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Hypomagnesia in Diabetics: A Survey in Gorgan

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Abstract: Several reports revealed that plasma level of essential trace elements like magnesium, calcium and phosphorus altered in diabetics. These micronutrients especially magnesium are suspected to have effective roles in pathogenesis and progression of diabetes. The studied subjects consisted of 96 diabetic volunteers (66.8%) females (mean age rate of 51.8±9.37) and (31.3%) males (mean age rate of 49.8±14.84) admitted in diabetes clinics of Gorgan city (Northeast of Iran). In these patients, the plasma level of Mg measured by simple sampling method due to a cross-sectional designated project. Glycated hemoglobin (HbA1c) also measured as a glycaemia control index. Hypomagnesia states were positive in 48 cases (50%). Housekeepers together with low educated individuals had significantly lower Mg plasma level as compared to other studied groups ($p<0.05$). No significant relationships were seen considering other variables. In respect to significant alterations of Mg plasma level that also reported in other such studies, it is recommendable to provide complementary supplication of such micronutrients for diabetics.

Key words: Diabetes, magnesium, plasma level, gorgan

Introduction

It is evident that Mg, as a cofactor, has an important role in carbohydrate, protein and fat metabolism. There are more than 300 Mg dependent enzymes with several vital effects that their roles in neuromuscular function are being the most important. Hypomagnesia and failure in Mg metabolism have evidently seen in CHD (Congestive Heart Disease), IHD (Ischemic Heart Disease), CVA (Cardiovascular Arrest), atherosclerosis, cardiac arhythmia and in cardiac ventricular problems (Chakraborti *et al*., 2002). Hypomagnesia (and probable Mg depletion states) had been a common clinical problem in bedridden and outpatient individuals; for example, based on a study, hypomagnesia had been seen in 10.2% of outpatients together with ward bedridden ones and in 61% of confined to bed in ICU ward post operation patients (Methency, 2000).

Hypomagnesia may occur because of DKA (diabetic ketoacidosis); in which increased plasma glucose, results in osmotic diuresis that in turn results in an increased renal excretion and following intracellular transition of Mg due to insulin therapy.

Associated metabolic effects of hypomagnesia that are consequences like hypokalemia, hypocalcaemia and hypophosphathemia, may influence the peripheral tissue reactions and secretion of insulin from pancreas (Methency, 2000).

The tendency to hypomagnesia is obviously evident in diabetics probably due to glucosuria, dietary states and hyperinsulinemia related Mg excretions (De Valk, 1999).

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Several studies have revealed the side effects of hypomagnesia to be consequences such as retinopathy, hypertension and cardiovascular problems in diabetics; so this study conducted to evaluate mean plasma level of Mg among diabetics in Gorgan.

Materials and Methods

The study groups consisted of 96 diabetic volunteers comprising 30 males (31.3%, mean age rate of 49.8 ±14.84) and 66 females (68.8%, mean age rate of 51.86±9.37). Majority of the patient subjects (63.3%) were within 20-40 years old and referring to the information recorded voluntarily in a questionnaire and their files there were 6(6.3%) IDDM (Insulin Dependent Diabetic Mellitus) and 90(93.7%) NIDDM (Non-insulin Dependent Diabetic Mellitus) cases. Considering the calculation of BMI (body mass index) the subjects were categorized in five body mass groups (thin<19, normal = 19-26, overweight 26-30, obese 30-35 and severe obese 35-40, morbid obese >40 uncommon). Of the studied subjects 71(74%) had a diabetes contraction history of less than 10 years and 25(26%) cases more than 10 years. Four cases were smokers, regarding their education state 34(35.4%) cases were illiterate, 39 (40.6%) were able to read (under high school diploma) and 23(24%) cases were certificated and belonged to a higher education state. HbA1c: Based on normal (4.5-6.9%) and borderline range of (7-9%), seven (7.3%) patient subjects had normal HbA1c level, 61(63.5%) cases higher than 9% and the rest were within 7-9 percentages. Professional state: The majority of the cases were females (housekeepers 58(60.4%) and 30% of the rest were employees, 10% farmers and 85% were Gorgan residents and 15% were located out of Gorgan . Physical activity: 72(75%) of cases had light physical activities, 20(20.8%) cases an ordinary and 4(4.2%) of them had very light physical activities. In all participants demographic information (sex, age, height, weight etc. were recorded with their free will (voluntarily). Two milliliter of whole blood sample collected in EDTA contained tubes for estimation of HbA1c and 4 mL in anticoagulant free tubes in order to serum preparation. These processes performed by expert personnel. Serum removed by centrifugation (2500 g rpm, for 5 min) and stored immediately at -20°C until analysis time (after separating the amount needed for FBS). Glucose, Mg and HbA1c determined based on colorimetric methods.

Results

Mean Mg level in studied subjects was 1.6±0.97 mg dL^{-1} (reference levels: normal = (1.5-2.5) mg dL^{-1}, hypomagnesia <1.5 mg dL^{-1} and for hypermagnesia state >2.6 mg dL^{-1}). Serum Mg level: 48(50%) cases defined to be hypomagnesic and 34(35.4%) cases had normal ranges of Mg level.

Mean Mg level was higher in females than males with no significant differences ($p>0.005$) and there was no significant correlations of Mg levels considering age parameter in different studied groups ($p>0.05$). Nineteen (40%) cases with hypomagnesia had normal BMI and 18(37.5%) of them were overweight. There was no significant relationship considering Mg level and BMI ($p>0.05$).

Hypomagnesia was more common in patients that had used glibenclamide (52.1% of hypomagnesic cases in comparison with others); while in those had used glibenclamide together with methformine and insulin with glibenclamide, it was 14.6 and 0-2.1%, respectively ($p>0.005$).

Mean serum Mg levels were lower in the patients considering the commencement of the illness, saying that, whatever the contraction history was earlier, the Mg level shown to be in lower ranges with no significant differences statistically ($p>0.05$). No one of the hypomagnesia diabetics were smokers and Mg level in subjects that had high school certificated or were in a higher educative state were in lower ranges in comparison with under high school diploma ones ($F; 1.94 = 2.866$: $p>0.05$).

Hypomagnesia were seen more commonly among women (56.3%) together with retired subjects (8.3%) than the others. The correlation of Mg level and professional state were not significant statistically. Hypomagnesia was shown to be more frequent in the subjects with light physical activities ($p>0.005$) and it was not correlated with blood sugar control in past three months duration ($p>0.005$).

Discussion

Mg is one of the most important cations that its plasma concentration always needs to be stay in a constant level. Intracellular and plasma (extra cellular) concentration of Mg regulated by the means of several factors that the most important one is being the insulin. *In vivo* and *in vitro*, studies have revealed the existence of a complex relationship between insulin and Mg as an important cathion. Mg shifts to the intracellular spaces by the aid of insulin; while on the contrary; intracellular concentration of Mg regulates the function of insulin (sp. Oxidative metabolism of glucose), calcium dependent processes and reductive depolarized stimulant dependent responses of soft tissues. Decreased intracellular level of Mg that is a common problem in NIDDM and hypertensive patients may result in insulin receptor dependent thyrosine kinase insufficiency and increased intracellular calcium concentrations that both may cause failures of insulin function (De Valk, 1999).

Resultant mean Mg plasma level in this study (Gorgan) was 1.61 ± 0.97 mg dL^{-1} that 50% of the studied diabetics were in hypomagnesic state.

Based on a study performed by Mostfavi *et al*. (2003) (Tehran med. Univ. related educative hospitals 1983-1986), serum and RBC Mg levels in diabetic pregnant women were significantly lower in comparison with non-diabetic pregnant and non-pregnant control groups (Mostafavi, 2003). Considering the results of a report (Walti *et al*., 2003), hypomagnesia state had shown to be 37.6% in diabetics (mean Mg level of 0.77 ± 0.08 mg dL^{-1}); while it was only 10.9% in comparison with normal subjects (Walti *et al*., 2003). Hassman *et al*. (1997) has reported plasma ionized Mg levels to be lower than normal control subjects (0.5 mmol L^{-1} contrary to 53 mmol L^{-1}) in diabetics. Based on a survey (Djurhuus *et al*., 1991) that evaluated the effects of hypomagnesia state on delayed type consequences of diabetes, there had been at least 30% of reported diabetics facing with hypomagnesia that had been in relationship with pectoral angina, MI and hyperlipidemic states (Djurhuus *et al*., 1991). Almost all the reports from all over the world, have confirmed most of the diabetics to be hypomagnesic. A report from India had confirmed hypomagnesia in all studied diabetic subjects with normal renal function (Srivastava *et al*., 1993). Nagse *et al*. (1996) had concluded that all diabetics faced with lower serum Mg levels than normal subjects. Frankel (1999) from USA has also confirmed hypomagnesia in almost 25% of their outpatients. Singh *et al*. (1997) concluded that hypomagnesia state and dietary Mg insufficiency might act as an effective role in commencement of diabetes and related consequences.

Present results considering the mean Mg levels were in line with the other similar reports; even present results have shown the hypomagnesia state to be more frequent finding in diabetics than the others have. According to the results of this survey, there were seen no significant correlations considering mean Mg level and HbA1c; while a study performed in Saudi Arabia had mentioned the urinary excretion of Mg correlated in a positive manner with the rate of HbA1c levels ($p<0.05$) (Yazigi *et al*., 1993). A group of Indian scientists has also reported hypoglycemia in diabetics conversely correlated with hypomagnesia state; however, serum concentration level of Mg had restored when insulin prescribed (Garber, 1996). Urinary excretion of Mg had been in a positive relationship

with glucosuria, as reported by a study group from Swiss (Roffi, 1994) and reports from Japan have correlated lower serum Mg levels in weakly controlled diabetics than well controlled ones Leeuw *et al*. (1992). Based on a study performed in Texas City (USA), serum Mg concentrations had shown to not correlated with HbA1c levels (Garber, 1996) that were in line with the results of present experiment.

All of the mentioned reports had correlated HbA1c associated with FBS levels and serum Mg concentrations to the increased urinary excretion due to osmotic diuresis and acidosis that are common findings in diabetics. Based on present results no correlation between serum Mg level and sex were existed; but in general, it was in higher ranges in females than males; while the serum and RBC Mg levels to be in a higher range in men than women (Leeuw, 1992). Other tudies also have mentioned some diversities for serum Mg level in consideration of sex in both types of diabetes (I,II) (Mostafavi *et al*., 2003; Walti *et al*., 2003; Husmann *et al*., 1997; Garber, 1996) that this was in line with the present results. There was also a discrepancy in the scope of aging and serum Mg level. Based on present results, lower mean concentrations of Mg level were evident with aging that was matched the other studies (De Valk, 1999; Husmann *et al*., 1997; Babagallo *et al*., 1997; Durlach *et al*., 1998; Wowang *et al*., 1999). Present study has revealed serum mean Mg level to be in higher ranges in subjects that were overweight with normal BMI ($p>0.05$); while based on a research performed on a group of fat children (Japan), there was a diverse relationship between serum Mg level and overweighing. It has suggested that due to increased level of fatty acids and following conjugation of active Mg in biologic microenvironments, the homeostasis of this vital ion disturbed in fats (Yakinici, 1997). There was also a negative correlation for mean Mg level in regard to education states ($p>0.05$); while returning to some other studies, serum Mg level has not shown to be in correlation with educational states of the studied subjects. Based on several studies, it seemed to be a positive correlation between educational and socio-economical and better dietary states (Wowang *et al*., 1999; Yakinici *et al*., 1997; Altura, 1991) but present results did not agree with that. As the confirmed effects of Mg level on commencement of delayed type clinical consequences such as retinopathy, cardiovascular problems for instance (CHD, IHD, CVA, Atherosclerosis and Cardiac Arhythmia states), it is strongly recommended that the diabetics considered to be screened and evaluated for microelements such as Mg and other vital micronutrients and educated to use them in a supportive complementary dietary regimen.

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