Magnesium deficiency: carbohydrate and lipid metabolism disorders and risk of type 2 diabetes

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ABSTRACT

In the pathophysiology of non-insulin dependent diabetes, characterized by hyperglycemia, at least three factors seem to be involved: a defect in insulin secretion, increased hepatic glucose production and insulin target. Over the past decade, significant advances in knowledge about the cellular mechanisms of action of insulin were performed. This has led to a better understanding of the mechanisms that could explain the insulin resistance in the type 2 diabetes, regardless of their primary or secondary origin. The deficit of magnesium is frequently associated with diabetes mellitus. This depletion ubiquitous cation in the body, alters glucose metabolism and insulin sensitivity and, is also implicated in the occurrence of complications and the risk of diabetes occurred among subjects predisposed who should receive a follow-up search of a magnesium deficiency, expression of a lack of intake and / or increased urinary loss. In our study, we found a correlation between magnesium deficiency and metabolic disorders affecting carbohydrate and lipid metabolism, labeled with revealing glycemic levels, insulin resistance, and lipid profile. The cause of magnesium deficiency in diabetic patients is not fully known. As the beneficial effects of magnesium supplementation, the long-term studies are needed before recommending routine supplementation in type 2 diabetes and subjects at risk with subclinical magnesium deficiency.

Key words: Magnesium deficiency-glucose level-lipid profile-insulin resistance

INTRODUCTION

Magnesium is an essential cofactor for some enzymes involved in the metabolism of glucose and insulin; it serves as a coenzyme in phosphorylation reactions necessary to activate the insulin receptor and the phosphorylation of adenosine triphosphate (ATP).

Magnesium is an intracellular cation but the concentration of magnesium in plasma or serum should not be considered a poor indicator of the total magnesium; this is the second-best indicator of the mineral magnesium pool after urinary magnesium, so his assessment should not be overlooked. It is important to emphasize that inadequate magnesium intake is usually diagnosed.

The calcium-magnesium balance is strictly mediated by the coordinated action of the intestines, kidneys and bones.

Since magnesium is essential because of its involvement in the magnesium-ATP complex that takes part in all the phosphate transfer reactions for cellular use and supply, it is not surprising that a deficiency of this mineral is involved in altering the metabolism and for chronic diseases in the genesis of additional complications.

Numerous studies have shown that there is magnesium deficiency in subjects with glucose intolerance, related to 1st degree T2D, women with a history of gestational diabetes and diabetic subjects.

Some authors propose supplementation with magnesium in the primary prevention of type 2 diabetes, in addition to diet and physical exercise.

The objective of our study, based on data from the literature, is to study the magnesium pool present in subjects at risk of developing type 2 diabetes.
The Magnesian status as well as the metabolic profile are carried out in each of the groups in order to isolate subjects likely to develop insulin resistance which, combined with the secretory defect of insulin, would lead to more or less long-term diabetes.

The purpose of this combined study is:
- to better understand the mechanisms of insulin resistance and insulin secretion disorders;
- to propose a nutritional education program in the context of preventive nutrition (correction of dietary errors, dietary monitoring and supplementation with magnesium) and an adapted physical activity program, capable of reversing and regularizing the anomalies responsible for of type 2.

**MATERIALS AND METHODS**

**Population**

This study, which is intended to be prospective, is carried out within a population divided into 4 groups:
- group 1: normal subjects (controls) (102)
- group 2: subjects with decreased glucose tolerance [(post prandial glucose between 1.40-1.99 g/L)] (168)
- group 3: subjects related to the first degree of patients with type 2 diabetes (133)
- group 4: patients with a history of gestational diabetes (172)

The results found in groups 2, 3 and 4 will be compared with those found in group 1.

All the subjects studied were recruited over a period of 14 months at the level of the internal medicine departments of the Blida University Hospital, the diabetes department of the EPH of Blida, the gynecological services - Obstetrics Unit Hassiba Ben Bouali (CHU Blida) and EPH Zeralda.

The study population meets the inclusion criteria:
- normal subjects aged between 35 and 55 years.
- subjects with decreases in glucose tolerance of males and females aged between 35 and 55 years.
- patients with a history of gestational diabetes, aged 30-49 years.
- first-degree subjects of male and female T2D between 35 and 55 years of age.

The exclusion criteria are:
- patients with associated tare, such as: hypertension, cardiopathy, endocrinopathy, dysparathyroidism, osteomalacia and other oncological diseases, which could interfere with the results.
- diabetics whose microalbuminuria is disturbed.
- patients with hemoglobin less than 10 g / dL.
- subjects whose feed can be rich in magnesium (fish and dried fruit)
- subjects whose water intake is based on mineral water (rich in magnesium)

**Samples**

The blood samples were taken on dry tubes, on EDTA tubes (K3 EDTA) and on heparinized tubes (lithium heparinate), in the morning on an empty stomach. Urine is collected in a plastic container (not metallic) = Urine pot.

All assays were performed on the same day, with the exception of insulin. For this hormone, aliquots of serum were stored in the freezer until assayed.

**Methods**

Dosages of the different biological parameters Magnesium nutritional status: Plasma and urinary magnesium assays were performed using the chlorophosphonazo III (CPZ III) colorimetric method on the Cobas C-501 analyzer Measurement of fasting and postprandial blood glucose: it was carried out on a Microlab 300 spectrophotometer using a glucose oxidase (GOD) colorimetric enzymatic method Determination of glycated hemoglobin was carried out on the Cobas Integra 400 (Roche) analyzer by TINIA (turbidimetric inhibition immunoassay).

Dosage of insulin: the dosage of insulin was carried out on the automaton Elecsys 2010 (Roche) by electrochimiluminescence “ECLIA” it is a method “sandwich”.

Determination of cholesterol: it was carried out on a Microlab 300 spectrophotometer using a colorimetric enzymatic method Determination of triglycerides: this was carried out by colorimetric enzymatic method (Glycerol PO-PAP method) Calculation of the HOMA insulin resistance index (Homoeostatic Model Assessment-insulin resistance): peripheral resistance to insulin is an early sign of diabetic risk and precedes by several years the proven appearance of type 2 diabetes.

In this case, it is essential to use a mathematical modeling technique, based on the knowledge of the quantitative responses of the main organs involved in glucose metabolism, as proposed by the Turner team.

The HOMA index makes it possible to demonstrate insulin resistance in a simple and reliable way. Calculated during the simultaneous measurement of fasting glucose and insulin, it allows early detection of subjects who may develop diabetes and thus undertake appropriate measures.

Its reproducibility in clinical routine is good. This index is all the more useful as the number of diabetics increases worryingly. The values of simultaneous fasting glucose and insulin assays should be systematically reported in the future with the HOMA index.

This parameter should assist in the identification of pre-diabetic conditions in large clinical or epidemiological studies and its use should be much broader.

There is a close correlation between the HOMA index and the reference test: the hyperinsulinic euglycemic clamp, a reference method for evaluating insulin resistance, reserved for clinical research, described by R DeFranzo.
Calculation: the HOMA index is calculated according to the formula:
\[ \text{Insulin (mU/L) \times glucose (mmol/L)} \div 22.5 \]

The normal value of the HOMA index is less than 2.44. Interpretation: a high HOMA score indicates the presence of insulin resistance. This is a risk factor for type 2 diabetes.

RESULTS
Comparison of the mean of the parameters of the 4 groups studied by the ANOVA test

Table 1: Comparison of the mean of the parameters of the 4 groups studied by the ANOVA test

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls (n = 102)</th>
<th>Glucose Intolerant (n = 168)</th>
<th>Related to 1st degree to type 2 diabetes (n = 133)</th>
<th>ATCD de DG (n = 172)</th>
<th>Statistical significance (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.69 ± 5.34</td>
<td>47.76 ± 6.28</td>
<td>44.75 ± 6.40</td>
<td>35.93 ± 4.53</td>
<td>0.001</td>
</tr>
<tr>
<td>Blood magnesium (mg/L)</td>
<td>20.31 ± 2.65</td>
<td>17.41 ± 2.77</td>
<td>18.45 ± 2.88</td>
<td>16.38 ± 2.77</td>
<td>0.001</td>
</tr>
<tr>
<td>Urinary magnesium (mg/L)</td>
<td>89.34 ± 47.78</td>
<td>105.71 ± 45.58</td>
<td>99.22 ± 48.80</td>
<td>112.51 ± 41.85</td>
<td>0.01</td>
</tr>
<tr>
<td>Fasting glucose (g/L)</td>
<td>1.01 ± 0.51</td>
<td>1.31 ± 0.04</td>
<td>1.41 ± 0.10</td>
<td>1.25 ± 0.09</td>
<td>0.001</td>
</tr>
<tr>
<td>Post prandial glucose (g/L)</td>
<td>1.31 ± 0.18</td>
<td>1.63 ± 0.18</td>
<td>1.78 ± 0.71</td>
<td>1.51 ± 0.17</td>
<td>0.001</td>
</tr>
<tr>
<td>Glycated Hemoglobin (%)</td>
<td>5.05 ± 1.64</td>
<td>6.18 ± 0.57</td>
<td>6.85 ± 0.49</td>
<td>6.10 ± 0.47</td>
<td>0.001</td>
</tr>
<tr>
<td>Insulin (µU/mL)</td>
<td>08.27 ± 2.37</td>
<td>10.27 ± 4.37</td>
<td>11.13 ± 4.94</td>
<td>10.76 ± 4.59</td>
<td>0.001</td>
</tr>
<tr>
<td>Cholesterol (g/L)</td>
<td>1.59 ± 0.46</td>
<td>1.99 ± 0.36</td>
<td>2.31 ± 0.37</td>
<td>2.17 ± 0.35</td>
<td>0.01</td>
</tr>
<tr>
<td>Triglycerides (g/L)</td>
<td>1.06 ± 0.80</td>
<td>1.53 ± 0.67</td>
<td>1.61 ± 0.64</td>
<td>1.80 ± 0.62</td>
<td>0.05</td>
</tr>
<tr>
<td>IR-HOMA</td>
<td>2.06 ± 1.48</td>
<td>2.41 ± 1.28</td>
<td>2.52 ± 1.19</td>
<td>2.55 ± 1.16</td>
<td>0.01</td>
</tr>
</tbody>
</table>

For the variables, the results are given as means ± SD;

n: number of patients; NS: not significant difference p> 0.05;

antecedent of DG: history of gestational diabetes; IR-HOMA: Homeostasis Model Assistance-Insulin resistance

The results of our work summarized in this table indicate, in subjects at risk for type 2 diabetes:
- a decrease in magnesemia
- an high level of fasting and postprandial glucose and glycated hemoglobin
- an characteristic insulin resistance index
- higher levels of lipids (cholesterol and triglycerides) than controls

DISCUSSION AND CONCLUSION

Magnesium deficiency is one of the factors involved in the genesis of primary abnormalities in relation to defects in signaling pathways, expression of mRNAs and proteins responsible for the final stages of secretion and exocytosis of insulin and, transport, phosphorylation, glucose oxidation in the β-cell, hepatic glucose production (glucose-6-phosphatase / glucokinase pair), and its peripheral use under the effect of insulin (post-reaction cascades Tyrosine kinase receptor resulting in the action of insulin).

Thus, all metabolic profiles at risk for type 2 diabetes, such as insulin resistance, subjects with glucose intolerance, subjects related to 1st degree diabetic subjects and women with a history of gestational diabetes, A follow-up in search of a magnesium deficiency, expression of an insufficiency of contribution and / or an increased urinary loss.

In investigations, the concentration of serum magnesium, of which 65-75% is diffusible, is the most clinically available test for assessing the state of body magnesium; However, it can not reflect the true total magnesium content of the body. In addition, serum levels of magnesium within normal limits may coexist with decreased intracellular concentrations; Magnesium content in muscles, red blood cells, lymphocytes and bone provides a more accurate assessment of the magnesia.
status of the body, but these compartments are not readily available for clinical use.

Recently specific ionic electrodes have become available to determine the ionized Mg in plasma and the first results suggest that this could be a better indication of the Mg state relative to the total concentration of serum magnesium. Further evaluation is required.

The effect of magnesium deficiency on degenerative complications remains difficult to determine.

The difficulty of the studies derives from the length of time necessary for the development of diabetic complications, the necessity and a good evaluation of the magnesic status, otherwise only correction or improvement of these complications under magnetic treatment would establish a causality.

Concerning the beneficial effects of magnesium supplementation, long-term studies are needed before recommending systematic supplementation in type 2 diabetics and at risk subjects with subclinical magnesium deficiency. In this pharmacological indication, the magnesium salt retained should be the one whose therapeutic coefficient (letal dose or LD 50 / effective dose or ED 50) would provide the widest margin of safety.

Any pharmacological parenteral therapy intervention study should only be performed with the magnesium salt which would have the highest therapeutic coefficient in the indication. Another path that deserves to be exploited is the modulation of oxidative stress. Under these conditions, oxidative stress may have beneficial effects on several biological functions and metabolic pathways; Its deleterious cellular effects and its initiating role of insulin resistance would be repressed.

REFERENCES


