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Hazelnut-enriched diet improves cardiovascular risk biomarkers beyond a lipid-lowering effect in hypercholesterolemic subjects

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BACKGROUND: Tree nuts, particularly almonds, walnuts, and pistachios, have been shown to possess cardioprotective effects. However, there is little information on the effects of hazelnut consumption on cardiovascular risk markers.

METHODS: The antiatherogenic effect of hazelnut before and after consumption in hypercholesterolemic subjects was investigated. Twenty-one hypercholesterolemic volunteers (18 men and 3 women) were recruited in a double control sandwich model intervention study with a single group and three isoenergetic diet periods. These were control diet I (4 weeks), hazelnut-enriched diet (4 weeks; hazelnut contributing 18%–20% of the total daily energy intake), and control diet period II (4 weeks). The cardiovascular risk biomarkers such as endothelial function, using flow-mediated dilation (FMD) technique, low-density lipoprotein (LDL) oxidation products and inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP), soluble intercellular adhesion molecule-1, and soluble vascular cell adhesion molecule-1 (sVCAM-1) as well as lipids and lipoprotein levels were monitored.

RESULTS: Consumption of a hazelnut-enriched diet significantly improved FMD (56.6%), total cholesterol (−7.8%), triacylglycerol (−7.3%), LDL-cholesterol (−6.17%), and high-density lipoprotein cholesterol (6.07%) compared with the control diet I. Oxidized-LDL, hs-CRP, and sVCAM-1 levels were significantly lower in the group ingesting a hazelnut-enriched diet compared with the control diets I and II. Modest correlations between sVCAM-1 and FMD and between sVCAM-1 and hs-CRP were observed ($r = -0.49$, $P < .025$; $r = 0.66$, $P < .001$, respectively).

CONCLUSION: Hazelnut-enriched diets may exert antiatherogenic effect by improving endothelial function, preventing LDL oxidation, and inflammatory markers, in addition to their lipid and lipoprotein-lowering effects. These beneficial effects appeared to be reversible after 4 weeks on a hazelnut-free diet. Therefore, hazelnut may be incorporated into daily diet without change in total caloric intake for sustained health benefit.

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Cardiovascular disease is a leading cause of death in many countries around the globe. The relationship between the consumption of nuts, particularly almonds, walnuts, and

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pistachios, and coronary heart disease (CHD) has been a major focus of health research. There is a large body of epidemiologic and controlled clinical studies related to nuts demonstrating their multiple beneficial effects on CHD.[1–3] Tree nuts are highly nutritious and provide macronutrients, micronutrients, and lipophilic bioactive compounds (or phytochemicals).[4–6] Although cardioprotective effects are generally attributed to all kinds of nuts, each nut has its own specific nutrition and bioactive compounds and may render different kind and degrees of benefit. In this regard, hazelnuts have the highest ratio of unsaturated to saturated fatty acids and a high level of monounsaturated fatty acids (MUFA), which play an important role in improving plasma lipid and lipoprotein levels. A high level of vitamin E, which protects low-density lipoprotein (LDL) against oxidation and a high level of L-arginine, which is precursor of nitric oxide and other bioactives, may contribute to its antiatherogenic effect of hazelnut. However, there are limited number of studies related to hazelnut consumption, and these are generally focused on lipid-lowering effects.[7–9] In a recent study, improving effects of hazelnut consumption on lipid and lipoprotein levels, LDL subfraction, and susceptibility of LDL to oxidation were reported in normolipidemic healthy volunteers.[9] Endothelial dysfunction plays a key role in the development and progression of CHD and is an independent predictor of future cardiovascular events.[10] Ros et al[11] showed that walnut intake improves endothelial function in hypercholesterolemic subjects by using a flow-mediated dilation (FMD) technique.

According to prospective epidemiologic studies, regular consumption of nuts is quite important to take advantage of their beneficial effect against cardiovascular events. However, in many case–control studies related to nut consumption, researchers have not focused on postconsumption on a nut-free diet. This study design, which is a double control sandwich model intervention study, is expected to shed light on diet changes resulting from hazelnut consumption after 4 weeks on a hazelnut-free diet. Here, we investigated the antiatherogenic effect of hazelnut consumption by evaluating cardiovascular risk biomarkers, namely endothelial function using FMD technique, LDL oxidation products, inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP), soluble intercellular adhesion molecule-1 (sICAM-1), and soluble vascular cell adhesion molecule-1 (sVCAM-1), as well as lipid and lipoprotein levels in hypercholesterolemic subjects.

Subjects and methods

Subjects

Twenty-one hypercholesterolemic volunteers (18 men and 3 women) with a mean age of 44.6 ± 10.4 years were recruited. The eligibility criteria were as follows: serum cholesterol level greater than 200 mg/dL with or without triacylglycerol greater than 150 mg/dL, not on a medication or supplementation known to alter lipid metabolism. Four of the hypercholesterolemic subjects (N = 21) had triacylglycerol levels lower than 150 mg/dL. Individuals were excluded if they had any systemic illness (diabetes mellitus, liver or kidney disease, or hypertension) or history of allergy to hazelnuts. Before starting the study, all participants were trained on the importance of maintaining their routine daily diet, physical activity, and other lifestyle habits. The study protocol was explained to each subject who signed an informed consent, approved by the Ethics Committee of the University.

Study design

It is well known that randomized controlled crossover study is a gold standard in the evaluation of dietary intervention studies. However, to evaluate the changes resulting from supplement consumption during the post-supplement period is complex and difficult. Therefore, this study was designed as a double control sandwich model intervention with a single group, isoenergetic three periods for a total of 12 weeks. All subjects consumed the diet according to three diet periods of control diet I in the first 4 weeks, followed by a hazelnut-enriched diet for the second 4 weeks, and finally control diet II during the last 4 weeks. With this study design we evaluated the effects of a hazelnut-enriched diet by comparing it with control diet I and control diet II. Caloric and nutrient composition of the study periods are given in Table 1.

Before starting the study, a 1-week pre-experiment training period was contemplated for all participants. Control diet I, National Cholesterol Education Program adult treatment panel (ATP) III step 2 diet (<7 % energy from SFA and <200 mg/d dietary cholesterol) was equivalent to control diet II. During the hazelnut-enriched diet period, hazelnut contributed 18%–20% to the total daily energy intake without increasing total daily energy intake. Subjects were instructed on reducing total food intake by approximately 18%–20%, which was the caloric value of the supplemented hazelnut, including reduction in starchy food intake (such as breads ext) by 8%–10%. Approximately 40–70 g/day of nuts were used in a previous clinical trial.[12] In the present study, 49–86 g/day natural or raw hazelnuts (Giresun quality Turkish Tombul hazelnut) were used.[13] The daily hazelnut supplement was provided in preweighed packages to each study participant. Subjects consumed hazelnuts as provided. Total daily amount of hazelnut was divided in two portions. One portion was consumed between breakfast and lunch and the other portion was taken between lunch and dinner. Only water was allowed with the hazelnut consumption. Participants were asked to eliminate hazelnut and other tree nuts from their diet other than those provided throughout the study. Anthropometric and biochemical parameters as well as endothelial functions were obtained at baseline and at the end of each diet period. Study participants were instructed by a dietitian to record their food intake for three consecutive days (two weekdays and one weekend day) at end of each period. Caloric and nutrient