A New Dietary Approach to Reduce the Risk of Type 2 Diabetes?

The projections for a continued rapid growth in the incidence of type 2 diabetes indicate the need of developing cost-effective approaches that can be widely employed to prevent or delay this major disorder. There is recent evidence that intensive lifestyle modification can be effective in reducing type 2 diabetes development (1). However, the role of particular micronutrients in the diet that may have a protective effect has not been well studied.

In this issue of Diabetes Care, there are two interesting prospective studies suggesting that an increased intake of magnesium (Mg) in the diet could have a protective role in reducing the risk of type 2 diabetes. Lopez-Ridaura et al. (2) evaluated dietary intake of different nutrients every 2–4 years in 85,060 women in the Nurses Health Study and 42,872 men in the Health Professional’s Follow-up Study. The medical history and lifestyle characteristics were followed for 18 years in the women and 12 years in the men. There was a significant reduction of relative risk of type 2 diabetes development in both men and women in the highest quintiles of Mg intake. These relationships remained significant after adjusting for age, total energy intake, family history of diabetes, physical activity, alcohol intake, or other dietary components analyzed. Adjustment for BMI somewhat attenuated the relationships, but the effect of Mg remained significant. Less than 5% of the cohort was taking Mg supplements, and of this group, there was no significant association with diabetes risk in multivariate models. Also, excluding participants with a history of hypertension or hypercholesterolemia at baseline or for diuretic use did not modify the results.

The careful design of this particular study has minimized recall and selection bias by its prospective nature, high rate of follow-up, and assessment of diet on repeated occasions throughout the study.

The second interesting report by Song et al. (3) used a validated semiquantitative food frequency questionnaire in a cohort of 39,345 U.S. women in the Women’s Health Study with no history of cardiovascular disease, cancer, or diabetes. The relative risks of type 2 diabetes development across quintiles of Mg intake were ascertained over 6 years, and in a smaller subgroup, fasting plasma insulin levels were examined in relationship to Mg intake.

The findings showed a significant inverse relationship between Mg intake and risk of developing type 2 diabetes. There was a significant interaction between Mg intake and BMI on the risk of type 2 diabetes, with the protective effect of Mg intake only seen in women with a BMI ≥25 kg/m². In a cross-sectional analysis of 349 healthy women in this study, a significant inverse association was seen between Mg intake and fasting plasma insulin levels.

What are the limitations of these two studies? Despite their careful design and analysis, it remains unclear whether something else in the higher Mg-containing foods participated in the beneficial effects observed. These studies also do not provide a clear explanation of why the effects are predominately seen in subjects with an increased BMI and whether the inverse of diabetes risk and Mg intake will be similar in all ethnic groups.

There are other prospective studies showing a relationship between Mg intake and disease risk. Whole-grain diets contain a high content of Mg. The Iowa Women’s Health Study showed a significantly reduced relative risk of diabetes in subjects with increased whole-grain and Mg intake (4). Whole-grain intake also reduced metabolic and cardiovascular risk factors in the Framingham Offspring Study (5). In this latter study, the results were most striking among overweight subjects and the benefit to reduce fasting insulin levels was attenuated after adjusting for Mg.

In men in the Honolulu Heart Program, increased Mg intake was associated with an almost twofold reduced risk of future coronary heart disease after 15 years of follow-up (6). These effects remained significant after adjustment for age, total kilocalories, and other known risk factors for coronary artery disease. Interestingly, the percentage of subjects with hypertension and diabetes also decreased with higher Mg intake.

However, there are other studies in which the results are not clear cut. A cross-sectional analysis of the Atherosclerosis Risk in Communities Study (ARIC) included 15,248 participants, male and female, black and white, aged 45–64 years (7). Fasting serum Mg was lower in participants with prevalent coronary artery disease, hypertension, and diabetes compared with those free of disease (7). In people without coronary artery disease, dietary Mg intake and serum Mg levels were inversely related to fasting insulin levels. In a later prospective analysis of the ARIC population (8), a graded inverse relationship between serum Mg levels and incident type 2 diabetes was seen over a 6-year follow-up period. However, the relationship was not observed among black participants, and there was not a significant effect seen with dietary Mg intake. The ARIC study results may be different given the shorter time of follow-up of the subjects and the different method of analysis; noting that both studies in this issue of Diabetes Care used Cox modeling as the primary method of analysis instead of the multiple logistic analyses approach in the ARIC study.

There have been laboratory, animal, and interventional human studies to provide a sound basis for suggesting a relationship between Mg and type 2 diabetes risk. Mg deficiency reduces insulin-mediated glucose uptake in rat adipocytes (9), and hypomagnesemic rats show impaired muscle insulin tyrosine kinase activity (10). In nondiabetic humans, dietary-induced Mg deficiency can lead to insulin resistance (11). Low dietary Mg was also associated with insulin resistance in a sample of young black Americans (12), and in a study of 18 nondiabetic volunteers, low serum Mg was associated with relative insulin resistance, glucose intolerance, and hyperinsulinemia (13).
Mg deficiency is common in type 2 diabetes, and Mg deficiency may be a factor related to insulin resistance (14–16).

In animal studies, dietary Mg supplementation can prevent fructose-induced insulin resistance and elevations of blood pressure in the rat (17). Furthermore, an increased dietary Mg intake can prevent the development of type 2 diabetes in male Zucker Diabetic Fatty rats, an animal model of spontaneous type 2 diabetes (18).

The results of Mg supplementation on glucose metabolism in established type 2 diabetes have been inconsistent (19–21). However, most of these studies have been relatively small and used different protocols and types of Mg replacement. To date, there have been no studies evaluating the effect of increasing Mg-rich foods in the diet.

In summary, there is now sufficient compelling evidence to justify support for a randomized prospective clinical trial to test the effect of consuming major food sources of Mg, such as whole grains, nuts, and green leafy vegetables, on the development of type 2 diabetes in a high-risk population. If increased Mg intake is beneficial, it could provide a new cost-effective way to reduce development of type 2 diabetes.

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References