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ORIGINAL ARTICLE

Substitution of red meat with legumes in the therapeutic lifestyle change diet based on dietary advice improves cardiometabolic risk factors in overweight type 2 diabetes patients: a cross-over randomized clinical trial

S Hosseinpour-Niazi[1,2], P Mirmiran[3], M Hedayati[4] and F Azizi[5]

BACKGROUND/OBJECTIVE: The objective of this study was to determine the effects of substitution of red meat with legumes in the Therapeutic Lifestyle Change (TLC) diet on cardiometabolic risk factors in type 2 diabetes patients based on dietary education.
SUBJECTS/METHODS: This study was a randomized, controlled, cross-over trial. Thirty-one participants (24 women and 7 men; age: 58.1 ± 6.0 years) with type 2 diabetes were randomly assigned to consume a control diet (legume-free TLC diet) and legume-based TLC diet for 8 weeks. Legume-based TLC diet was the same as the control diet, but the legume-based TLC group was advised to replace two servings of red meat with legumes, 3 days per week. After the interventional period, a washout period was conducted for 4 weeks. The groups were then advised to follow the alternate treatment for 8 weeks. Cardiometabolic risk factors were measured.
RESULTS: Compared with the legume-free TLC diet, the legume-based TLC diet significantly decreased fasting blood glucose ($P = 0.04$), fasting insulin ($P = 0.04$), triglyceride concentrations ($P = 0.04$) and low-density lipoprotein cholesterol ($P = 0.02$). Total cholesterol concentrations decreased after consumption of both TLC diet and legume TLC diet; however, the data did not differ significantly between the two diets. body mass index (BMI), waist circumference, systolic and diastolic blood pressures did not change significantly after consumption of either the legume-free TLC diet or the legume-based TLC diet.
CONCLUSIONS: Dietary advice given for substitution of red meat with legume intakes within a TLC diet-improved lipid profiles and glycemic control among diabetes patients, which were independent from BMI change. This trial was registered in the Iranian Registry of Clinical Trials (http://www.irct.ir) as IRCT201202251640N7.

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INTRODUCTION

Cardiometabolic risk factors are the most frequent problems among type 2 diabetes patients;[1] consequently, interventions that decrease these cardiometabolic risk factors are considered beneficial to health. In previous investigations, intakes of meat,[2] fruit and vegetable,[3] dairy products[4] and whole grains[5] appeared to influence the risk of cardiometabolic factors among diabetes patients, either positively or negatively, but legume intakes have not been emphasized enough.[6] Legumes, including beans, lentils, peanuts, peas and soybeans, could reduce the risk of the cardiometabolic risk factors through their beneficial components, that is, complex carbohydrate, vegetable protein, soluble fiber, low-glycemic-index and high content of isoflavones.[7,8] Current dietary guidelines for Americans recommend consumption of at least three cups of legumes per week for health promotion and disease prevention.[9]

A therapeutic approach that can control cardiometabolic risks might have beneficial effects for diabetes patients. The Therapeutic Lifestyle Change (TLC) diet is currently recommended by the Adult Treatment Panel of the National Cholesterol Education Program to lower the risk of cardiometabolic risk factors.[10] In previous studies, inclusion of soy in the TLC diet or Dietary Approach to Stop Hypertension had beneficial effects on cardiometabolic risk factors;[11,12] however, soybean intake is not usually part of a traditional dietary pattern, whereas the intakes of other legumes is traditional. The current study examined the effects of substitution of red meat with non-soy legumes in the TLC diet on cardiometabolic risk factors among overweight type 2 diabetes patients, based on dietary education.

MATERIALS AND METHODS

Participants

Type 2 diabetes patients who had serum glucose levels and medication doses that had been stable for 3 months were recruited from the clinic of Taleghani hospital, Tehran, Iran, during 2012. Participants were considered having diabetes if fasting blood glucose (FBG) was $\geqslant 126$ mg/dl or they were using oral glucose-lowering agents. Eligible participants had a clinical

[1]Nutrition and Endocrine Research center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [2]Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [3]Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [4]Cellular and Molecular Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran and [5]Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Correspondence: Dr P Mirmiran, Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
E-mail: mirmiran@endocrine.ac.ir
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diagnosis of type 2 diabetes, body mass index (BMI) 25–30 kg/m^2, were aged 40–75 years, were non-smokers, were not currently receiving insulin therapy and did not have any cardiac, hepatic or renal function disorders. A total of 40 type 2 diabetes patients were screened for inclusion in the study. All participants provided informed written consent. This study was approved by the research council and ethics committee of the Research for Endocrine Sciences, Shahid Beheshti University of Medical Sciences (registered in http://www.irct.ir; ID number IRCT201202251640N7).

Study design

This was a randomized cross-over study. During the run-in period (2 weeks), the participants consumed their own usual diet (50% of energy from carbohydrate, 15% of energy from protein and 35% of energy from fat) with restrictions that included no type of legume. After 2 weeks of the run-in period, patients were randomly assigned to one of the two diet intervention groups: legume-free TLC diet or legume-based TLC diet. Random allocation of patients to intervention groups was performed using random sequencing generated in the Statistical Package for Social Science (SPSS Inc., Chicago, IL, USA) at the end of the run-in period, and randomization was performed by an assistant. After the interventional period, a washout period was conducted for 4 weeks; then, the groups followed the alternate treatment for 8 weeks. Because this was a dietary intervention, patients and investigators were not blinded.

For assessing the diet compliance, the participants were visited every week for 30–45 min per patient, at the baseline and during intervention. Compliance was assessed by during each weekly visit, when the 3-day diet records were collected; the participants were educated by dieticians on substitution of red meat by legumes, and advised to reduce saturated fatty acid and cholesterol intakes and increase fiber intakes. Participants also received education on using an exchange list of foods and preparation of the diet record. Every participant had to bring her 3-day diet record, including 2 weekdays and 1 weekend day, at each visit. Each food and beverage was then coded according to the prescribed protocol and analyzed for content of energy and the other nutrients by using NUTRITIONIST III software (version 7.0; N-Squared computing, Salem, OR, USA), which design for Iranian foods. Estimated nutrient intakes from all records collected during the intervention were averaged for the determination of dietary compliance. In the legume-free TLC diet, mean intake of energy, protein, fat, saturated fatty acid, monounsaturated fatty acid and carbohydrate was determined by the diet record divided by the recommended amounts of these nutrients according to calorie requirements of each patient, based on equations suggested by the Institute of Medicine, and Food and Nutrition Board.[13,14] Compliance was defined >90%. In addition, intakes of cholesterol and fiber were according to the TLC diet (<200 mg cholesterol and 25–30 g fiber intake). In the legume-based TLC diet, in addition to the above, intakes of legume >90% of those prescribed were considered as good compliance. Participants were asked not to change their habitual physical activity levels for the duration of the study. In the current study, patients were not on a weight-reducing diet, because weight loss was not a goal of the current study.

Diets

Two diet interventions were used in the current study: (1) control diet, which was a legume-free TLC diet that consisted of 50–60% carbohydrate, 15% protein and 25–35% of energy from fat (<7% saturated fat, up to 20% monounsaturated fat and up to 10% polyunsaturated fat) and <200 mg cholesterol and 25–30 g fiber intake; and (2) legume-based TLC diet, which was the same as the control diet, but the participants were advised to replace two servings of red meat with different types of cooked legumes such as lentils, chickpeas, peas and beans 3 days per week. Half a cup of cooked legumes was considered as one serving of red meat; nutrient compositions of the legume-free TLC diet and legume-based TLC diet consumed by the study participants are shown in Table 1.

Measurement

Cardiometabolic factors included FBG, blood pressure, BMI, waist circumference and lipid profiles. Weight was measured using digital scales (Seca, Hamburg, Germany), while the participants were minimally clothed and not wearing shoes, and it was recorded to the nearest 100 g. Height was measured while participants were standing without shoes, with their shoulders in a normal position, using a tape fixed to the wall, and it was recorded to the nearest 0.5 cm. BMI was calculated as weight (kg) divided by the square of height (m^2). Waist circumference was measured at the level of the umbilicus site, using an outstretched tape meter, without pressure to body surfaces, and it was recorded to the nearest 0.5 cm. Systolic and diastolic blood pressures were measured using a standard mercury sphygmomanometer, on the right arm after a 15-min rest in a sitting position. Two measurements were taken at 1-min intervals, and the average of the measurement was recorded as the participant's blood pressure. Additional information about age, medical history, current use of medications and cigarette smoking were obtained using an oral questionnaire. Physical activity was assessed using an oral questionnaire, including a list of common activities of daily life; the frequency and the amount of time spent on activities per week over the past 12 months were documented. Levels of physical activity were expressed as metabolic equivalent hours per week.

Biochemical assessment

After 12–14 h of overnight fasting, blood samples were drawn into vacutainer tubes in a sitting position, from all study participants. Serum was separated and frozen at −70° C, on the day of blood collection for biochemical analysis. All blood analyses were performed at the TLGS research laboratory, using a Selectra 2 autoanalyzer (Vita; Scientific, Spankeren, The Netherlands). The laboratory staff was blinded to the treatment status. Serum triglyceride concentrations were measured using triglyceride kits (Pars Azmoon Inc., Tehran, Iran) by the enzymatic calorimetric test with glycerol phosphate oxidase. HDL cholesterol was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungistic acid. Serum fasting glucose concentration was assayed using an enzymatic colorimetric method with the

Table 1. Dietary intakes of the participants by intervention period

Daily dietary intake	*Legume-free TLC diet*	*Legume-based TLC diet*[a]	P	*Washout*
Nutrients				
Energy (kcal)	2058 ± 27[b]	2030 ± 25	0.75	2078 ± 20
Carbohydrate (% energy)	52.2 ± 1.7	53.6 ± 1.3	0.89	54.5 ± 1.5
Total fat (% energy)	33.9 ± 0.8	32.5 ± 0.6	0.32	32.3 ± 0.9
Protein (% energy)	14.6 ± 0.7	13.9 ± 0.5	0.41	13.3 ± 0.7
Saturated fatty acid (% energy)	8.4 ± 0.5	7.1 ± 0.5	0.25	12.3 ± 0.6
Monounsaturated fatty acid (% energy)	17.1 ± 0.9	17.5 ± 0.9	0.87	14.9 ± 0.4
Polyunsaturated fatty acid (% energy)	8.3 ± 0.4	7.9 ± 0.4	0.41	5.1 ± 0.2
Cholesterol (g)	169 ± 14	129 ± 9	0.04	225 ± 13
Total fiber (g)	26.9 ± 1.3	31.4 ± 1.5	0.03	24.2 ± 0.9
Magnesium (mg)	408 ± 4.2	450 ± 5.4	0.03	340 ± 3.4
Meat (serving per day)	4.9 ± 0.2	3.8 ± 0.2	0.04	3.5 ± 0.2
Legume (serving per week)	1.1 ± 0.1	6.1 ± 0.1	< 0.001	0.7 ± 0.1

Abbreviation: TLC, therapeutic lifestyle change. [a]This diet was the same as legume-free TLC diet; two servings of red meat were replaced with non-soy legume such as lentils, chickpeas, peas and beans, 3 days per week. Half a cup of cooked legume was considered as one serving of red meat or poultry. [b]Mean and s.e.m. (all such values).

glucose oxidase technique. Total cholesterol was assessed with cholesterol esterase and cholesterol oxidase using the enzymatic colorimetric method. Low-density lipoprotien (LDL) cholesterol was measured enzymatically using commercially available kits (Pars Azmun). Inter- and intra-assay coefficients of variations were both 2.2% for serum glucose, 2 and 0.5% for high-density lipoprotein (HDL-C) and total cholesterol and 1.6 and 0.6% for triglycerides, respectively.

Statistical analysis

The Statistical Package for Social Science (version 15.0; SPSS Inc) was used for statistical analyses. Baseline and end-of-intervention values were used to calculate the changes in each of the cardiometabolic factors. Paired *t*-test was used to compare baseline and end-of-intervention values in each group. Repeated-measures analysis of variance was used to compare means of cardiometabolic factors at the end of the intervention diets, with baseline values, age and physical activity as covariates. Results are expressed as mean ± s.e. A P value < 0.05 was considered significant.

Baseline and end-of-intervention values only for compliant participants ($n = 31$) were used in the analysis (patients completing two intervention diets during 8 weeks of treatment with compliance). Subsequently, according to the intent-to-treat approach, all analyses were done using data for participants with compliance and non-compliance of diet intervention ($n = 38$). Finally, analyses using imputation of missing data was done ($n = 40$); the amount of missing data was small and the results were consistent across the various approaches.

In the current study, LDL cholesterol was the primary outcome and total cholesterol and FBG were other prespecified outcomes. Blood pressure, triglycerides and HDL cholesterol and insulin were secondary outcomes.

RESULTS

Thirty-one of the 40 participants who began the diet intervention completed the entire cross-over study. Nine participants dropped out because of changes in medications or because they had a poor compliance with the intervention protocol (Figure 1). The mean age of participants who completed the study was 58.1 ± 6.0 years; 77.4% were women. Activity levels of participants remained the same across all study periods (in legume-free TLC diet group: 2.56 ± 0.2; in legume-based TLC group: 2.49 ± 0.2). Analysis of the diet records is shown in Table 1. The legume-based TLC diet that emphasized substitution of red meat with legume intake had higher amounts of legume intake (6.1 vs 1.1 serving per week; $P < 0.001$) and lower amounts of meat intake (3.8 vs 4.9 serving per day; $P = 0.04$), compared with the legume-free TLC diet; there was no significant difference in energy intake between the two groups ($P = 0.75$). The results were the same with regard to the intake of percentage of the protein ($P = 0.41$), total fat ($P = 0.32$), carbohydrate ($P = 0.89$), saturated fatty acid ($P = 0.25$), monounsaturated fatty acid ($P = 0.87$) and polyunsaturated fatty acids ($P = 0.41$). The legume-based TLC diet had a higher amount of

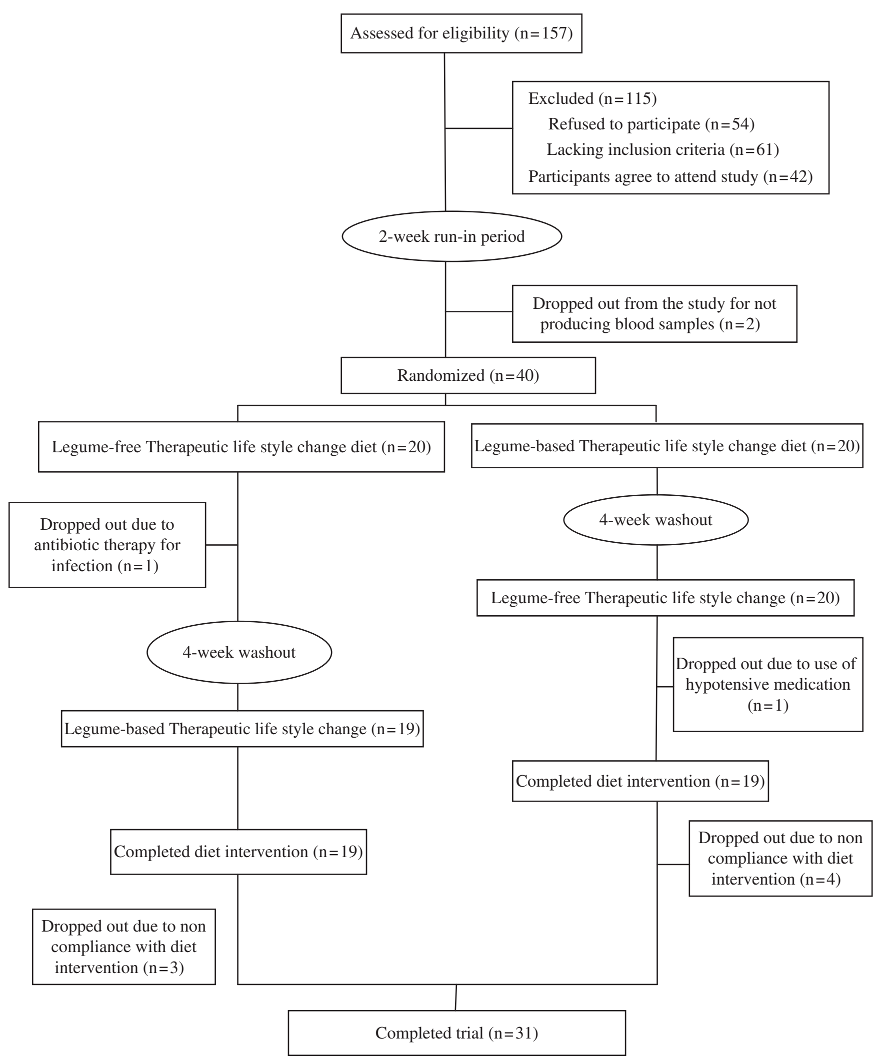

Figure 1. Flowchart for the participants.

total fiber (31.4 vs 26.9 g per day; $P = 0.03$) and magnesium (450 vs 408 mg per day; $P = 0.03$) and lower cholesterol (129 vs 169 g per day; $P = 0.04$) compared with the legume-free TLC diet.

Cardiometabolic factors

No significant differences in the baseline characteristics of patients were observed across the diet periods. Effects of the two diets on cardiometabolic factors are shown in Table 2. After consumption of both the legume-free TLC and legume-based TLC diets, FBG, fasting insulin, triglyceride concentrations, LDL cholesterol and serum total cholesterol showed significant decreases from baseline values. Compared with the legume-free TLC diet, the legume-based TLC diet significantly decreased FBG (−19.5 ±5.5 vs −28.7 ± 6.7, $P < 0.001$), fasting insulin (−1.5 ± 0.5 vs −3.5 ± 0.4, $P = 0.006$), triglyceride concentrations (−19.5 ± 6.4 vs −38.5 ± 6.6, $P = 0.02$) and LDL cholesterol (−8.7 ± 2.7 vs −15.6 ± 5.1, $P = 0.02$). Total cholesterol concentrations decreased after consumption of both TLC and legume TLC diets; however, the difference was not significant. BMI, waist circumference and systolic and diastolic blood pressures did not change significantly after consumption of either of the two diets (Table 2).

Table 2. Means of cardiometabolic factors at baseline and after 8 weeks of intervention in type 2 diabetic patients[a]

	Control diet[b]	*Legume-based TLC diet*[c]	P[c]
n	31	31	
BMI (kg/m²)			
Baseline	27.8 ± 0.6	27.7 ± 0.6	0.51
End of trial	27.9 ± 0.6	27.2 ± 0.6	0.01
Change	0.06 ± 0.4	− 0.4 ± 1.7	0.18
Waist circumference (cm)			
Baseline	98.5 ± 1.6	97.1 ± 2.5	0.10
End of trial	97.1 ± 1.4	95.2 ± 2.8	0.37
Change	− 1.3 ± 2.9	− 3.5 ± 1.8	0.33
SBP (mm Hg)			
Baseline	13.6 ± 0.4	12.5 ± 0.2	0.51
End of trial	13.2 ± 0.3	12.0 ± 0.3	0.01
Change	− 0.4 ± 0.3	− 0.4 ± 0.3	0.90
DBP (mm Hg)			
Baseline	8.1 ± 0.3	7.8 ± 0.1	0.32
End of trial	7.7 ± 0.2	7.5 ± 0.3	0.65
Change	− 0.4 ± 0.3	− 0.4 ± 0.3	0.69
FBG (mg/dl)			
Baseline	147.6 ± 9.6	143.3 ± 10.0	0.14
End of trial	128.1 ± 8.9[d]	114.5 ± 7.3[d]	0.001
Change	− 19.5 ± 5.5	− 28.7 ± 6.7	< 0.001
Fasting insulin (μIU/ml)			
Baseline	7.5 ± 0.7	8.1 ± 0.6	0.426
End of trial	6.0 ± 0.5[d]	4.5 ± 0.3[d]	0.011
Change	− 1.5 ± 0.5	− 3.5 ± 0.4	0.006
TG (mg/dl)			
Baseline	144.0 ± 10.5	151.0 ± 9.9	0.28
End of trial	124.5 ± 10.5[d]	122.6 ± 10.6[d]	0.03
Change	− 19.5 ± 6.4	− 38.5 ± 6.6	0.02
HDL-C (mg/dl)			
Baseline	48.6 ± 2.7	47.3 ± 2.4	0.34
End of trial	46.9 ± 2.6	48.0 ± 2.6	0.44
Change	− 1.7 ± 1.3	0.64 ± 1.2	0.29
LDL-C (mg/dl)			
Baseline	97.8 ± 5.4	100.1 ± 5.6	0.39
End of trial	89.1 ± 5.2[d]	79.4 ± 5.0[d]	0.04
Change	− 8.7 ± 2.7	− 15.6 ± 5.1	0.02
Total cholesterol (mg/dl)			
Baseline	179.2 ± 6.6	174.4 ± 7.2	0.41
End of trial	161.5 ± 7.0[d]	156.1 ± 6.3[d]	0.50
Change	− 17.7 ± 4.9	− 18.3 ±5.4	0.51

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride; TLC, Therapeutic Lifestyle Changes. [a]Data are mean ± s.e. [b]The control diet was a legume-free TLC diet. [c]The legume-based TLC diet was the same as the control diet, but two servings of red meat was replaced with different types of cooked legumes such as lentils, chickpeas, peas and beans, 3 day per week. [d]$P < 0.05$ compared with baseline.

DISCUSSION

In the current study, we observed that both the TLC diet with and without legumes had favorable effects on some cardiometabolic factors; however, compared with the TLC diet without legumes, consumption of a TLC diet with legumes for 8 weeks significantly improved FBG, insulin concentration and some disturbances in lipid profiles in overweight type 2 diabetes patients. This may be explained in part by comparison of the nutrient profiles between the two diets. For example, legume diets had higher concentrations of magnesium and fiber and a lower concentration of cholesterol; they are known to be associated with decreased levels of cardiometabolic risk factors and to improve diabetes and insulin resistance.[15,16]

The National Institute of health considers serum total cholesterol and cholesterol lipid fractions LDL and HDL as valid biomarkers for the risk of cardiovascular disease.[17] Triglyceride concentrations are also relevant as indicators of cardiovascular disease risk in diabetes patients.[18] In the current study, compared with the TLC diet without legumes, the legume-based TLC diet had beneficial effects on serum concentrations of total cholesterol, LDL cholesterol and triglycerides in type 2 diabetes patients; these results are consistent with the results of previous trials demonstrating that the ingestion of legumes has a cholesterol-lowering effect. In a clinical study, incorporation of a 1.5 serving of legume in a high-fiber and low-glycemic-index diet for 4 weeks decreased total cholesterol, LDL cholesterol and triglyceride concentrations by 10–14.8%.[19] In addition, among obese participants, a calorie-restricted legume-based diet for 8 weeks decreased weight, serum TC and LDL-C.[20] Crujeiras *et al.*[21] reported that an addition of four servings of legumes/week to a hypocaloric diet for 8 weeks led to improvements in both total cholesterol and ox-LDL cholesterol, malondialdehyde and urinary 8-iso-PGF2α. The reduction observed in LDL cholesterol is consistent with that reported in a previous meta-analyses of 26 randomized controlled trials of the effect of dietary pulses (beans, chickpeas, lentils and peas) on cardiovascular risk factors, which concluded a significant reduction in LDL cholesterol of 0.17 mmol/l at a median dose of 130 g/d of pulses (about one serving daily) over a median follow-up of 6 weeks.[22] Most of the previous studies investigate the effect of legume in the framework of a hypocaloric diet.[19–21] In the current study, we found that dietary advice on replacement of two servings of red meat with legumes for 3 days per week in an isocaloric TLC diet had beneficial effects on disturbances of lipid profiles in diabetes patients, independent of BMI change.

Legumes are a good source of soluble fiber, which have been shown to have cardiometabolic protective effects, and are believed to bind to bile acids in the intestines and prevent reabsorption into the body. Consequently, an increase in the production of bile acids decreases the liver pool of cholesterol and increases the uptake of serum cholesterol by the liver, thereby decreasing circulating cholesterol in the blood.[23] In addition, specific phytochemicals such as phytosterols may reduce cardiovascular disease by lowering blood cholesterol concentrations.[24]

In the current study, replacement of red meat in the TLC diet by legumes-improved concentrations of glucose and insulin among overweight diabetes patients, independent of BMI change. Some previous studies investigating the effects of legume inclusion in the diet on biomarkers of insulin sensitivity and diabetes have documented conflicting results.[25–29] In a clinical trial, incorporation of 1 cup of legumes as part of a low-glycemic-index diet improves HbA1c in diabetes patients.[25] In another study, inclusion of chickpeas in the habitual ad libitum intake of 45 healthy participants for 12 weeks resulted in a reduction in serum total cholesterol, fasting insulin concentration and homeostasis model of assessment-insulin resistance.[26] In a cross-sectional study of non-diabetes participants, substituting a serving of total red meat intake with alternative protein food in a combination of poultry, fish, legumes and nuts was associated with significantly lower fasting insulin, HbA1c and C-reactive protein.[27] A previous meta-analysis of 39 trials showed that pulses, alone or in low-GI or high-fiber diets, improved markers of longer-term glycemic control in humans. Pulses alone (11 trials) lowered FBG (−0.82, 95% confidence interval (CI) − 1.36 to − 0.27) and insulin (−0.49, 95% CI − 0.93 to − 0.04). Pulses in low-glycemic-index diets (19 trials) lowered glycosylated blood proteins (GP), measured as HbA_{1c} or fructosamine (−0.28, 95% CI − 0.42 to − 0.14). Finally, pulses in high-fiber diets (11 trials) lowered FBG (−0.32, 95% CI − 0.49 to − 0.15) and GP (−0.27, 95% CI − 0.45 to − 0.09).[30] In addition, a large prospective study shows that a traditional Mediterranean food pattern, which is rich in plant-based foods such as legumes, is associated with a significant reduction in the risk of developing type 2 diabetes.[31] However, others found no beneficial effects; Hartman *et al*.[28] found that a high-legume diet did not improve insulin sensitivity and inflammation after a 4-week intervention compared with a healthy American diet among insulin resistance participants. In another study, compared with whole-grain-based foods, inclusion of 140 g of chickpeas in the diet did not improve insulin sensitivity, insulin and homeostasis model of assessment-insulin resistance and glucose concentrations among healthy participants.[29] Comparison of the legume-based diet with a healthy diet such as the healthy American diet [28] and whole-grain-based foods [26] may explain the non-significant effect of legumes on insulin sensitivity. In the current study, the legume-based TLC diet had a more beneficial impact on glycemic control; more fiber, magnesium, phytoestrogen and isoflavone intakes owing to legume consumption might be responsible for these effects.[15,16]

Besides abnormalities in lipid metabolism, elevated blood pressure is another cardiometabolic risk factor among diabetes patients. In the current study, neither the TLC diet nor the TLC diet with legumes had significant effects on systolic or diastolic blood pressure. Previous trials examining the effect of legume consumption on blood pressure reported conflicting results. Some trials did not observe significant decreases in systolic and diastolic blood pressures after inclusion of legumes to the diet among peripheral artery disease and obese subjects;[32,33] however, others have found improvements in blood pressure resulting from the addition of legumes to the diets of obese or hypertensive patients.[11,20,34] Given the variability in the findings of these trials, it remains unclear whether legume consumption improves blood pressure, and in which population or at what amounts a benefit may be conferred.

To mention limitations, in the present study, we only recommended the types of intervention diets to be consumed, and no particular pre-prepared diets were given to participants; therefore, the diets may not have been followed as carefully as in trials in which prepared food was provided. In addition, owing to a limited budget, we could not measure the biochemical indices of legume intake in this project, and compliance of participants was assessed by analyzing the 3-day diet self-record. However, our results suggest that compliance of legume-based TLC diet could have benefits on cardiometabolic risk factors. The rate of non-compliance was also a limitation in the present study. About one-fourth of the study participants were lost to follow-up, which might be considered another limitation of this study; however, this was a cross-over trial, and cross-over trials are usually carried out over a longer time period, which results in a greater number of patient exclusions. However, after analysis of data for both compliance and non-compliance of participants, no difference was shown with analysis of compliance participants. In addition, the rate of non-compliance in the legume-based TLC diet and control diet was the same, and thus compliance did not differ. Furthermore, because this was a dietary intervention, patients and investigators were not blinded.

CONCLUSIONS

Dietary advice for diabetic patients on the substitution of red meat with legume intake within a TLC diet-improved glycemic control and lipid profiles such as triglycerides, total and LDL cholesterol, independent of any BMI change.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

The project idea for this study was from S.H. The project was designed by P.M, S.H and F.A. S.H, and M.H analyzed and interpreted the data; S.H and P.M prepared the manuscript. All authors read and approved the final manuscript. Overall F.A supervised the project and approved the final version of the manuscript to be submitted.

REFERENCES

1 Kalofoutis C, Piperi C, Kalofoutis A, Harris F, Phoenix D, Singh J. Type II diabetes mellitus and cardiovascular risk factors: current therapeutic approaches. *Exp Clin Cardiol* 2007; **12**: 17–28.
2 White DL, Collinson A. Red meat, dietary heme iron, and risk of type 2 diabetes: the involvement of advanced lipoxidation end products. *Adv Nutr* 2013; **4**: 403–411.
3 Mursu J, Virtanen JK, Tuomainen TP, Nurmi T, Voutilainen S. Intake of fruit, berries, and vegetables and risk of type 2 diabetes in Finnish men: the Kuopio Ischaemic Heart Disease Risk Factor Study. *Am J Clin Nutr* 2014; **99**: 328–333.
4 Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Am J Clin Nutr* 2013; **98**: 1066–1083.
5 Aune D, Norat T, Romundstad P, Vatten LJ. Whole grain and refined grain consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Eur J Epidemiol* 2013; **28**: 845–858.
6 Villegas R, Gao YT, Yang G, Li HL, Elasy TA, Zheng W, Shu XO. Legume and soy food intake and the incidence of type 2 diabetes in the Shanghai Women's Health Study. *Am J Clin Nutr* 2008; **87**: 162–167.
7 Bazzano LA, Thompson AM, Tees MT, Nguyen CH, Winham DM. Non-soy legume consumption lowers cholesterol levels: a meta-analysis of randomized controlled trials. *Nutr Metab Cardiovasc Dis* 2011; **21**: 94–103.
8 Hamden K, Jaouadi B, Carreau S, Aouidet A, Elfeki A. Therapeutic effects of soy isoflavones on α-amylase activity, insulin deficiency, liver-kidney function and metabolic disorders in diabetic rats. *Nat Prod Res* 2011; **25**: 244–255.
9 US Department of Agriculture, US Department of Health and Human Services Dietary Guidelines for Americans 2010: www.dietaryguidelines.gov.

10 National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the NationalCholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; **106**: 3143–3421.
11 Welty FK, Lee KS, Lew NS, Zhou JR. Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women. *Arch Intern Med* 2007; **167**: 1060–1067.
12 Miraghajani MS, Esmaillzadeh A, Najafabadi MM, Mirlohi M, Azadbakht L. Soy milk consumption, inflammation, coagulation, and oxidative stress among type 2 diabetic patients with nephropathy. *Diabetes Care* 2012; **35**: 1981–1985.
13 Institute of Medicine of the National Academies, Food and Nutrition Board. *Dietary reference intakes: for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids*. The National Academy Press: Washington, DC167. 2002, pp 1060–1067.
14 Institute of Medicine of the National Academies, Food and Nutrition Board. *Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids*. The National Academy Press: Washington DC. 2005, pp 107–264.
15 Rebello CJ, Greenway FL, Finley JW. A review of the nutritional value of legumes and their effects on obesity and its related co-morbidities. *Obes Rev* 2014; **15**: 392–407.
16 Bouchenak M, Lamri-Senhadji M. Nutritional quality of legumes, and their role in cardiometabolic risk prevention: a review. *J Med Food* 2013; **16**: 185–198.
17 Venter CS, Vorster HH, Cummins JH. Effects of dietary propionate on carbohydrate and lipid metabolism in healthy volunteers. *Am J Gastroenterol* 1990; **85**: 549–553.
18 Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. *J Cardiovasc Risk* 1996; **3**: 213–219.
19 Zhang Z, Lanza E, Kris-Etherton PM, Colburn NH, Bagshaw D, Rovine MJ *et al.* A high legume low glycemic index diet improves serum lipid profiles in men. *Lipids* 2010; **45**: 765–775.
20 Hermsdorff HH, Zulet MÁ, Abete I, Martínez JA. A legume-based hypocaloric diet reduces proinflammatory status and improves metabolic features in overweight/obese subjects. *Eur J Nutr* 2011; **50**: 61–69.
21 Crujeiras AB, Parra D, Abete I, Martínez JA. A hypocaloric diet enriched in legumes specifically mitigates lipid peroxidation in obese subjects. *Free Radic Res* 2007; **41**: 498–506.
22 Ha V, Sievenpiper JL, de Souza RJ, Jayalath VH, Mirrahimi A, Agarwal A *et al.* Effect of dietary pulse intake on established therapeutic lipid targets for cardiovascular risk reduction: a systematic review and meta-analysis of randomized controlled trials. *CMAJ* 2014; **186**: E252–E262.
23 Galisteo M, Duarte J, Zarzuelo A. Effects of dietary fibers on disturbances clustered in the metabolic syndrome. *J Nutr Biochem* 2008; **19**: 71–84.
24 Rochfort S, Panozzo J. Phytochemicals for Health, the Role of Pulses. *J Agric Food Chem* 2007; **55**: 7981–7994.
25 Jenkins DJ, Kendall CW, Augustin LS, Mitchell S, Sahye-Pudaruth S, Blanco Mejia S *et al.* Effect of legumes as part of a low glycemic index diet on glycemic control and cardiovascular risk factors in type 2 diabetes mellitus: a randomized controlled trial. *Arch Intern Med* 2012; **172**: 1653–1660.
26 Pittaway JK, Robertson IK, Ball MJ. Chickpeas may influence fatty acid and fiber intake in an ad libitum diet, leading to small improvements in serum lipid profile and glycemic control. *J Am Diet Assoc* 2008; **108**: 1009–1013.
27 Ley SH, Sun Q, Willett WC, Eliassen AH, Wu K, Pan A *et al.* Associations between red meat intake and biomarkers of inflammation and glucose metabolism in women. *Am J Clin Nutr* 2014; **99**: 352–360.
28 Hartman TJ, Albert PS, Zhang Z, Bagshaw D, Kris-Etherton PM, Ulbrecht J *et al.* Consumption of a legume-enriched, low-glycemic index diet is associated with biomarkers of insulin resistance and inflammation among men at risk for colorectal cancer. *J Nutr* 2010; **140**: 60–67.
29 Nestel P, Cehun M, Chronopoulos A. Effects of long-term consumption and single meals of chickpeas on plasma glucose, insulin, and triacylglycerol concentrations. *Am J Clin Nutr* 2004; **79**: 390–395.
30 Sievenpiper JL, Kendall CW, Esfahani A, Wong JM, Carleton AJ, Jiang HY *et al.* Effect of non-oil-seed pulses on glycaemic control: a systematic review and meta-analysis of randomised controlled experimental trials in people with and without diabetes. *Diabetologia* 2009; **52**: 1479–1495.
31 Martínez-González MA, de la Fuente-Arrillaga C, Nunez-Cordoba JM, Basterra-Gortari FJ, Beunza JJ, Vazquez Z *et al.* Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study. *BMJ* 2008; **336**: 1348–1351.
32 Zahradka P, Wright B, Weighell W, Blewett H, Baldwin A, O K *et al.* Daily non-soy legume consumption reverses vascular impairment due to peripheral artery disease. *Atherosclerosis* 2013; **230**: 310–314.
33 Abete I, Parra D, Martinez JA. Legume-, fish-, or high-protein-based hypocaloric diets: effects on weight loss and mitochondrial oxidation in obese men. *J Med Food* 2009; **12**: 100–108.
34 Tovar J, Nilsson A, Johansson M, Björck I. Combining functional features of whole-grain barley and legumes for dietary reduction of cardiometabolic risk: a randomised cross-over intervention in mature women. *Br J Nutr* 2014; **111**: 706–714.