EDITORIAL

Towards a link between magnesium, exercise, and risk of type 2 diabetes mellitus

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Exercise represents a potent stressor for both healthy and unhealthy individuals, causing the alteration of body homeostasis. In managing type 2 diabetes mellitus (T2DM), exercise is considered one of the three key counteracting strategies, along with a healthy diet and suitable medications. However, the full understanding of the mechanisms explaining the negative effects of magnesium deficiency remains unclear. Nevertheless, exercise can also manipulate blood magnesium levels, particularly in patients with T2DM,[1] as demonstrated by the lower level of serum magnesium in patients with T2DM reporting higher amount of daily physical activity.[1]

Magnesium is an important intracellular cation that plays an important role in carbohydrate metabolism and insulin release.[2] T2DM is often associated with magnesium deficits, especially in patients with poorly controlled glycemic profiles.[3] Reduced intracellular Mg^{2+} is evidenced to decrease the insulin receptor activity and increase the insulin resistance.[4] Chronic magnesium deficiency can cause postreceptorial insulin resistance, and consequently reduce glucose utilization in the cells, worsening the reduced insulin sensitivity occurring in patients with T2DM. Hypomagnesemia affects insulin resistance and is a risk factor for T2DM. Increased magnesium intake reduces the fasting glucose, insulin resistance, and progression from prediabetes to diabetes.[5] Furthermore, it can be assumed that a relationship exists between magnesium, exercise, and the risk of T2DM, due to the impairment of glucose and insulin metabolism as a consequence of magnesium deficit.

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2019) 82: 527-528.

Received April 30, 2019; accepted April 30, 2019.

doi: 10.1097/JCMA.0000000000000120.

Magnesium homeostasis is maintained by several molecules. Cyclin and CBS domain divalent metal cation transport mediator 2 (*CNNM2*), transient receptor potential melastatin 6 and 7 (*TRPM6* and *TRPM7*), and solute carrier family 41 members 1 and 2 (*SLC41A1* and *SLC41A3*) were studied in this article.[6] *CNNM2* is as a gene involved in renal Mg^{2+} handling and regulates renal Mg^{2+} reabsorption.[7] Mutated *CNNM2* was observed in dominant hypomagnesemia.[7] At present, there are no reported correlations between *CNNM2* and diabetes. Both *TRPM6* and *TRPM7* are members of cation channels and regulate the magnesium homeostasis.[8] The role of *TRPM6* and *TRPM7* in diabetes is still controversial. However, without insulin-induced activation, *TRPM6* magnesium channels impaired the glucose tolerance during pregnancy. *SLC41A1* and *SLC41A2* are upregulated in hypomagnesemia,[9] while *SLC41A1* is downregulated during exercise.[10] Insulin modulates intracellular Mg^{2+} concentration by regulating *SLC41A1* activity.[11] Therefore, *TRPM6* and *SLC41A1* might have the key roles in a three-way link between exercise, magnesium, and insulin metabolism.

Exercise prescription should take into account the two most important parameters (ie, volume and intensity) and the entire duration of the exercise program. Indeed, the acute changes in plasma magnesium strongly rely on exercise intensity and duration.[12] Furthermore, different magnitudes of training adaptation could be reached when short, moderate, and long periods of exercise programs are prescribed. Additionally, exercise selection has an important role, as some exercises may involve specific muscle groups (eg, cycling) or the majority of muscle groups (eg, running and swimming). Further research is necessary to clarify this bidirectional link between magnesium manipulation and exercise, especially in patients with T2DM undergoing cycling exercise. Physical activity improves insulin sensitivity and diminishes the elevated blood glucose levels. However, there are still patients with poor response to aerobic exercise, such as patients with diabetics who have chronic hyperglycemia.[13] In contrast, metabolic and bariatric surgery shows high efficacy in remitting T2DM even 2 years after intervention.[14,15]

In the current issue of *J Chin Med Assoc*, Chiang and his colleagues conducted a prospective study to investigate changes in blood glucose and magnesium levels and the expression of genes encoding magnesium transporters after a 3-month exercise period in 15 adult patients with diabetes (eight males and seven females).[6] They found that fasting blood glucose, HbA1c, and waist circumference significantly decreased, and *CNNM2*, *TRPM6*, and *TRPM7* were significantly downregulated. It is difficult to differentiate whether the changes of magnesium-responsive genes are related to the chronic exercise or to the improvement of hyperglycemia. Another weakness is the change of plasma magnesium in patients with T2DM after exercise. These patients frequently have magnesium deficits,[3] and hypomagnesemia is known to increase insulin resistance.[4] In this study, patients with T2DM exhibiting normal plasma magnesium levels have significantly decreased plasma magnesium levels after exercise. Therefore, the three-way link between hypomagnesemia, expression of genes encoding magnesium transporters, and status of T2DM still requires further advanced investigation.

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