**ORIGINAL ARTICLE**

# Magnesium deficiency in type 2 diabetes

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**Background**. Controversial reports are available regarding the effect of magnesium (Mg) on glycaemic control and lipids profile in diabetic patients. The present study was designed to compare serum Mg levels of type 2 diabetic patients with those of non-diabetic controls and to assess the relationship between serum Mg levels and metabolic parameters of type 2 diabetic patients and healthy control subjects.

**Patients and Methods**. The study was randomized, cross-sectional and 90 healthy blood donors and 38 patients with Type 2 diabetes were recruited serum glucose, insuline, total cholesterol, triglycerides, total $Mg^{++}$ and $Ca^{++}$ were measured. Wight, height and blood pressure were recorded. BMI and IR were calculated.

**Results**. Plasma glucose level, and calculated IR HOMA were significantly higher in diabetic subjects, as we expected (glucose 3.98±0.10mmol/l vs. 6.60± 0.70mmol/l, p=0.04, IR 3.28±0.21mU/l vs. 6.39±0.15mU/l, p=0.01). Plasma lipids, Total cholesterol (Total ch) and triglycerides (5.42±0.98mmol/l vs. 7.30±2.20mmol/l, p=0.04, 1.78±1.12 mmol/l vs. 3.5±1.87mmol/l, p=0.01) were also significantly higher in diabetic patients Serum Mg was lower significantly in diabetic subjects (0.83±0.03mmol/l vs. 0.77±0.09mmol p=0.04). In healthy subjects serum Mg level negatively correlated with body mass index (BMI) (r=-0.316, p<0.01), systolic blood pressure (SBP) (r=-0.326, p<0.01), and diastolic blood pressure (DBP) (r=-0.346, p<0.01). In diabetic group serum Mg level negatively correlated with serum insulin (r=-0.233, p=0.05), IR HOMA (r=-0.280, p=0.04), Total ch (r=-0.331, p=0.02), triglycerides (r=-0.378, p<0.01) and with SBP (r=-0.380, p<0.01) and DBP (r=-0.272, p=0.04).

**Conclusion**. The results of the present study have shown lower serum Mg level in type 2 diabetic patients and demonstrated that almost all components of metabolic syndrome in diabetic patients were associated with serum Mg level.

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Magnesium is one of the most prevalent intracellular cation which plays a crucial role in many physiological processes, as neuromuscular excitability, muscle contraction, hormone secretion, and metabolic processes. Its plasma concentrations represent only 1% of total amount. Hypomagnesaemia is common and is usually asymptomatic [1, 2]. However, a prospective study of Rubeiz and al[3], and other studies showed a significant impact of hypomagnesemia on survival in critically ill patients[4]. Improved methods for assessing magnesium status in the clinic have contributed to the further understanding of magnesium disequilibria in pathogenesis of many diseases[5].

Magnesium deficiency is commonly found in people with type 2 diabetes and may have a negative impact on metabolic syndrome parameters, dyslipidemia, hypertension, as well as on the associated complications as retinopathy and thrombosis [6, 7]. A poor intracellular magnesium concentration, as found in noninsulin-dependent diabetes mellitus and in hypertensive patients, may result in defective tyrosine-kinase activity at the insulin receptor level and exaggerated intracellular calcium concentration [8,9]. Both events are responsible for the impairment in insulin action and a worsening of insulin resistance in noninsulin-dependent diabetic and hypertensive patients. However, previous studies have reported inconsistent results about the effects of intracellular magnesium concentration on insulin action and incidence of diabetes mellitus type 2 in healthy subjects [9,10,11,12]. We assessed the serum level of magnesium in healthy persons and type 2 diabetic subjects, and investigated is there any relationship between serum magnesium levels and components of metabolic syndrome (MS), in healthy subjects and diabetic patients, separately.

## Patients and methods

The study was randomized, cross-sectional, with two groups of subjects, 90 healthy blood donors and 38 patients with Type 2 diabetes (mean age 31.56±10.35 years vs. 37.66±9.62 years, p=0.08), with diabetes duration 0.9±0.5 years, treated with diet only and without late manifestations of diabetes.

*Anthropometrics determination*. Weight and height were measured using standard techniques. BMI was calculated as weight (kg) dividing by height (cm) squared.

Metabolic and cardiovascular determinations: serum glucose, insulin, total Ch, triglycerides, total magnesium and calcium ion ($Ca^{2+}$) were collected in the morning after the participants had been fasting for at least 8h.

Using this data, the degree of insulin resistance (IR) was calculated according to the homeostasis model assessment (HOMA), which is good index for assessing insulin resistance in subjects with different degree of insulin resistance and has a good correlation with insulin mediated glucose uptake calculated by euglycemic hyperinsulinemic glucose clamp [13]. Baseline blood pressure was recorded by standard mercury sphygmomanometer.

*Analytical methods*. Plasma insulin was measured by commercial double-antibody, solid phase radioimmunoassay (INEP, Zemun, Serbia). Serum glucose, total Ch, and triglycerides were measured by commercial enzymatic tests. Serum levels of total magnesium were determined by colorimetric method[14].

*Calculations and Statistical analysis*. The differences between groups were calculated by student's t test. Pearson's correlations were used to test associations among serum level of magnesium and other variables.

## Results

The clinical characteristics of the study groups are indicated in Table 1. The group of type 2 diabetic subjects didn't differ from healthy group for sex, age, gender, BMI, and diastolic blood pressure.

Plasma glucose level and calculated IR were significantly higher in diabetic subjects than control group (glucose 3.98±0.10 mmol/l vs. 6.60±0.70 mmol/l, p=0.04; IR 3.28±0.21 mU/l vs 6.39±0.15 mU/l, p=0.01). Plasma lipids, total ch and triglycerides (5.42±0.98 mmol/l vs. 7.30±2.20 mmol/l, p=0.04; 1.78±1.12 mmol/l vs 3.5±1.87 mmol/l, p=0.01) were also significantly higher in diabetic patients (Table 1). SBP was significantly higher in diabetic subjects than control group (126±8.26 mmHg vs. 149.16±11.14, p=0.03). Serum Mg was lower significantly in diabetic subjects (0.83±0.03 mmol/l vs 0.77±0.09 mmol p=0.04) (Table 1). The values of serum $Ca^{2+}$ didn't differ significantly between groups.

In healthy subjects serum Mg level correlated negatively with age, BMI, SBP, and DBP, and positively with serum Ca (Table 2). In diabetic group, serum Mg level correlated negatively with SBP, DBP, serum insulin, and insulin resistance index (Table 2). A negative correlation between serum Mg and plasma concentration of total cholesterol and triglycerides were also found in both groups (Table 2).

## Discussion

In this study, total serum magnesium level of type 2 diabetic patients was considerably lower than the magnesium level in healthy controls, of similar age and nutritional status. Nadler et al. reported that 25-39% of type 2 diabetics have low levels of serum magnesium in USA[6]. The reasons why magnesium deficiency is common in diabetic patients are not clear and include increased losses of urinary magnesium, due to glucosuria and osmotic diuresis, or due to treatment with thiazides or loop diuretics. The other serious reasons could be lower magnesium dietary intakes of or lower magnesium absorption. The ARIC study investigated prospectively dietary magnesium intake and serum level in cohort of non-diabetic middle-aged adults and concluded that low serum magnesium level is independent predictor of incident type 2 diabetes, but no association was detected between dietary magnesium intake and the risk for incident type 2 diabetes [11]. In Swiss adults with type 2 diabetes dietary intake of magnesium appears sufficient, as reported Walti et al.[12]. Our patients were middle-aged slightly overweight, with short duration of diabetes and unfortunately, we didn't undergo dietary assessment in both groups of participants. We demonstrated lower level of insulin sensitivity index in diabetic group, with significantly higher SBP and higher plasma level of triglycerides, as the components of MS. The level of insulin and insulin sensitivity index were associated with serum

**Table 1.** *Baseline characteristics of study groups*

| | Controls (n=90) | DM type 2 (n=38) | P value |
|---|---|---|---|
| Sex(%men) | 67% | 55% | NS |
| Age(years) | 31.56±10.35 | 37.66±9.62 | NS |
| BMI(kg/m$^2$) | 24.83±0.50 | 27.32±1.07 | NS |
| SBP(mmHg) | 126.69±8.26 | 149.16±11.14 | 0.03 |
| DBP(mmHg) | 82.70±4.87 | 85.83±3.76 | NS |
| Glucosa(mmol/l) | 3.98 ±0.10 | 6.36±0.70 | <0.01 |
| Insulin(mU/l) | 17.93±0.91 | 23.10±3.66 | NS |
| IR HOMA | 3.28±0.21 | 6.39±1.15 | <0.01 |
| Total Ch(mmol/l) | 5.05±0.12 | 7.00±0.72 | 0.02 |
| Triglycer(mmol/l) | 1.40±0.12 | 2.89±0.99 | <0.01 |
| $Ca^{2+}$(mmol/l) | 1.10±0.09 | 1.07±0.02 | NS |
| Mg(mmol/l) | 0.82±0.03 | 0.77±0.09 | 0.04 |

*Data are means+/-SE; p values were derived from paired Student's test*

**Table 2.** *Correlations between Mg level and antropometric and metabolic parameters in control group and diabetic patients*

| | Control Gp r | P value | Diabetic pts r | P value |
|---|---|---|---|---|
| Age | -0.615 | <0.01 | 0.225 | NS |
| BMI | -0.316 | <0.01 | -0.228 | NS |
| SBP | -0.326 | <0.01 | -0.380 | <0.01 |
| DBP | -0.346 | <0.01 | -0.272 | 0.04 |
| Glucosa | 0.241 | NS | 0.155 | NS |
| Insulin | 0.009 | NS | -0.233 | 0.05 |
| IR HOMA | 0.056 | NS | -0.280 | 0.04 |
| Total Ch | -0.369 | <0.01 | -0.331 | 0.02 |
| Triglycerides | -0.363 | <0.01 | -0.378 | <0.01 |
| $Ca^{2+}$ | 0.334 | <0.01 | 0.179 | NS |

magnesium level only in diabetic group, and SBP, DBP and triglycerides were related to serum Mg in both groups. We have shown that almost all components of MS in type 2 diabetic subjects were associated with serum Mg level, and that is consistent with statement that low serum Mg level could be responsible for the pathogenesis of MS, and type 2 diabetes[7-9]. Barbagallo M suggests defective tyrosine-kinase activity at the insulin receptor level and decrease smooth cell responsiveness to depolarizing stimuli could be a consequence of low intracellular Mg concentration, as found in type 2 diabetes and in hypertensive patients, [9]. In cross-sectional population-based study Romero F and Rodriguez-Moran M compared subjects with MS and disorder-free controls and revealed a strong relationship between decreased serum magnesium and MS[15]. Among the components of MS, dyslipidemia and hypertension were strongly related to low serum magnesium levels[15]. Takaya J et al examined the basal levels and changes in intracellular Mg ion of platelets, in diabetic and obese children, and reported that decreased intracellular Mg might underline the initial pathophysiologic events leading to insulin resistance and abnormality of platelet coagulation[8]. Our findings show that hypomagnesaemia, if it is present in subjects without diabetes, could be followed by hypertension and hyperlipoproteinaemia, and that particulary in diabetic subjects, serum Mg level is closely related to parameters of insulin resistance or MS. Rodrigez-Moran et al demonstrated improved insulin sensitivity and metabolic control in type 2 diabetic patients who received magnesium supplementation[16].

In conclusion, the results of the present study revealed lower serum Mg level in type 2 diabetic patients and demonstrated a strong relationship between decreased serum magnesium and almost all components of MS in these patients. In healthy subjects serum Mg level was associated with systolic and diastolic blood pressure.

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