Nuts for Diabetes Prevention and Management

ALISON KAMIL AND C-Y. OLIVER CHEN*

Antioxidants Research Lab., JM USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, U.S.A.

ABSTRACT

Type 2 diabetes mellitus is an important preventable disease and a growing public health problem. Epidemiologic and clinical studies suggest that healthy eating, physical activity, and BW control are the main driving forces to reduce diabetes risk. Owing to their low available carbohydrate content, favorable fat and protein profile as well as phytonutrient content, nut consumption has been associated with a reduced risk of development and management of diabetes. Nuts, by virtue of its cardioprotective actions, have also been shown to reduce biomarkers of risk factors for diabetic complications. Although more studies are warranted, the emerging picture is that nut consumption beneficially influences diabetes risk and management beyond blood glucose control.

Key words: Nuts, diabetes, glycemia, body weight, lipids, endothelial function, hypertension, antioxidant, anti-inflammatory

INTRODUCTION

The topic of this review is the health benefits of nuts in diabetes prevention and management. We first provide background information about diabetes. We next discuss nuts as components of a healthy diet for glycemic control in people with diabetes or at risk for developing diabetes. Finally, as nuts contain a variety of nutrients exerting cardioprotective, antioxidant, and anti-inflammatory actions, we will present studies demonstrating how nuts could ameliorate biomarkers of risk factors for diabetic complications.

DIABETES INCIDENCE AND MANAGEMENT

Diabetes is characterized by hyperglycemia and glucose intolerance due to insulin deficiency and/or impaired effectiveness of action. As of 2007, roughly 6% were affected worldwide and it is estimated that this will increase to 7.3% by 2025[1]. Fueled by rapid urbanization, nutrition transition, and increasingly sedentary lifestyles, Asia accounts for 60% of the world's diabetic population[2]. Type 2 diabetes mellitus (T2DM) is by far the most common disorder, affecting 90 - 95% of the U.S. diabetes population[3].

Several factors contribute to the development of T2DM, including family history, ethnicity, age, genetics, lifestyle, diet, and body weight (BW). Excess BW, particularly abdominal adiposity is the most important modifiable risk factor for development of diabetes. The incidence of diabetes clearly rises as obesity prevalence increases[4,5]. Furthermore, diet quality especially of fats and carbohydrates (CHO) play an important role, independent of BMI and other risk factors[5]. There is also strong evidence for an inverse association between physical activity and the risk of diabetes[6].

Healthy eating, physical activity, and BW control are the cornerstones of diabetes prevention or management. The major medical nutrition therapy recommendations provided by the American Diabetes Association (ADA) include moderate weight loss and regular physical activity, with dietary strategies including reduced calories and intake of dietary fat. Recommended foods include: healthy CHO such as whole grains, fruits, vegetables, legumes, and low-fat dairy; heart healthy fish; good fats high in monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA). Foods to limit include: bad fats high in saturated (SFA) or trans-fatty acids; sodium; and alcohol[7]. Hence, the application of nutritional therapy to lower the risk or delay the onset of diabetes is important.

NUTRITION COMPOSITION

"Tree-nuts" or nuts are a nutrient dense food that contains diverse macro and micronutrients and other phytochemicals that may have beneficial effects on T2DM and other health complications[8]. Nuts are rich in magnesium, which helps regulate blood sugar levels and is involved in energy metabolism. Nuts are also a good source of dietary fiber which decreases gastric emptying, in turn decreasing the rates of CHO breakdown and glucose absorption. Furthermore, nuts are high in unsaturated fats, mostly high in MUFA in most nuts and PUFA in walnuts. Their unsaturated fats appear to exert anti-inflammatory and lipid lowering effects. L-arginine is also an important constituent of nuts that is essential to vascular function. Nuts contain an

*Author Correspondence. Tel: 617-556-3128;
Fax: 617-556-3344; Email: Oliver.Chen@tufts.edu

array of phytonutrients, e.g., carotenoids, phenolics, and phytosterols, which exert antioxidant and anti-inflammatory actions as well as an inhibitory effect on starch digestive enzymes. Incorporation of nuts into a diet may therefore improve the overall nutritional quality of the diet.

NUTS AND DIABETES PREVENTION

Jiang *et al*.[9] observed in the Nurses' Health Study that women consuming a 1 oz serving of nuts >5 times/wk had a 25% lower risk of developing T2DM compared with women who never ate nuts. Recently, the PREDIMED study[10] with 418 persons at high cardiovascular risk showed that a traditional high-fat Mediterranean diet enriched with mixed nuts (30 g/d) or olive oil decreased the incidence of diabetes by 50% after a median follow-up of 4 yrs compared to a control diet consisting of advice on a low-fat diet.

Owing to their low available CHO content and favorable fat profile, nuts may decrease the risk of diabetes by reducing postprandial blood glucose levels. This is important as chronic hyperglycemia causes damage to the eyes, kidneys, nerves, and blood vessels. Kendall *et al*.[11] examined the effect of pistachios on postprandial glycemic response, in a two stage study with 10 healthy overweight subjects. Addition of pistachios to 50 g available CHO resulted in a significant reduction in the glycemic response of the composite meal in a dose-dependent manner for the 28 g (5.7%), 56 g (3.8%), and 84 g (9.3%). Likewise, addition of 56 g pistachios to CHO foods significantly attenuated their glycemic response: parboiled rice (19%) and pasta (40%). Similarly, Josse *et al*.[12] found that the addition of almonds to white bread with 50 g CHO resulted in a progressive reduction in the glycemic index of the composite meal in a dose-dependent manner for the 30 g (105.8), 60 g (63.0), and 90 g (45.2) in 9 healthy volunteers. Furthermore, since the nutrient bio-accessibility of nuts consumed in different physical forms might be different, Mori *et al*.[13] reported in a randomized crossover trial with 14 patients with impaired glucose tolerance (IGT) that 42.5 g whole almonds, but not comparable amounts of almond butter or defatted almond flour, added to a 75 g available CHO-matched meal decreased postprandial glucose response compared to a no almond vehicle.

Given the rapidly increasing obesity prevalence, nuts may decrease the risk of diabetes through weight management. Bes-Rastrollo *et al*.[14] reported in the Nurses' Health Study II with an 8 yr follow-up that women eating nuts >2 times/wk had slightly less mean weight gain (5.04 kg) than did women who rarely ate nuts (5.55 kg). Moreover, Wien *et al*.[15] assessed the effect of an almond-enriched (84 g/d) or complex-CHO-enriched low calorie diet (1012 kcal/d) on anthropometric, body composition and metabolic parameters in a randomized prospective 24 wk trial with 65 overweight and obese subjects. As low fat diets (≤ 20% kcal) have been shown to have poor adherence in the outpatient treatment of obesity[16], alternative approaches with more moderate fat content (35% kcal, < 10% from SFA) which increases palatability may enhance compliance to weight loss diets. Wien *et al*. reported reductions in BW, BMI, waist circumference, and fat mass being 62, 62, 50, and 56% greater, respectively, than the control diet. The above lack of effect of nut consumption on weight gain could be attributed to the observed calorie displacement from other foods, satiating and palatability properties of nuts, and the probable modest malabsorption of nut fats[17]. Thus, nuts could be a part of a balanced, healthy diet for glycemic and BW management.

NUTS AND DIABETES MANAGEMENT

According to the ADA, the primary objective in management of diabetes is achievement of targeted glycemic control (HbA_{1C} < 7%)[18]. Besides the acute trials above showing reductions in postprandial glycemia in individuals at risk for development of T2DM, up to date there are 4 clinical trials demonstrating the effect of nuts on glycemic control in T2DM patients. Cohen & Johnston [19] reported in a 12 wk randomized crossover trial with T2DM patients that consumption of 28.4 g/d almonds at a frequency of 5 d/wk decreased HbA_{1c} as compared to a control diet without almonds (4% reduction vs. 1% increase, respectively). Li *et al*.[20] demonstrated in a randomized, crossover, controlled trial that almonds (60 g/d) replacing 20% calories of the control National Cholesterol Education Program (NCEP) Step 2 diet significantly decreased fasting blood glucose and insulin and HOMA insulin resistance as compared to the control diet. After a 42 wk intervention with an almond-based, high fat and protein diet (40, 22, and 25% kcal from fat, MUFA, and protein, respectively) vs. a contemporary American Heart Association diet (30, 15, and 15% kcal, respectively) in 17 patients with metabolic syndrome or T2DM, Scott *et al*.[21] noted that the former diet was modestly better in glycemic control. Jenkins *et al*.[22] reported in a 3 mo randomized parallel study with 117 T2DM subjects that supplementation with mixed nuts (75 g/d) to a 2,000 kcal diet in replacement for CHO foods significantly reduced HbA_{1c} 21% compared to supplementation with half-nut dose or muffin. Hence, frequent nut consumption has a beneficial effect for blood glucose control in T2DM patients as part of a strategy to improve diabetes control.

BENEFITS BEYOND GLUCOSE CONTROL

Diabetes is associated with a myriad of other health complications that include cardiovascular disease (CVD), hypertension, cancers, and renal and gallstone disease. More specifically, of these patients with diabetes or IGT, 75% will die of some form of CVD[23]. Thus, the expanded

goals of diabetes management, besides slowing or stopping disease progression, must include optimizing the reduction of all risk factors associated with disease complications. A pooled analysis of epidemiologic studies shows a clear dose response between nut consumption and a reduced risk of coronary heart disease (CHD)[24]. Collectively, these findings provide compelling evidence of the cardioprotective benefit of nut consumption.

Dietary intervention studies have shown that nut consumption can reduce the risk of heart disease by improving serum lipid profile, endothelial function and blood pressure, in addition to lowering oxidative stress and inflammation. A pooled analysis of 25 intervention studies[25] evaluating the effect of nuts on blood lipids among people with normolipidemia and hypercholesterolemia, demonstrated significant reductions in both total cholesterol (5.1%) and LDL-C (7.4%) with a mean daily consumption of 67 g of nuts and greatest among subjects with high LDL-C or with lower BMI consuming Western diets. Moreover, walnuts are the only nuts that have been formally studied for effects on endothelial function, which is important as endothelial dysfunction has been shown to be predictive of future adverse cardiovascular events. In a randomized, controlled crossover trial with 24 participants with T2DM[26], endothelial function as measured by flow-mediated dilation (FMD) was significantly improved after consumption of a walnut enriched diet (56 g/d) compared to a control diet without walnuts (2.2 vs. 1.2%, respectively). Similarly, Ros *et al*.[27] demonstrated in a randomized crossover design with 21 hypercholesterolemic subjects that replacement of ~32% of the energy with walnuts significantly improved FMD compared to a control diet without walnuts with a similar energy and fat content. Further studies are needed to confirm that overall nut intake influences endothelial function. To note, few studies have examined the effect of nut consumption on incidence of hypertension. However, the result of the Physicians' Health Study I showed there was an inverse relation between nut intake and hypertension among U.S. male physicians (BMI < 25)[28]. Further examination of the relation between nuts and incident of hypertension in the general population and differential effects of types of nuts consumed is warranted, as well as mechanism of action.

Evidence also suggests a protective role of nuts against biomarkers of CVD such as susceptibility to oxidation and inflammation. Oxidation markers after feeding nuts have been examined in several clinical trials. Jenkins *et al*.[29] compared diets supplemented for 4 wks with 2 almond doses (36.5 or 73 g/d) with a similar diet supplemented with muffins in 27 hypercholesterolemic subjects. The almond diets significantly increased the resistance of LDL-C to oxidation and decreased serum MDA and urinary isoprostanes. Furthermore, in a randomized crossover clinical trial with 60 healthy young male soldiers who were habitual smokers, Li *et al*.[30] reported that supplementation with 84 g almonds daily for 4 wks resulted in a significant decrease in lymphocyte DNA strand breaks as compared to isocaloric pork (120 g/d). They also demonstrated that adding almonds led to increased activities of serum superoxide dismutase and glutathione peroxidase, but not changed after pork. Inflammation also plays a critical role in the risk for and progression of CVD and T2DM such that biomarkers like C-reactive protein (CRP) and interleukin-6 (IL-6) are independent predictors of their pathology. An anti-inflammatory action by nuts is consistent with the observation that frequency of nut and seed consumption is inversely associated with each of these biomarkers[31]. In a randomized, controlled, crossover clinical trial with healthy adults, Rajaram *et al*.[32] found incorporating almonds into the diet at 10 and 20% of calories (34 and 68 g/2000 kcal, respectively) for 4 wks lowered CRP compared to a nut-free control diet, although no dose-response relationship was observed. E-selectin, a cell adhesion molecule activated by cytokines during inflammation, was also significantly lower, but only with the higher almond dose. These results suggest that nuts can enhance antioxidant defenses and diminish inflammation and oxidative stress. More studies are warranted to elucidate the mechanism of actions for these reductions in biomarkers.

CONCLUSION

The available data demonstrate that nuts as replacement for CHO have beneficial effects on diabetes risk and management. In general, the nutrient composition of nuts and emerging clinical evidence provide a strong justification in support that they could be a part of a balanced, healthy diet for glycemic, BW management, and cardioprotection. More research with robust study designs are needed to better identify differential effects of different types of nuts as well as the benefits in the longer term.

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