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Editorial

Nutritional life-style and Diabetes

Diabetes mellitus (type II) has become a significant threat to public health worldwide: it has been estimated that at least 171 million people are affected and it is assumed that by 2030 this figure will have more than doubled to 366 million people. While the developing countries will experience the highest burden, the impact in the developed countries is also considerable. Reasons for the continuing rise in the diabetes prevalence include the rising life expectancy and aging of populations, the increasing prevalence of obesity and associated life-style factors of low physical activity and inappropriate diet. The latter refers to both the quantitative and qualitative aspects of eating behaviour. In this context, one issue of ongoing research interest is the question about the role of a high intake of fruits and vegetables in diabetes prevention. Current research results from both observational and experimental research clearly show that life-style changes – increased physical activity and improved diet – are able to substantially reduce diabetes incidence. However, the independent effect of a diet rich in fruits and vegetables have not been convincingly demonstrated. This issue of the IFAVA newsletter highlights the present research findings on this issue in the article "The role of fruits and vegetables in diabetes" by K. Hoy.

The underlying mechanisms linking fruit and vegetable intake to diabetes risk include improved weight control, and increased fibre and antioxidant intake. Carotenoids have been considered to play a crucial role in this context, as outlined by M. Schulze in the next article of this issue "Carotenoids and the development of type 2 diabetes". Finally, BMI and the development of overweight and obesity during the life course are an inevitable topic when talking about diabetes prevention. In the third article of this issue A. Schienkiewitz focuses in "BMI history and risk of type 2 diabetes" on the importance of a life-long weight maintenance.

Anja Kröke, Prof. Dr.
Fulda University of Applied Sciences, Germany

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HEAD OFFICE
International Fruit And Vegetable Alliance
c/o Canadian Produce Marketing Association
9 Corvus Court
Ottawa, ON K2E 7Z4 Canada

IFAVA

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The Role of Fruits and Vegetables in Diabetes

— Kathy Hoy —
Produce for Better Health Foundation, Germany

Intake of fruits and vegetables, and prevention of type 2 diabetes

The increase in the incidence of type 2 diabetes has been attributed in part to high-fat, high calorie diets, overweight and obesity - particularly excess abdominal fat, and lack of exercise[1,2]. These factors are associated with insulin resistance and metabolic syndrome- important risk factors for type 2 diabetes and cardiovascular disease[3]. Estimates suggest that up to a 75% reduction in risk for type 2 diabetes could be achieved by preventing obesity[4].

Observations from population-based studies suggest that fruit and vegetable consumption may be associated with a reduced risk of diabetes[5-8] or may be protective[9], although results have not always been consistent[10-12]. A positive association between fruits and vegetables and reduced risk is supported by an inverse association between serum carotenoids, a marker for fruit and vegetable intake, and type 2 diabetes and impaired glucose metabolism in adults[13].

Dietary patterns that include fruits and vegetables have been associated with a reduction in fasting blood glucose[14-16], improved results on glucose tolerance tests[17,18] lower glycosylated hemoglobin values[19] and enhanced insulin sensitivity[20]. However, energy intake may modify these associations[21]. Taken together, these studies suggest that fruit and vegetable intake is potentially beneficial for prevention and management of diabetes.

Fruits and vegetables and weight management

The relationship of obesity and type 2 diabetes is well established[22]. Further, weight reduction is an integral part of treatment for type 2 diabetes, leading to improved glycemic control and often a reduction or elimination of the need for medication[22]. Weight management may also minimize the increased risk of people with diabetes for cardiovascular diseases.

Research suggests that advice to increase intake of fruits and vegetables coupled with advice to decrease energy intake is an effective recommendation for weight management[23-25], as they are less calorically dense and more nutrient rich per serving than many foods[26].

Fruits and Vegetables, Fiber and Glycemic Control

Results from studies that have evaluated fiber and blood glucose control are inconsistent. Large amounts of fiber appear to be necessary for beneficial effects on glycemia, hyperinsulinemia and plasma lipids in people with diabetes. A recent study[27] addressed the potential issue of acceptability of a high fiber diet. In a randomized, crossover study, 13 patients with type 2 diabetes consumed a standard ADA diet (24 g total fiber) or a high fiber diet (50 g total fiber), achieved by including fruits and vegetables and grains, especially those high in soluble fiber. Results indicated that the high fiber diet improved glycemic control compared to the ADA diet, and patients accepted the high fiber diet with few side effects.

The fiber content of fruits and vegetables may also contribute to a lower glycemic index and hence glycemic load of the diet. A recent meta-analysis indicates that the use of this technique can provide an additional benefit over that observed when total carbohydrate is considered alone[28]. Although scientists worldwide do not agree that using the glycemic index is the best way to plan carbohydrate intake for individuals including those with diabetes[29,30], the potential health benefits of fruits and vegetables for those with diabetes are becoming obvious.

Fruits and vegetables, antioxidants and diabetic complications

Newer research is revealing additional benefits of fruit and vegetable consumption for health in diabetes. Elevated blood glucose levels can lead to oxidative stress. This damage may play an important role in the development of complications in diabetes, such as lens cataracts, kidney disease and neurological disease[31]. Animal studies suggest the mechanisms by which antioxidants in the diet may help counteract this damage[32]. Data from the Third National Health and Nutrition Examination Survey (1988-1994) (NHANES III) showed that adults with metabolic syndrome have suboptimal concentrations of several antioxidants in the blood, as well as a lower consumption of fruits and vegetables compared to adults without metabolic syndrome[33]. Further research is needed to determine the role of antioxidants for improving glycemic control and/or exerting antioxidant activity.

Conclusions

Overall the body of evidence strongly supports that healthy diets which include ample fruits and vegetables, whole-grains, and high-fiber foods without excess fat or calories, in conjunction with regular physical activity—can improve control of blood sugar among individuals with type 2 diabetes and may offer some protection against its development.

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Carotenoids and the development of type 2 diabetes

— Matthias B. Schulze —

German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany

Potential mechanisms for antioxidants and reduction in risk for type 2 diabetes

One major action of antioxidants in cells is to prevent damage resulting from the action of reactive oxygen species. Reactive oxygen species include hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl), and free radicals such as the hydroxyl radical (OH) and the superoxide anion (O_2^-). Reactive oxygen species are highly reactive chemicals that attack molecules by capturing electrons and thus modifying chemical structures. Antioxidative effects have been observed for a number of plant compounds, among them polyphenols, vitamin C, tocopherols, and carotenoids. Carotenoids are a widely distributed group of naturally occurring pigments. Carotenoids with molecules containing oxygen, such as lutein and zeaxanthin, are known as xanthophylls. The unoxidized carotenoids such as alpha-carotene, beta-carotene and lycopene are known as carotenes. Although major sources of carotenoids in the diet are plant foods, carotenoids are used extensively as safe, natural colorants for food and also in animal feeding.

The development of type 2 diabetes is associated with a combination of pancreatic beta-cell dysfunction and insulin resistance. Normal beta-cells can compensate for insulin resistance by increasing insulin secretion or beta-cell mass. However, insufficient compensation leads to the onset of glucose intolerance. Once hyperglycemia becomes apparent beta-cell function gradually deteriorates and insulin resistance aggravates. Under conditions of chronic hyperglycemia and elevated free fatty acids oxidative stress is provoked in pancreatic beta-cells and the mechanisms for glucotoxicity and lipidoxicity seem, at least in part, to be mediated by overloads of reactive oxygen species[1, 2]. Beta-cells might be rather vulnerable to oxidative stress due to their relatively low expression of antioxidant enzymes such as catalase and glutathione peroxidase[3]. Thus, it is likely that oxidative stress is involved in beta-cell deterioration in type 2 diabetes. This is further supported by animal studies which suggest potential usefulness of antioxidants for diabetes prevention[1, 2]. The role of carotenoids in the development of type 2 diabetes has therefore received considerable scientific interest in recent years.

Carotenoid intake and risk for type 2 diabetes in observational studies

Montonen et al.[4] observed a significant lower diabetes risk among participants with high total carotenoid intake in the Finnish Mobile Clinic Health Examination Survey. Among single carotenoids, beta-cryptoxanthin intake was significantly associated with a reduced risk of type 2 diabetes in this prospective cohort study. However, no adjustments for other dietary characteristics were made in this study. In the Women's Health Study, there was no association between dietary intake of lycopene or lycopene-containing foods and the risk of incident type 2 diabetes[5].

Carotenoid concentrations and risk for type 2 diabetes in observational studies

Plasma beta-carotene levels were not significantly associated with the incidence of diabetes in a study by Reunanen et al. after adjustment for risk factors[6]. In the Women's Health Study, there was no prospective association between baseline plasma carotenoids (total, lycopene, alpha-carotene, beta-carotene, beta-cryptoxanthin and lutein/zeaxanthin) and the risk of type 2 diabetes[7]. In contrast, serum carotenoids were associated with lower diabetes risk among nonsmokers in the CARDIA Study[8]. This association was evident for total carotenoids and beta-carotene, while alpha-carotene, lutein/zeaxanthin and lycopene were not significantly associated with risk. Interestingly, no association between carotenoids and diabetes was observed among smokers, suggesting an effect modification by smoking.

Carotenoid supplementation and risk for type 2 diabetes in intervention studies

The efficacy of beta-carotene supplements for primary prevention of type 2 diabetes among apparently healthy men was tested in the Physician's Health Study, a randomized placebo-controlled trial[9]. Over 12 years of follow-up, there was no significant difference in diabetes incidence between the intervention group (receiving 50 mg on alternate days) and the placebo group. In the SU.VI.MAX trial, participants in the intervention group received 120 mg vitamin C, 30 mg vitamin E, 6 mg beta-carotene, 100 µg Se, and 20 mg Zn daily. There was no difference in glucose levels after follow-up between the intervention group and the placebo group[10].

Discussion

Although study findings are generally conflicting, the results of the Cardia Study suggest that a beneficial effect of beta-carotene may be present among non-smokers. However, most participants in the Physician's Health Study randomized trial did not smoke at the time of the study[9]. The lack of effect observed in the trial speaks against a role of beta-carotene in the prevention of diabetes. There is also little evidence to suggest that other carotenoids may reduce the risk of type 2 diabetes. Although carotenoids are naturally occurring in plant foods, particularly fruits and vegetables, beta-carotene is also extensively used in many countries as a colorant and for fortification in food processing and animal feeding. Supplements are an additional source of beta-carotene, and blood levels may therefore be not a good indicator of fruit and vegetable intake[11]. Although studies of blood concentrations of beta-carotene consider the hypothesized antioxidative compound, the results of these studies cannot be interpreted as a lack of effect of fruit and vegetable intake. The same applies to the prevention trial which tested beta-carotene but not fruits and vegetables. These studies therefore leave the question as to whether fruit and vegetables consumption are important in diabetes prevention unanswered. Because fruit and vegetables contain not only carotenoids, but also fibers, polyphenols, vitamin C and other bioactive compounds, it seems straight forward to assume beneficial effects. Unfortunately, there is also only limited evidence supporting a role of fruit and vegetable consumption in diabetes prevention.

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BMI history and risk of type 2 diabetes

— Anja Schienkiewitz —
German Institute of Human Nutrition Potsdam-Rehbrücke, Department of Epidemiology, Germany

Evidence from several epidemiologic studies indicates that obesity and weight gain are causally related to type 2 diabetes. Many studies have reported a higher diabetes risk in men[1-5] and women[4,6,7] with increasing BMI (kg/m^2) and weight gain in adolescence[1,6]. The duration of overweight seems to be another significant risk factor for diabetes independent of the current degree of obesity[8,9]. Although considerable scientific work has been done on the association between overweight and diabetes, no study has explicitly quantified whether or how body weight changes during different periods in adult life are related to risk of type 2 diabetes. The topic is even more interesting since the prevalence of obesity and diabetes have increased substantially over the last decades[10] and large segments of the population are starting to gain weight early in adult life, after settling into an occupation or family life. Data from adults in westernized countries show that the largest increase in the prevalence of obesity in men and women is seen in younger life, between age 20 and 40 years[11-13].

Observations from the EPIC Study

An investigation was conducted to compare two different periods in adult life with regard to the association between weight change and risk of diabetes[14]. The study population included 7,720 men and 10,371 women from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam cohort[15], a population sample of 27,548 participants contributing to the (EPIC)-Potsdam Study, a large multicenter cohort to study the association between nutrition and chronic disease[16]. The baseline examinations included anthropometric measurements and face-to-face interviews on sociodemographic characteristics. Follow-up questionnaires for information on incident diseases were collected every two to three years and self-reported diabetes cases were verified by the treating physician.

The mean percentage of BMI change between ages 25 and 40 y was highest (10%) in men and women with a BMI less than 23.0kg/m^2 at age 25 years. For a BMI between 23.0 and 25.0 the mean percentage change of BMI was 7%-8%, and for overweight men and women it was 5.5%. Women had higher percentages of BMI change between 40 to 55 y in all categories of BMI at age 25 y (12%-14%) whereas the percentage of BMI change for men increased slightly by 8%-10% compared with the earlier period. Using a multivariate model, the relative risk of diabetes for men and women was slightly higher for a BMI change between 25 and 40 y (about 25% higher risk for a 1-unit increase in BMI) than for a BMI change between 40 and 55y (12% higher risk). The stronger association of risk with weight gain in early adulthood than in later life might be explained by the longer duration of exposure to excessive body fat. Previous studies already identified that obesity lasting 5 y and longer is an important risk factor for type 2 diabetes[8,9].

Effect of weight history

To determine risk related to different weight change histories, the BMI changes were categorized into three groups: "loss or stable" (loss or gain of less than 1 BMI unit over 15 y), "moderate gain" (gain of 1.0-4.0 kg/m2) and "severe gain" (gain of more than 4.0 kg/m2). Severe weight gain between age 25 and 40 y and stable weight management between 40 and 55 y was associated with a 1.5-times higher risk for diabetes in men and a 4.3-times higher risk in women compared with those of stable management in early adulthood and severe gains later in life. An explanation for the higher risks among women than men with moderate or severe BMI gain during early adulthood could be the relation between parity and obesity. The childbearing years have been identified as a critical period for substantial excess weight gain and development of obesity, which cannot be explained by behavioural changes[17]. Risk was not increased for those who were overweight at age 25 y and had lost weight or maintained weight during the same periods compared with normal weight people whose weight was stable until age 55 y. However, even modest weight gain in adult life is associated with a substantial risk of developing type 2 diabetes, and moderate or severe weight gain in early life is a stronger risk factor for diabetes than is weight gain after age 40 y. This stresses the importance of maintaining a healthy body weight throughout life.

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