Original Article

A study to access the Impact of Magnesium Deficiency in the Obese Individuals

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ABSTRACT

Background: Obesity is an important health problem among developed and developing countries. Magnesium (Mg) deficiency is seen in obese individuals. **Aim**: To investigate the effect of Mg deficiency on insulin resistance in obese subjects. **Methods**: In this retrospective study, patients admitted to our hospital between 1 January 2016 and 31 December 2016 were included and data were retrieved from their medical records. We collected values of HbA1c, Mg, Glucose and Homa-IR and other biochemical tests. According to Body Mass Index (BMI), patients were divided into 3 groups. The relationship between Mg level and BMI was analyzed. Meanwhile, we also observed the relation between insulin resistance and BMI and relation between Hba1c and BMI. **Results**: A total of 134 patients, 21 male and 113 female, were included in the study. There was no statistical significance in serum Mg levels between the groups and there was a weak negative correlation between BMI and serum Mg levels. The correlation between BMI and insulin resistance was found to be moderately positive. On comparing, BMI and HbA1c between groups; it was statistically significant the groups consisting of BMIs below 25 and between 25-35, and the groups consisting of BMIs below 25 and >35. There was moderate positive correlation between BMIs and HbA1c levels. A negligible positive correlation between Mg levels and insulin resistance was observed. A weak negative correlation was found between Mg and HBA1C levels. **Conclusion**: Serum MG deficiency can be seen in obese individuals. Low serum Mg levels may accelerate the development of diabetes in obese individuals.

Key words: Obesity, Magnesium, Insulin resistance, diabetes

Obesity has become an important health problem in developed and developing countries. Dietary intake of high calories decreased physical activity and sedentary life plays a role in the development of obesity. Increased body weight can lead to diseases such as type 2 diabetes, cardiovascular disease, hypertension and cancer [1]. In the development of obesity, environmental and genetic factors are thought to be influenced by neuro endocrine mechanisms regulating energy balance [2]. Magnesium (Mg) is the second common cation in extracellular and intracellular fluids. It is also a cofactor of nucleic acid and protein synthesis [3].

Mg is necessary to maintain normal muscle and nerve function as well as the heart rhythm and bone integrity. It is also responsible for protein synthesis and energy metabolism. Mg deficiency frequently developed by; urinary system disease causing Mg loss and lack of Mg absorption due to gastrointestinal system disease and chronically low uptake of Mg [4]. In previous study, it was observed that Mg replacement may play a role in decrease of insulin resistance and diabetes [5]. Insulin resistance; is defined as an impaired biological response to endogenous or exogenous insulin [6]. According to the Turkish Diabetes, Hypertension, Obesity and Endocrinological

Diseases Prevalence Study-II (TURDEP-II) data published in 2010, the prevalence of obesity in Turkey has reached 32% in the adult age group. Compared to TURDEP I study data in 1998, obesity in our country increased by 44% in 12 years and increase was 34% in women and 107% in men [7]. Studies have shown that magnesium intake is significantly correlated with steatosis, insulin resistance, hyperinsulinemia, hypertriglyceridemia, low HDL cholesterol and hypertension [8]. In this study, we aim to show the relationship between serum Mg level and insulin resistance in young obese individuals.

METHODS

This retrospective study was conducted between January 1, 2016 and December 31, 2016 in the University Research Hospital patients who were followed up and treated in the internal clinics and were directed to a dietician. All patients who applied to the hospital with any complaint were included in the study in which 21 were male and 113 female patients. Patients with known diabetes, metabolic disease with liver and kidney dysfunction were excluded from the study. This study was ethical approved by Amasya University Sabuncuoğlu Serefeddin Education and Research Hospital (Amasya, Turkey) in the scientific meeting at 29.04.2016.

Demographic profile and data of included patients were retrieved from their medical records. After examining the patients' data, 3 groups were formed based on their BMI. First group consist of patients whom BMI were under 25. The second group consist of patients whose BMI is between 25 and 35. The third group consist of patients whose BMI is upper 35. The BMI <25 was considered to be normal, between 25- 29.9 was overweight people and if it was >30, the person was said to be obese. The relationship between Mg level and BMI was analyzed. Meanwhile, we also observed the relation between insulin resistance and BMI and relation between Hba1c and BMI. Insulin resistance was calculated by; HOMA index (fasting insulin (pmol/l) x fasting plasma glucose (mg/dL) / 405) and BMI calculated by; Body Weight (kg) / Squared Length (m2) formula. Serum Mg (normal values: 1.9 - 2.5 ng / ml) was studied in the Olimpus AU 5800 by direct method in which magnesium ions form a complex with xylidine blue. Serum insulin measurements (normal values: 2,6-37,6 pmol/l) were performed on the Siemens Advia Centaur xp with electrochemiluminescence method. Serum glucose measurements (normal values: 74- 109 mg/dl) were performed on the Olympus AU 5800 instrument using the glucose oxidase method. HBA1C measurements (normal values: 4-6%) were performed on the Trinity / Menarini Premier device by HPLC boranat method.

GraphPad Prism version7.00 was used for statistical analysis. (GraphPad Software, La Jolla California USA). One-Way ANOVA was used to compare quantitative data while the multiple logistic regression analysis was performed to investigate how dependent variables were affected by independent variables. The Chi-Square test was used to understand gender differences. The results were evaluated in 95% confidence interval and significance level of p <0.01. Correlation between the parameters was done by Pearson correlation analysis. Correlation coefficient (r) was evaluated as weak between 0.00-0.24, moderate between 0.25-0.49, strong between 0.50-0.74, very strong relation between 0.75-1.00.

RESULTS

Total 134 people were included in this study and the mean Mg level was 1.7±2.2 mg/ dl and Hba1c level was 4-6. In our study, 32 (23.8%) of the participants had BMI <25, 84 (62.6%) patients had BMI between 25-35 and 18 (13.4%) patients had BMI >35 and over. 10 of the patients with BMI <25 (31.25%) were male and 22 (59.75%) were female. 8 (9.5%) of the patients with BMI between 25 and 35 were male and 76 (90.5%) were female. There were 3 male (16.6%) and 15 (83.4%) female with BMI 35 and over. Table 1 shows the gender differences in BMI. Although there is a difference between the genders, there is no difference between male and female groups by one way Anova (p> 0,05).

Table 1. Gender differences according to body mass index

	BMI<25 (n=32)		BMI25-35 (n= 84)		BMI≥35 (n=18)		χ^2	p
Gender	n	%	n	%	n	%		
Female	22	59.75	76	90.5	15	83.4	8.29	0.015
Male	10	31.25	8	9.5	3	16.6		

Table 2. Analysis of correlation between parameters

Parameters		Mg	Insulin resistance	BMI	HBA1C
Mg	r	1	0.014	-0.149	-0.053
	p	--	0.870	0.085	0.543
Insulin resistance	r	0.014	1	0.277	0.141
	p	0.870	--	0.001	0.104
BMI	r	-0.149	0.277	1	0.385
	p	0.085	0.001	--	0.0004
HBA1C	r	-0.053	0.141	0.385	1
	p	0.543	0.104	0.0004	--

There was a weak negative correlation between BMI and Mg levels (r = -0,149, p <0,085). Also, there was a moderate positive correlation between BMI and insulin resistance (r = 0.277 p <0.001) and a moderate positive correlation between BMI and HBA1C levels (r = 0.385, p <0.0004). A negligible positive correlation between Mg and insulin resistance was observed (r = 0.014, p <0.870). There was a weak negative correlation between Mg and HBA1C (r = -0.053, p <0.543) and a weak positive

correlation between insulin resistance and HBA1C (r = 0.141, p <0.104) (Table 2).

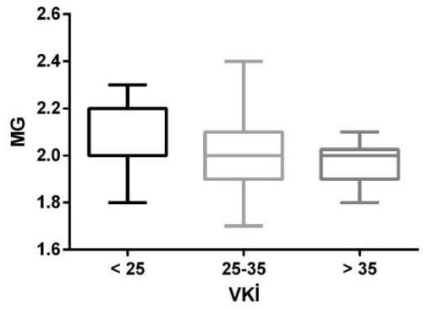

Fig 1: Mg level of among the BMI groups

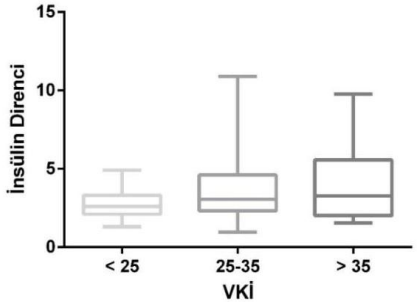

Fig 2: Levels of Insulin Resistance among BMI groups

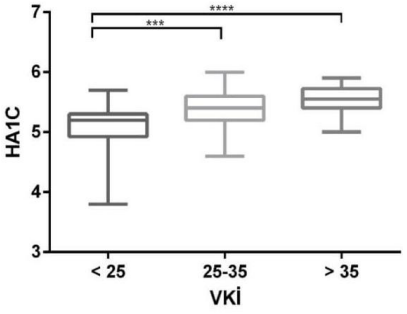

Fig 3: HbA1C levels between BMI groups

There was no statistical significance between the groups (P>0,05) according to the levels of Mg levels among the BMI groups (Figure 1). Levels of insulin resistance among BMI groups were not statistically significant (P> 0.05) (Figure 2). HbA1c levels between BMI groups had following outcomes: BMI between 25-35 group is statistically significant with the group that constitutes the BMI <25 (p=0.0007), and the group with BMI >35 is statistically significant than the group that had patients with BMI <25 (p <0.0001), (Figure 3).

The linear regression analysis showed the following observations: 2.2% of BMI is attributed to an increase in MG levels (r2 = 0.02234, p = 0.0848) (Figure 4); a very low increase in insulin resistance is attributed to a 0.2% increase in MG levels (r2 = 0.000203, p = 0.8702) (Figure 5); and0.2% of the change in HA1C levels is attributed to the increase in MG levels (r2 = 0.002803, p <0.5435) (Figure 6).

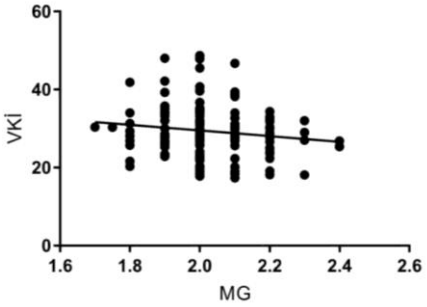

Fig 4: Linear regression analysis between BMI & Mg

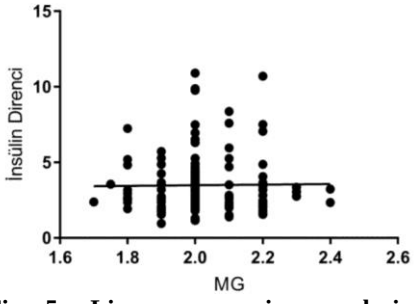

Fig 5: Linear regression analysis between insulin resistance and Mg

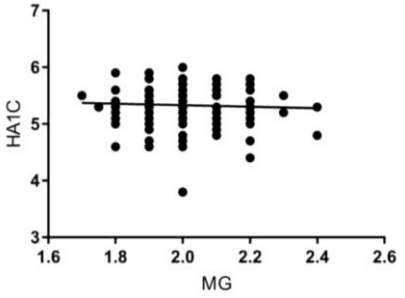

Fig 6: Linear regression analysis between HA1C & Mg

DISCUSSION

Mg may play a role in pancreatic insulin secretion, insulin action in peripheral tissues, and glucose homeostasis and many mechanisms have been presented to support this fact. Firstly; it is the cofactor for many critical enzymes that use high-energy phosphate bonds in glucose metabolism. It has been observed that reduced Mg levels increase intracellular Ca levels, decrease insulin signalling, decrease troxin kinase activity in insulin receptor. Therefore, intracellular Mg levels are important in maintaining insulin sensitivity in adipose tissue and skeletal muscle. In addition, intracellular Mg levels can affect insulin secretion stimulated by glucose by altering the pro inflammatory response, endothelial function, oxidative stress, and cellular iron metabolism in pancreatic cells [9].

In a previous study, dietary magnesium intake was found to be inadequate in non-diabetic individuals with metabolic syndrome. Dietary magnesium intake has a protective effect on insulin resistance [10]. Changes in the cellular Mg, and may alter glucose entry into the cell, leading to insulin resistance development [11]. Another study investigated whether oral mg supplementation improves insulin sensitivity and metabolic control in patients with low Mg levels in type 2 diabetes. Total 63 patients with type 2 diabetes whose serum Mg levels were low and who were using glibenclamide, were included in the study. As a result, in Mg supplemented patients, HOMA-IR index, fasting glucose levels, and HBA1C levels were lower compared to control group. Decreased Mg levels in patients with type 2 diabetes are important in the development of metabolic control of type 2 diabetes and insulin sensitivity [12].

In a study, hypomagnesaemia is found to be associated with the development of impaired glucose tolerance and type 2 diabetes [13]. Plasma and intracellular Mg concentration is strictly regulated by many factors. The most important of these seem to be insulin. Invitro and in vivo studies show that insulin has been implicated in the passage of Mg into the extracellular and intracellular space. Intracellular Mg concentration has been shown to be effective in regulating insulin action.

Insulin independent type 2 diabetes and hypertensive patients have low intracellular Mg concentration. This may result in defective tyrosine kinase activity at the insulin receptor level and exogenous intracellular Ca activity. In the case of insulin independent type 2 diabetes, daily Mg supplementation creates a more favourable intracellular Mg concentration and contributes to insulin-mediated glucose uptake. Several studies have shown that Mg may play a key role in vascular tone and insulin-mediated glucose uptake [14].

In a study of 4637 patients, the risk of developing metabolic syndrome was lower in people with high Mg intake [15]. Takaya J et al showed that Mg is necessary for glucose metabolism and utilization and Mg deficiency is associated with insulin resistance [16]. The relationship between obesity and Mg is not clear. Various studies have evaluated the relationship between BMI and Mg uptake in adults, but the results are still controversial [17]. There is a relationship between Mg deficiency and IR in children. In obese children, serum magnesium deficiency may be developed as a secondary due to reduced Mg intake in diet. Mg supplementation may be important in protecting from type 2 diabetes in obese children [18]. In a study conducted on 276 white South Asian and 315 Canadian women, the relationship between serum Mg concentrations, DM, glucose control, IR and BMI was investigated. Serum Mg concentration was lower in both sexes and in females of South Asian females. Serum Mg and racial differences were not significant after being checked for diabetes drug use. The use of diabetes medications, bad glucose control indicators, insulin resistance, and obesity were thought to be associated with low Mg levels in women [19]. The incidence of type 2 diabetes is thought to be inversely related to Mg. These findings have suggested that consumption of Mg-rich foods such as cereals, beans, nuts, and green leafy vegetables may reduce the risk of type 2 diabetes [20].

If we look at another study, serum Mg levels in the obese group with insulin resistance were significantly lower as compared to the control group. At the same time, there was a positive correlation between serum Mg level and BMI deviation score in obese patients. Low serum magnesium levels may contribute to the development of insulin resistance in obese children [21]. In a study of 536318 participants, 24.516 patients had a significant inverse relationship between Mg intake and type 2 diabetes risks. This was not observed in normal weight subjects when a significant inverse relationship was detected in overweight subjects. These differences were not statistically significant [22]. More than 1 million individuals were studied in 40 studies ranging the age group of 4 to 30 years. The relationship between increased dietary Mg and total cardiovascular disease was observed in these study groups. It was observed that Mg intake was associated with decreased cardiac insufficiency, stroke, type 2 diabetes and all-cause mortality [23]. The relationship between Mg, type 2 diabetes and lipid profile was evaluated. Two grups were made consistig of 50 control groups and 50 patient groups were included in the study. There was a negative correlation between serum Mg levels and fasting blood glucose levels and lipid profiles [24].

Fat tissue is considered as an endocrine organ; it produces reactive oxygen species that cause lipid peroxidation. Mg deficiency causes oxidative stress development. This mineral is the cofactor of many enzymes. It is effective in the cell membrane stability. Mg acts as antioxidant. Low Mg was found as a marker of high oxidative stress in obese individuals [25].

In a study of Libiyan patients, 100 type 2 diabetes and 50 control groups were studied to measure serum Mg levels. According to the control group, a significant decrease in Mg was observed in patients with Libyan diabetic patients. There was a significant negative correlation between serum Mg levels and HBA1C levels and duration of diabetes. There was a negative correlation between fasting plasma glucose and Mg levels. There was no correlation between Mg levels and age [26]. Increased levels of Mg in our study were among the BMI groups. No statistical significance was found between the groups. There is a correlation between BMI and Mg levels in the weak negative direction. This suggests in the unlikely

event that Mg deficiency may lead to weight gain in individuals. There is no statistical significance between the levels of insulin resistance among the BMI groups. Again, there was a moderate positive correlation between BMI and insulin resistance. This was thought to be due to decreased insulin sensitivity in obesity-related peripheral tissues.

Levels of HBA1C between BMI groups; the group consisting of 25-35 of BMI, was statistically significant with the group consisting of the lower than 25 of the BMI, and the group consisting of over 35 was statistically significant with the group consisting of BMI lower 25. There was a moderate positive correlation between BMI and HBA1C levels. This increase may be due to increased insulin resistance due to obesity and consequently increased HBA1C levels with increased blood sugar in individuals. A negligible positive correlation between Mg levels and insulin resistance was observed. This is because our study is conducted as a retrospective data search, so there is no information about the dietary patterns and lifestyle of the patients. A weak negative correlation was found between Mg and HBA1C levels. Elevated serum Mg level may help control blood glucose levels. Accordingly, it may have caused the HBA1C level to decrease. It is thought to be arising from reduced glucose transit in the cells and increased blood glucose levels due to increased insulin resistance.

Since this study was conducted retrospectively, there were certain limitations to this study. Among these, information on the amount of Mg intake in the diet, which may affect the serum Mg levels of patients, could not be obtained from patient records. There was no availability information about the patients' lifestyles and daily physical activity. Another important issue is whether Mg deficiency contributes to the development of obesity or whether Mg levels have changed depending on obesity-related eating habits. For the elucidation of these issues, there is a need for more patients and more detailed information from the patients.

CONCLUSION

In conclusion, Mg deficiency can be seen in obese individuals, although our findings are not very strong. Low serum Mg levels may contribute to the development of diabetes in obese individuals. We cannot fully understand the contribution of low serum Mg levels to the development of diabetes in obese individuals. Therefore, when the patient benefit and the treatment cost of these diseases are taken into account, serum Mg levels should be determined by routine controls and necessary treatment should be done in obese individuals. This can delay obesity and the development of diabetes in individuals. It may be useful in the treatment of obesity.

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