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Effect of non-soy legume consumption on inflammation and serum adiponectin levels among first-degree relatives of patients with diabetes: A randomized, crossover study

Sahar Saraf-Bank M.Sc. [a,b], Ahmad Esmaillzadeh Ph.D. [a,b], Elham Faghihimani M.D. [c], Leila Azadbakht Ph.D. [a,b,*]

[a] *Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*
[b] *Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran*
[c] *Isfahan Endocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*

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ABSTRACT

Objective: First-degree relatives of patients with diabetes are at more risk for endothelial dysfunction and inflammation. The aim of the present study was to determine the effects of a non-soy legume-enriched diet on inflammatory biomarkers and serum adiponectin levels among first-degree relatives of these patients.
Methods: Twenty-six participants (14 women and 12 men) with a family history of diabetes were recruited to this randomized, crossover study. Participants were randomly assigned to a legume-enriched or a habitual diet for 6 wk that was separated by a 2-wk washout. The inflammatory markers—high-sensitivity C-reactive protein (hs-CRP), interleukin-6, tumor necrosis factor-α, and serum levels of adiponectin—were measured at the beginning and the end of each intervention period according to the standard protocol.
Results: Energy intake of participants was not statistically different between the two diets (1821.5 ± 100.11 versus 1788.2 ± 92.68 kcal/d, respectively). After consumption of a legume diet, percent change of hs-CRP reduced significantly compared with consumption of a habitual diet (−4.86% ± 1.86% versus 3.55% ± 1.97%, $P = 0.002$) and among the women in the study (−12.96% ± 1.96% versus 3.24% ± 2.65%, $P = 0.004$). The percent change of other inflammatory markers and serum concentrations of adiponectin were not significantly different between the two diet groups.
Conclusion: The results of this study showed that a legume-enriched diet significantly reduced the hs-CRP concentrations in first-degree relatives of patients with diabetes after 6 wk of intervention compared with a habitual diet.

Introduction

Diabetes is a multifactorial disease in which interaction of multiple genes and environmental factors can play an important role [1,2]. It has been demonstrated that individuals with a family history of diabetes are at two to five times higher risk for developing diabetes [3]. Cross-sectional studies have found that the first-degree relatives of patients with diabetes are at higher risk for decreased levels of adiponectin and increased levels of inflammatory markers. It has been demonstrated that the non-obese insulin-resistant first-degree relatives of patients with diabetes had lower adiponectin levels [4]. Additionally, it has been shown that the association of low concentrations of adiponectin and family history of diabetes was independent of the effects of obesity, glycemia, and insulin sensitivity [5], whereas the association of high levels of C-reactive protein (CRP) with family history of diabetes was mediated through overweight and obesity [6].

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* Corresponding author. Tel: ++98 311 792 2791; fax: +98 311 668 2509.
E-mail address: Azadbakht@hlth.mui.ac.ir (L. Azadbakht).

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One way to modify high levels of inflammatory markers and increase the serum levels of adiponectin is a dietary approach. Other available methods include exercise, cardiovascular drugs, insulin sensitizers, and combination therapies [7]. It has been established that nonhydrogenated vegetable oils such as olive oil [8], fruits and vegetables [9], low- and high-fat dairy [10], soy nut [11], dietary patterns [12] and a Mediterranean diet [13] provide anti-inflammatory effects.

Legumes are a part of dietary components. Legumes contain high amounts of soluble and insoluble fibers and resistance starches that make them low-glycemic and low-energy dense foods [14,15]. Additionally, legumes have vegetable proteins; oligosaccharides; phytochemicals; vitamins; and minerals like folic acid, potassium, and magnesium; saponins; and polyphenols [16,17]. There are limited clinical trials assessing the effects of legume consumption on inflammation and adiponectin serum levels and the results of these studies are controversial. A significant reduction in body weight, CRP, and complement C3 has been documented in overweight and obese individuals after consumption of a legume-based hypocaloric diet. After adjusting for observed weight loss, the reduction in inflammatory markers remained significant [17]. One study was unable to show the beneficiary effects of legume consumption on CRP and adiponectin in overweight and obese adults [14]. Only one cross-sectional study assessed the association between legume intake and inflammation and showed an inverse significant relationship among Iranian women [18].

To the best of our knowledge, there are trials studying the effects of non-soy legumes on inflammatory markers among first-degree relatives of patients with diabetes. So the aim of this study was to determine the effects of non-soy legume-enriched diet on high-sensitivity (hs)-CRP as a primary end point and other inflammatory biomarkers and serum adiponectin levels as secondary outcomes among these individuals.

Materials and methods

Participants

According to available files in the Isfahan Endocrine and Metabolism Research Center, of 346 potential eligible first-degree relatives of patients with type 2 diabetes, 320 did not meet all or one of the inclusion criteria or were not interested in participating in the present study. In all, 26 eligible individuals were recruited to this randomized clinical trial. Furthermore, this number was adequate to cover potential losses during the study period. Men and women with the mean age of 50 $\pm$ 1.29 y (14 women and 12 men) were enrolled. Inclusion criteria included being at risk for diabetes according to the American Diabetes Association's standards [19]; age >30 y; not being pregnant or lactating; no history of liver or kidney disease, cancer, allergy, hyperthyroidism, hypothyroidism, gastrointestinal problems (bloating and irritable bowel syndrome); not using anti-inflammatory or glucose-lowering medications; being a nonsmoker; no weight change >3 kg during previous 2 mo; and not adhering to a specific diet. Before the start of study, a questionnaire asking about demographic information, medical history, and medication use was completed. An overview of the study course was given to the participants, following which participants were asked to provide written informed consent. This study was conducted according to the guidelines of the Declaration of Helsinki and all procedures involving human subjects were approved by the research and ethics committee of the Isfahan University of Medical Sciences, Isfahan, Iran (No. 191015).

Study design

This randomized, crossover study was conducted between September 2012 and January 2013 in Isfahan Endocrine and Metabolism Research Center, Isfahan, Iran. The aim of the present study was to determine the effects of legume consumption on inflammatory markers and serum levels of adiponectin. With regard to previous studies [11,20], the sufficient sample size for this study was calculated by the use of following formula $n = 2[(z_{1-\alpha/2} + z_{1-\beta})^2 \times s^2/\Delta^2$, in which $\alpha = 0.05$ and $\beta = 80\%$. In this formula, S was considered as variance of serum level of CRP (S = 0.2) and Δ was considered as difference in mean of serum level of CRP (Δ = 0.18) [11,20]. Finally, the sufficient sample size for this study was 19 adults. Due to the crossover nature of the study and the length of the intervention, which resulted in potential losses, 26 individuals were recruited. Anthropometric indices and blood pressure levels were measured at baseline and at weeks 6, 8, and 14. Furthermore, by using dietary and physical activity records, physical activity and dietary intakes were assessed before study entry and throughout the intervention. The participants were randomly divided into two groups and then randomly assigned to their habitual diet (control diet) or a habitual diet enriched with legumes (legume diet) by a third person who was not aware of the groups. All participants completed a 1-d dietary record before the start of study. According to this completed form, legume, meat, and energy intakes, as well as all macro- and micronutrients were the same between participants assigned to the intervention and control groups. Therefore, the diets of participants in the legume diet group and the habitual diet group were similar before the start of study. Each phase of study was 6 wk in duration, separated by 2-wk washout. According to the Legume Inflammation Feeding Experiment Study [15], 2 wk were enough for washout period. After randomization, fasting blood samples were drawn for biochemical measurements for the first time. The participants completed 1-d dietary and physical activity records at baseline and by 2-wk intervals until the end of study. Participants were shown how to complete the dietary and physical activity records, and written instructions were given. Eight records were completed for each participant; one record before the start of study, three in each intervention phase, and one during the washout period. In each intervention period, two weekdays and one weekend day were registered by the participants. The average of three dietary records was entered for analysis. Furthermore, participants were asked to record their daily physical activities in a way that total recorded time reached ≤24 h. Then the recorded physical activities were multiplied by the relevant metabolic equivalents (MET) coefficients and finally converted to MET-h/d. At the end of weeks 6, 8, and 14, anthropometric indices and blood pressure were measured and fasting blood samples were taken.

At the beginning of study, healthy eating recommendations were given to all participants. The participants in both groups were advised to modify their lifestyles and improve their dietary intakes. Raw legumes were measured on a digital scale and packed by study staff. For the legume diet period, 12 raw packs of legumes (65 g raw in one pack that is equivalent to one serving of cooked legume) for the first 3 wk of the intervention phase were given to the legume-enriched diet group (4 packs/1 wk). Participants were asked to use the prescribed legumes in addition to their ordinary use of legumes. Legumes that were used in this study consisted of pinto beans and brown lentils. In this study, these two types of legumes were chosen because they can be cooked apart from family food and can be eaten as a separate meal (i.e., evening meal). Additionally, these legumes are the most commonly used by Iranians. After completing the first 3-wk, participants received 12 raw packs of the second 3 wk of the legume phase. In all, 24 packs of legume (12 pinto beans and 12 brown lentils) were consumed during the legume phase. The participants were instructed to ingest 4 packs of legumes per week according to the kind of legumes they wished to eat. The participants were asked to soak the legumes for ≤2 h and to discard the water before consuming. A written instruction describing the cooking method was also given to the participants. In the control period, participants were asked to continue their usual diet. To assess the compliance of participants, a trained dietitian was in contact with participants during all phases of the study. At individual visits, the completed dietary records were reviewed to evaluate the amount of consumed legumes. Additionally, for participants in the legume diet group, legume packages were provided. Furthermore, a phone call was made by a dietitian every fortnight to remind participants to complete their record forms and to consume four packs of legumes per week. If needed, participants were instructed about their dietary plan. To ensure that the prescribed legumes were consumed and to ensure adherence, larger packs of legumes (one 480 g pack of pinto bean and one 480 g pack of brown lentil) were given for use by the family.

Anthropometric and blood pressure measurements

Anthropometric indices including weight, height, waist circumference, body mass index (BMI), and systolic and diastolic blood pressure were measured before and after each intervention phase by a trained expert. Using a Seca scale, weight was measured nearest to 0.1 kg. During weight measurement, participants wore light clothing and were barefoot. Height was measured with a Seca stadiometer without shoes, with 0.1 cm accuracy. Waist circumference was measured at narrowest part with an inelastic tape nearest to 0.1 cm, with minimal clothing. BMI was calculated by dividing weight (kg) by the height square (m^2). Blood pressure was measured in a sitting position after 5 min rest with a mercury sphygmomanometer.

Laboratory analysis

Blood samples were taken before starting the study (week 1) and at weeks 6, 8, and 14. After 12 to 14 h of fasting, all blood samples were drawn between 0700