dL)	1.88±0.92
Systolic Blood Pressure (Mean ± SD mmHg)	144.2 ± 11.31
Diastolic Blood Pressure (Mean ± SD mmHg)	89.56±10.23

Discussion

The primary objective of our study was to evaluate the relationship between magnesium and blood pressure (SBP and DBP) in patients with Diabetic. Using correlation (Table 2) and linear regression analyses (Table 3), our study found a significant negative correlation between serum magnesium and blood pressure (SBP and DBP).

Table 2. Association of serum magnesium with SBP and DBP

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Variable	r	P value
Systolic Blood Pressure (Mean ± SD mmHg)	-0.43	0.01
Diastolic Blood Pressure (Mean ± SD mmHg)	-0.38	0.05

Table 3. Association of serum magnesium with SBP and DBP using linear model analysis (adjusted for covariates)

Variable	β ± SE	P value
Systolic Blood Pressure (Mean ± SD mmHg)	5.46±2.31	0.01
Diastolic Blood Pressure (Mean ± SD mmHg)	2.89±0.59	0.02

Adjusted for covariates—Age, sex, and BMI.

According to previous research, magnesium is a crucial cofactor for various enzymes involved in the metabolism of glucose. It is important for bringing out phosphorylation of enzyme muscle insulin tyrosine. (6) Thus, lack of magnesium affects the insulin's post receptor signaling, affecting glucose absorption resulting in hyperglycemia.(7) In a study conducted on maternal magnesium restricted rats, the metabolic disturbances

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associated with insulin resistance, glucose intolerance, and irreversible alterations in body composition was seen in their pups (8)

The effects of magnesium supplementation on glucose metabolism in type 2 diabetes have varied. In a meta-analysis of nine randomised double-blind controlled studies, the advantages of oral magnesium supplementation on glycemic control in patients with type 2 diabetes were evaluated (9). While a supplement was effective in lowering plasma fasting glucose levels and raising HDL cholesterol. On the other hand it did not have any effect on long-term glycemic control while measuring the glycated haemoglobin, weight control, and blood pressure [20]. But the published trials were of smaller sample size.

Magnesium alters the tone and contractility of vascular smooth muscle by altering calcium ion concentrations. As a moderate calcium-channel blocker, it works by preventing calcium-related excitation-contraction coupling and calcium dependent depolarization. By bringing this effect magnesium helps in relaxing the vascular system (10). In addition, the activated magnesium-ATP complex, which contains magnesium, is necessary for calcium ATPases and all other ATP and phosphate transfer-associated enzymes, including protein kinases (11). Therefore, hypertension may develop as a result of a magnesium deficiency and affect blood pressure measurements. There is an inverse correlation between blood pressure readings and magnesium levels, as established by numerous human studies on

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serum level and dietary supplements of magnesium (12, 13). As discussed earlier the meta-analysis of 12 randomised controlled studies found that magnesium supplementation did not affect the diastolic readings and there was no significant changes observed in lowering the systolic blood pressure either (14) [35]. There are now strong events showing the direct impact of magnesium consumption on metabolic and cardiovascular risk factors. An intracellular magnesium depletion experiment also identified insulin resistance, affects vascular tone leading to hypertension, induces pro-inflammatory changes and endothelial dysfunction, and ultimately increases the risk for cardiovascular disease.

Our study's strengths include the use of statistical tests to explore for correlations between variables, the fact that it was a pilot study, and the achievement of the target sample size. To investigate the relationship between magnesium and blood pressure in Diabetic patients, regression analysis was used. This study, which is also a pilot/exploratory one, can give population estimates to help establish the right sample size to study the impact of magnesium on blood pressure in future research.

Our study has a number of limitations that affect both its internal and external validity. First of all, the fact that our study was conducted in a single center limits its applicability to patients at other institutions. The conclusions from this single-center study should therefore be cautiously generalised to specific patients

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and patient demographics experiencing diabetics. Due to the fact that this study was retrospective in nature, data from the electronic medical record was not routinely obtained at predetermined intervals as would be the case in a prospective study. Because our study was retrospective and non-randomized, significant variables were not gathered or taken into consideration, which could have skewed the results.

Conclusion

This finding revealed a significant negative correlation between magnesium and blood pressure in diabetic patients. After controlling for confounders, the negative relationship between serum magnesium and systolic and diastolic blood pressure remained. The results of this study suggest to a potential role for magnesium in reducing blood pressure in diabetic patients. We do not, however, advise altering current clinical practise with regard to the monitoring of magnesium in diabetic patients in context of the study's limitations and strengths.

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