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Magnesium - An Essential Factor in Glucose Metabolism

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Abstract: ***Plasma and intracellular magnesium concentrations are tightly regulated by several factors. Insulin seems to be one of the most important. The studies have demonstrated that insulin may modulate the shift of magnesium from extracellular to intracellular space. Intracellular magnesium concentration affect insulin action, mainly by oxidative metabolism of glucose. Intracellular magnesium deficiency may affect the development of insulin resistance and alter the glucose entry into the cell. Low levels of magnesium have been associated with a number of chronic diseases, such as insulin resistance and diabetes, hypertension, disorders of the cardiovascular system, retinopathy, nephropathy or neuropathy. Experimental studies in animals and cross-sectional studies in humans suggest that low levels of magnesium levels may impair glucose metabolism and lead to type 2 diabetes. Magnesium supplementation leads to an improvement fasting glucose levels and insulin sensitivity indices. Magnesium supplementation improves insulin sensitivity in overweight patients even in normomagnesemic and without diabetes. This suggests the need for early optimize the level of manganese to the prevention of insulin resistance and progression of diabetes in people with overweight. Because recent data suggest a relationship impairment of glucose homeostasis with hypomagnesemia it is right to routinely monitor magnesium levels in these patients.***

Keywords: magnesium, TRP channel, hypomagnesemia, glucose metabolism, insulin resistance, diabetes

1. Introduction

Many ions play an important role in the body's metabolic processes, including the maintenance of glycemic homeostasis. This is indicated by both clinical observations and experimental studies. The function TRPM7(transient receptor potential melastatin-subfamily member 7) plays an important role in these processes. [1]

Magnesium is a very important elektrolyte that plays a manifold role in human body. [2]

Magnesium deficiency may cause varius disorders, its deficiency may cause disturbances of the cardiovascular or nervous system function, as well as disorders of glucose metabolism. [3]

Magnesium plays a key role in metabolism of glucose and insulin, mainly due to its influence on tyrosine kinase activity of insulin receptors, on activity of glucose transporter protein 4 (GLUT4) and on control of glucose translocation to cells.

Low levels of magnesium result in aberrant kinase activity and reduced cellular glucose utilization, which in turn increases insulin resistance [4]

The importance of magnesium to glucose metabolism and insulin sensitivity was revealed in experimental as well as clinical researches. [5 - 10]

It has been shown that patients with hypomagnesemia and type 2 diabetes have an increased risk of developing complications. [11] The question of interdependence requires further investigation.

In clinical practice, the magnesium content in human body is evaluated based on its serum level. In special cases, more sensitive tests are required. [12]

Magnesium plays an important role in insulin effect while insulin stimulates magnesium absorption in insulin-sensitive tissues. Magnesium deficiency causes insulin resistance, hence it may also be one reason for glucose intolerance. The mechanisms of these processes are not completaly understood. However, it is believed that the hypomagnesemia may interfere cellular glucose transport, decrease insulin secretion or interfere interaction between insulin and its receptor.

Comprehensive overview of hypomagnesemia in diabetes progression, based on literature and own studies, was presented by American authors. [13]

Authors believe that magnesium supplementation may have significantly beneficial influence on slowness of prediabetes progression to clinically obvious diabetes, what is associated with proper insulin secretion and decrease of insulin resistance.
Canadain authors, based on studies on 2295 patients, stated that higher magnesium intake causes insulin resistance dilution. [14]

The relation between magnesium deficiency and insulin resistance was observed in obese children. [15]

Authors performed the test of magnesium serum level and insulin resistance index (IR) in group of 24 children with BMI ≥ 85 percentiles. They stated that magnesium supplementation or higher intake of magnesium rich food may be an important tool in prevention of type 2 diabetes in obese children.

Celik et al. presented the study on correlation between magensium serum level and insulin resistance index in group of obese children. [16]

Authors observed significantly lower magnesium level in group of obese children with higher IR. They stated that the decreased magnesium level may favor progression of insulin resistance in obese children.

American scientists analyzed the influence of magnesium intake on progression of metabolic syndrome in young adults. [17]
Authors stated that the young adults who consumes higher magnesium doses have lower risk of metabolic syndrome progression.

Brazilian authors studied magnesium deficiency in patients with metabolic syndrome [18].

This relation may be connected with postreceptor insulin resistance.

Type 1 as well as type 2 diabetes are closely linked with magnesium deficiency. The frequency of hypomagnesemia in patients with type 2 diabetes is estimated in wide range between 13,5 - 47,7%.

Recently, many researches demonstrated magnesium deficiency in patients with type 2 diabetes. [19.20,21]

In type 2 diabetes, insulin resistance plays the major role. Therefore magnesium deficiency that leads to insulin resistance increase, may be one of reason for higher incidence of type 2 diabetes and also its chronic complications. [21]

An extensive analyze of relation between magnesium intake and the risk of type 2 diabetes progress, based on literature from 1966-2007, was presented by Swedish scientists. [22]

Based on this overview, authors suggested that the intake of magnesium rich food may reduce the risk of type 2 diabetes occurrence.

Recently, Chinese authors presented results od diagnostic study in a group of 178 patients with glucose metabolism disorder: 33 patients with type 2 diabetes diagnosed and145 patients with prediabetes diagnosed. Additionally, magnesium serum levels were evaluated. The results were compared with control group. The relation between low magnesium level and incidence of glucose metabolism disorder was stated. According to authors' opinion, the results indicate that the low magnesium level is an independent risk factor in prediabetes progression and type 2 diabetes' [23]

Evaluation of the correlation between inuslin resistance and magnesium deficiency in patients with type 2 diabetes was performed by Indian authors who observed distinctively low magnesium level with high HOMA-IR level in 38 patients. [24]

The research involved children, youth and young adults. The significant reduction of magnesium level was identified in patients with diabetes.

In the Chutia and Lynrah study in group of 38 patients with type 2 diabetes, the lower magnesium serum level was revealed also in patients with diabetes in comparison to control group [25]. The strong relation between magnesium serum level and insulin sensitivity indexes was revealed.

The negative correlation between magnesium level and IR index and the positive correlation between magnesium level and QUICKI index (quantitative insulin sensitivity check index) were stated.

The reduction of magnesium serum level was observed also in other than type 2 diabetes types.

Lin and Huang revealed the relation between lower magnesium level (and other ions) and incorrect metabolic control in patients with type 1 diabetes [26].

Authors proposed the opinion that supplementation of magnesium, zinc and chromium ions improves metabolic control, what was revealed in experimental studies on mince.

Recently, reports about hypomagnesemia occurrence in patients with monogenic diabetes (HNF1β mutation). [27]

Iranian authors conducted research on magnesium suplementation effects in pregnant patients with GDM (gestational diabetes). [28]

They stated that the magnesium suplementation has a positive effect on metabolic state of examined patients and reduces incidence of hyperbilirubinemia and necessity of new born children hospitalization. Lower magnesium serum levels in pregnant with GDM were observed also by other scientists. [29]

Many studies revealed that magnesium deficiency increases the risk of chronic diabetes complications occurence, eg. retinopathy, nephropathy, neuropathy.

Dasgupta et al. analyzed concomitance of lower magnesium levels and chronic complications in 150 patients with type 2 diabetes. [30]

Hypomagnesemia was identified in patients with worse metabolic control and presence of complications, ia. retinopathy, nephropathy and foot ulceration.

Shaikh and Karira observed concomitance of lower magnesium level and symptoms of cardiac failure in patients with diabetes. [31]

Pham et al. study revealed that lower potassium level accelerates occurrence of renal disorder in patients with type 2 diabetes. [32]

Kondu et al. proposed that hypomagnesemia may be a prognostic indicator of diabetic retinpathy progression [33].

It was observed that the reduction of magnesium level in patients with diabetic kidney disorder potentaites osteoporosis. [34]

The analysis of stories of diabetic patients hospitalized in the intensive care performed by Curiel-Garcia et al. revealed that hypomagnesemia diagnosed at the moment of admission is linked to high death rate in critically ill patients with type 2 diabetes [35].

Recently, extensive coverage of experimental studies on the effects of extracellular Mg2 + concentrations on insulin secretion has been published. The results of these studies are not conclusive and the authors believe that further research is needed to clarify whether modulation of intracellular concentrations of Mg2 + by TRPM7 affect β-cell functions and glucose-stimulated insulin secretion. [36]

2. Conclusions

In the opinion of many authors, further research is necessary for the final explanation of this problem.

These numerous and various reports regarding hypomagnesemia in glucose homeostasis disorders, underline the need of controling magnesium level and considering this test as a regular one for all diabetic patients, regardless of diabetes type and also for patients with pre-diabetic state. [12,25]

Although the risk of hypomagnesemia caused by insufficient dietary magnesium supply is low because of mechanisms that limit the renal excretion of this element. However, bacause of the role of magnesium in glucose metabolism in patients with disorder of this metabolism, the magnesium level should be controled carefully and magnesium supplementation should be applied if necessary. There are more and more studies devoted to the mechanisms of magnesium deficiency in diabetes and the possible role of Mg supplementation in the prevention and treatment of disease. [37,38,39]

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