Extended Abstract
Volume 4:9, 2021

Food Safety and Health

Open Access

Target approach in diabetes prophylaxis

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Abstract

The violation of glucose transport to the muscle cell plays the key role in the mechanism of development of insulin resistance. The phosphorylation of glucose into glucose-6-phosphate with the participation of the hexokinase enzyme is the first step of intake of glucose by muscle. Therefore, endocrinologists believe that insulin should activate hexokinase, but this is not confirmed by biochemical science. However, there is evidence data that the activity of hexokinase is under the control of the ATP/ADP coefficient, i.e. the intake of glucose is inhibited by reducing the cells energy requirement and increasing the ATP/ADP ratio. Therefore, it can be suggested that the activation of energy-dependent processes should contribute to an increase in the rate of glucose entry into the cell and lead to a decrease of insulin resistance. The ATP/ADP coefficient decreases with physical activity, with activation of protein synthesis at the translation stage (leucine) and with elevation of heat production (thyroxine), at which the blood glucose level decreases. Insulin itself promotes the initiation of the peptide chain, i.e. activation of protein synthesis at the stage of translation (kinase activation of translation). Factors contributing to polysomic disaggregation (hyperkinesia, cortisol, and inflammatory cytokines) lead to a reduction in the expenditure of glucose energy on the anabolic process and promote the development of hyperglycaemia. Therefore, the targeted approach in the prevention of diabetes is to increase the efficiency of activities of energy-dependent processes, in particular, to improve the process of protein synthesis. The NIDDK-sponsored Diabetes Prevention Program (DPP) and ongoing DPP Outcomes Study (DPPOS) are major studies that changed the way people approach type 2 diabetes prevention worldwide. The DPP showed that people who are at high risk for type 2 diabetes can prevent or delay the disease by losing a modest amount of weight through lifestyle changes (dietary changes and increased physical activity). Taking metformin, a safe and effective generic medicine to treat diabetes, was also found to prevent the disease, though to a lesser degree. The DPPOS has continued to follow most DPP participants since 2002. To date, the DPPOS has shown that participants who took part in the DPP Lifestyle Change Program or are taking metformin continue to prevent or delay type 2 diabetes for at least 15 years. The DPPOS has also shown that the DPP Lifestyle Change Program is cost effective (costs are justified by the benefits of diabetes prevention, improved health, and fewer health care costs) and metformin is cost-saving (leads to a small savings in health care costs) after 10-years. DPPOS researchers are also continuing to follow other health problems in participants such as cancer, cardiovascular diseases (heart and blood vessel disease), nerve damage, kidney disease, and eye disease. As participants age, researchers are following age-related health problems such as trouble with physical function and difficulties with thinking or memory. The NIDDK funded the landmark Diabetes Control and Complications Trial (DCCT) to see if people with type 1 diabetes who kept their blood glucose levels as close to normal as safely possible with intensive diabetes treatment (three or more shots of insulin per day or an insulin pump with self-monitoring of blood glucose at least four times per day) could slow the development of eye, kidney, and nerve disease, compared with people who used the conventional treatment at the time of the study (one or two shots of insulin per day with daily self-monitoring of urine or blood glucose). The DCCT ended after 10 years in 1993—a year earlier than planned—when the study proved that participants who kept their blood glucose levels close to normal greatly lowered their chances of having eye, kidney, and nerve disease. A follow-up study to the DCCT, the ongoing Epidemiology of Diabetes Interventions and Complications (EDIC) study, has continued to follow DCCT participants since 1994. EDIC has shown that there are long-term benefits of early and intensive blood glucose control on the future development of diabetes-related complications such as heart, eye, kidney, and nerve disease, and that early and intensive blood glucose control also lengthens life. EDIC has also shown that scheduling eye exams based on personal risk for retinopathy, rather than once a year, results in fewer eye exams, lower costs, and quicker diagnosis and treatment of advanced diabetic eye disease. Findings from DCCT/EDIC have changed the way diabetes is treated worldwide. As a result of DCCT/EDIC and other studies, early and intensive blood glucose control is now the standard treatment for people with type 1 and some people with type 2 diabetes, and it helps people with diabetes live longer and healthier lives. The Special Statutory Funding Program for Type 1 Diabetes Research, or Special Diabetes Program, is a special appropriation that supports research on the prevention and cure of type 1 diabetes and its complications. Since 1998, the Special Diabetes Program has enabled the creation of unique, innovative, and collaborative research consortia and clinical trials networks. These have made significant research progress as noted in program reports and also generated numerous research resources for use by the broad scientific community. The NIDDK administers the Special Diabetes Program on behalf of the Secretary of the Department of Health and Human Services, in collaboration with multiple NIH Institutes and Centres and the CDC, and with input from the Diabetes Mellitus Interagency Coordinating Committee.

Learn more about the Program's background. The Special Diabetes Program supplements type 1 diabetes research supported by the NIDDK and NIH's regular appropriation. Therefore, the links on this site do not represent the entirety of type 1 diabetes research supported by the NIDDK and the NIH, but rather focus only on research supported by the Special Diabetes Program. Learn more about NIDDK diabetes research.

This work is partly presented at *2nd International Conference on Nutrition, Food Science and Technology*
April 08-09, 2019