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Serum ionized magnesium in diabetic older persons☆,☆☆

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ABSTRACT

Objective. Several alterations of magnesium metabolism have been associated with type 2 diabetes pathophysiology, a condition particularly frequent in older persons. We aimed to evaluate serum total (Mg-tot) and serum ionized magnesium (Mg-ion) in older persons with type 2 diabetes in order to explore clinically applicable methods for the detection of magnesium deficit.

Material/Methods. Mg-tot and Mg-ion were measured in 105 fasting subjects with type 2 diabetes (mean age: 71.1 ± 0.8 years; M/F: 45/60) and in 100 age-matched non-diabetic control persons (mean age: 72.2 ± 0.8 years; M/F: 42/58).

Results. Mg-ion concentrations were significantly lower in diabetic persons compared with controls (0.49 ± 0.05 mmol/L vs. 0.55 ± 0.05 mmol/L; $p < 0.001$). Mg-tot was also slightly but significantly lower in diabetic patients (0.82 ± 0.007 mmol/L vs. 0.84 ± 0.006 mmol/L; $p < 0.05$). There was an almost complete overlap in the values of Mg-tot in older diabetic patients and controls; conversely, 44.8% of diabetic patients had Mg-ion values below 0.47 mmol/L, while none of the controls did. After adjustment for age, sex, BMI, and triglycerides, Mg-tot was significantly associated with FBG in all the participants ($p < 0.05$) and Mg-ion was significantly associated with FBG in all the participants ($p < 0.01$) and with HbA1c in diabetic participants ($p < 0.001$).

Conclusions. Alterations of magnesium serum concentrations are common in type 2 diabetic older adults; Mg-ion evaluation may help to identify subclinical magnesium depletion (i.e. in patients with normal Mg-tot); the close independent associations of Mg-tot and Mg-ion with FBG and with HbA1c reinforce the possible link between magnesium homeostasis and altered glucose metabolism.

1. Introduction

There is compelling evidence suggesting that magnesium depletion may play a role in the pathophysiology of insulin-resistance and/or altered glucose homeostasis in type 2 diabetes mellitus [1–3]. Magnesium is the second most abundant intracellular cation after potassium, and it is involved in a number of fundamental biochemical processes, comprising all ATP transfer

Abbreviations: ATP, adenosine triphosphate; BMI, body mass index; DBP, diastolic blood pressure; ESRD, end stage renal disease; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; ISE, ion-selective electrode; NADPH, nicotinamide adenine dinucleotide phosphate-oxidase; NMR, nuclear magnetic resonance; Mg-tot, total serum magnesium; Mg-ion, extracellular free levels of magnesium; SBP, systolic blood pressure.

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reactions. Magnesium ion plays a key role in the regulation of insulin actions, including insulin-mediated glucose uptake [1].

Type 2 diabetes has been associated with extracellular and intracellular magnesium depletion. Epidemiologic studies have found a high prevalence of hypomagnesemia in persons with type 2 diabetes [4–7], especially in those with poorly controlled glycemic values [4,5], and with micro and macrovascular chronic complications [8]. Recently, a close and independent relationship of low serum Mg concentrations and ventricular ectopy in patients with type 2 diabetes has been reported [7]. Hypomagnesemia is currently considered an accurate predictor of death and of progression to ESRD in patients with type 2 diabetic nephropathy [9,10]. Two meta-analyses of prospective studies concluded that magnesium intake is inversely associated with type 2 diabetes [11,12]; magnesium intake has been also strongly and inversely associated with the metabolic syndrome [13,14], while hypomagnesemia has been independently associated with the development of impaired glucose tolerance [15]. A recent study showed a close relationship between the presence of diabetes and the lower levels of magnesium in obese subjects who undergo bariatric metabolic surgery [16].

Although the importance of magnesium homeostasis in glucose metabolism is well appreciated, magnesium metabolism has not become the focus of routine attention for the care of type 2 diabetes patients in the clinical practice. The main reasons for this include the difficulties in obtaining an easily available, accurate, and reproducible measure of magnesium status since the concentrations of total serum magnesium (Mg-tot), commonly used as an estimation of magnesium in the clinical practice, are extremely constant and do not accurately reflect the body magnesium status [1]. Depletion of intracellular as well as of ionized serum magnesium has been reported in the presence of normal levels of Mg-tot [17,18]. Because aging represents a major risk factor for Mg insufficiency [19], it is possible that older diabetic subjects are at further risk of magnesium deficit, which may not always be clinically apparent.

The present study was designed to evaluate magnesium metabolism in older type 2 diabetes patients measuring Mg-tot and the extracellular free levels of magnesium (Mg-ion) with a Mg-specific ion-selective electrode (ISE) in order to explore clinically applicable methods for the detection of magnesium deficit in older persons with type 2 diabetes.

2. Methods

2.1. Subjects

Two hundred and five older persons (aged ≥ 60 years), 105 type 2 diabetic patients (mean age: 71.1 ± 0.8 years; M/F: 45/60) and 100 age-matched non-diabetic controls (mean age: 72.2 ± 0.8 years; M/F: 42/58) were consecutively recruited from the Outpatient Clinic of the Geriatric Unit at the University Hospital of Palermo, Italy. Anthropometric and laboratory data including Mg-tot and Mg-ion were measured (Table 1). All type 2 diabetic persons recruited for the present study were recently being diagnosed with diabetes, treated with diet therapy only and had never been treated before with insulin or hypoglycemic agents. In order to avoid possible interferences with dietary components and physical exercise that may alter serum magnesium concentrations, we advised participants not to modify their dietary and physical activity usual habits during the study period. None of the patients had been on diuretic therapy for at least 1 month before the study and none had significant renal dysfunction, as assessed by serum creatinine levels and calculated glomerular filtration rate (GFR) [20].

Table 1 – Clinical characteristics of study participants.

Parameter	Controls	type 2 diabetes	p
N	100	105	
Age (years)	72.2 ± 0.8	71.1 ± 0.8	NS
M/F	42/58	45/60	NS
BMI	28.4 ± 0.9	28.8 ± 1.0	NS
Systolic BP (mm Hg)	145.8 ± 2.1	146.9 ±2.0	NS
Diastolic BP (mm Hg)	75.7 ± 0.9	76.1 ± 1.0	NS
HR (bpm)	74 ± 5.1	76 ± 4.1	NS
GFR (mL/min/1.73 m^2)	80.4 ± 2.25	83.3 ± 3.2	NS
FBG (mg/dL)	98.1 ± 1.6	142.6 ± 5.2	$p < 0.001$
Triglycerides (mg/dL)	113.3 ± 5.2	141.6 ± 8.3	$p < 0.01$
Mg-tot (mmol/L)	0.84 ± 0.006	0.82 ± 0.007	$p < 0.005$
Mg-ion (mmol/L)	0.55 ± 0.05	0.49 ± 0.05	$p < 0.001$

BMI: body mass index; BP: blood pressure; bmp: beats per minute; GFR: glomerular filtration rate; FBG: fasting blood glucose. Mg-tot: serum total magnesium; Mg-ion: serum ionized magnesium. To convert mg/dL of glucose in mmol/L multiply by 0.5551.

No differences in age, sex, race, blood pressure levels, GFR, and body mass index (BMI) were present between the groups (Table 1). It is well known that alcohol abuse may alter magnesium metabolism by means of different mechanisms, i.e. malnutrition, increased urinary magnesium loss, among others [21]. Therefore, we excluded persons with alcohol abuse (intended as alcohol consumption higher or equivalent to more than 1 glass of wine per day) and requested the participants specifically not to change their usual alcohol consumption habits since this could affect magnesium circulating concentrations.

The study was approved by the ethical committee of our Institution and was conducted in accordance with the guidelines of the Declaration of Helsinki for human research. An informed consent was signed by all participants. Exclusion criteria included: not compensated acute disease, such as severe congestive heart failure, severe chronic obstructive pulmonary disease, angina pectoris, acute myocardial infarction or stroke in the previous 6 months of the study, severe uncontrolled hypertension (SBP ≥ 180 mm Hg and/or DBP ≥ 90 mm Hg), moderate to severe renal or hepatic disease, and/or alcohol abuse.

2.2. Magnesium measurements

Blood samples were obtained from participants after they had fasted for 10 h and after they had been in a sitting or supine position for 15 min. Serum Mg-tot concentrations were measured by standard colorimetric techniques with an