

A sesame seeds-based breakfast could attenuate sub-clinical inflammation in type 2 diabetic patients: A randomized controlled trial

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Abstract: *Background and aim:* The aim of this study was to investigate the effects of Tahini, a traditional functional food made from ground un-hulled sesame seeds, on glucose homeostasis parameters and serum high-sensitive reactive protein (hs-CRP) in diabetic patients. *Methods:* This randomized clinical trial included 41 patients with type 2 diabetes, who were randomly assigned to one of two groups: Group A (Tahini 30 g/d, n=21) and group B (control, n=20). After an initial 2-week washout period, patients in group A, replaced a part of their usual breakfast with 2 tbsp (~28 g) Tahini, while group B patients continued the usual breakfast meal for 6 weeks. Insulin and hs-CRP levels were measured, and insulin sensitivity index and homeostasis model assessment of insulin resistance index (HOMA-IR) at were calculated baseline and 6 weeks intervention. *Results:* After 6-weeks, there was a significant 21.1% decrease in serum hs-CRP levels in group A. Slight but non-significant decrease in fasting serum glucose, serum insulin, insulin sensitivity index and HOMA-IR was observed during Tahini supplementation. *Conclusion:* Replacing a part of regular diet with Tahini as a functional food could attenuate sub-clinical inflammation in type 2 diabetic patients.

Keywords: High-Sensitive C Reactive Protein, Inflammation, Insulin Resistance, Sesame Seeds, Tahini, Type 2 Diabetes

1. Introduction

Systemic and sub-clinical inflammatory processes are considered as important pathogenic factor in the development of insulin resistance, type 2 diabetes and its complications especially vascular dysfunction and cardiovascular diseases [1,2]. Among proposed clinical markers of inflammation, high-sensitive C-reactive protein (hs-CRP), an acute phase 2 protein that releases from hepatocytes through stimulation by cytokines (interleukin-6, tumor-necrosis-factor-alpha and interleukin-1beta), was considered as a sensitive and reliable marker [3]. Even minor hs-CRP elevation has been shown to be associated with increased risk of cardiovascular events and clinically, serum hs-CRP levels <1 mg/L, 1-3 mg/L and >

3 mg/L have been considered as low, medium and high risk, respectively [4].

In patients with type 2 diabetes, hsCRP levels significantly correlate with hemoglobin A1C, lipid disorders, the stage of beta-cell dysfunction, insulin resistance and future cardiovascular risk; anti-inflammatory therapeutic approaches are now considered to be important in the management of type 2 diabetes and prevention of micro- and macro-vascular diseases [5,6].

The major pharmacological approaches to attenuate inflammatory processes are oral anti-diabetic drugs and non diabetic drugs such as aspirin, statins, cyclooxygenase-2

inhibitors, and fibrates; however use of some functional foods and their bioactive components may also be more effective. Sesame seed (*seamen indicum L.*) is one of these unique healthy foods with multiple beneficial effects including anti-aging, anti-cancer, anti-oxidative activity, anti-hypertensive, modulation of lipid metabolism and lipid peroxidation, enhancement of liver function, immunoregulatory and anti-thrombosis properties [7,8].

High level of mono and poly-unsaturated fatty acids, vitamin E, fiber, phytosterols, and other nutraceutical components such as bioactive lignans, sesamin, sesamol, episesamin and sesamolin have made sesame seeds and their byproducts functional foods beneficial in the prevention and treatment of chronic disease and metabolic disorder [9,10]. Anti-inflammatory properties of sesame seed and its byproducts have been shown in animal models [11,12], however in humans these effects have seldom been studied [13,14].

In this study we assessed the effects of 6-week consumption (in breakfast meal) of Tahini, a traditional food stuff produced from grounded un-hulled sesame seeds (*seamen indicum L.*), on fasting serum glucose, serum insulin, homeostasis model assessment of insulin resistance index (HOMA-IR), and serum hs-CRP as inflammatory marker in type 2 diabetic patients.

2. Material and Methods

2.1. Patients and Study Design

This was a parallel, randomized, and controlled study. Type 2 diabetic patients, aged 30-60 years with a clinical diagnosis of type 2 diabetes (for at least one year) were recruited from the Iran Diabetes Society; they were excluded if they had severe impairment of cardiac, hepatic or renal function, gestation or lactation or if they used insulin injection or consumed antioxidant supplements. Forty-one patients, initially eligible, were included in the study. Subjects were randomly assigned to one of two groups: Group A (Tahini 28 g/d, n=21) and group B (control, n=20). Random allocation of patients to treatment groups was performed by sequentially numbered containers. Randomization was performed by an assistant and group allocation was blinded for the investigator and participants.

Ethics approval for the trial was obtained from ethical committee of the Research Institute for Endocrine Sciences of the Shahid Beheshti University of Medical Sciences. This clinical trial registered in the "Iranian Registry of Clinical Trials" at <http://www.irct.ir> with the following identification: IRCT201105161640N4, was conducted between March and July 2011. The methods and results of the current study are reported according to Consolidated Standards of Reporting Trials guidelines [15].

2.2. Interventions

During an initial 2-week washout period following recruitment, energy content of breakfast meal was adjusted

for all patients within the range of 270 kcal, without any changes in regular breakfast pattern. The patients were advised to avoid intake of foods containing sesame seeds or sesame oils. After this period, patients in group A, replaced a part of their usual breakfast with 2 tbsp (~28 g) Tahini, so that energy content of breakfast be maintained in the same range; in group B patients continued with the usual breakfast meal. Each patient in group A received 2 boxes (1200 g) of Tahini (grounded un-hulled sesame seeds without any additives) purchased from Oghab Halva Company (Tehran, Iran). Patients were recommended to maintain their regular lifestyle, including diet and physical activity throughout the study period. Patients were contacted every week to evaluate compliance to the intervention and to enquire regarding any possible side effects such as allergic reactions.

2.3. Measurements

To monitor dietary compliance and assess nutrient intakes three-day dietary recalls, including 2 weekdays and 1 weekend day, were collected at baseline and again after 6 weeks from subjects. Weight, height, and waist circumference were measured at baseline and 6 weeks later. Weight was measured to the nearest 100g with digital scales, while the subjects were minimally clothed without shoes. Height was measured to the nearest 0.5 cm, in a standing position without shoes, using a tape meter. Waist circumference was measured to the nearest 0.1 cm, at the umbilical level and that of the hip, at the maximum level, over light clothing, using an unstretched tape meter, without any pressure to the body. Body mass index was calculated as weight (kg) divided by square of the height (m²). For blood pressure measurements, after a 15-minute rest in the sitting position, two measurements of blood pressure were taken, on the right arm, using a standardized mercury sphygmomanometer; the mean of the two measurements was considered as the participant's blood pressure.

2.4. Biochemical Analysis

At baseline and again 6 weeks after intervention, 12-h fasting blood samples were collected into tubes containing 0.1% EDTA and centrifuged at 4°C and 500g for 10 min to separate serum. Serum frozen at -70° C, on the day of blood collection for biochemical analysis. Fasting plasma glucose was measured by the enzymatic colorimetric method using a glucose oxidation kit (Pars Azmun Company, Tehran, Iran). Serum insulin concentration was measured by using enzyme-linked immunosorbent assay (ELISAs) kit (Mercodia, Uppsala, Sweden). The fasting glucose to insulin ratio was estimated as the insulin sensitivity index [16]. Insulin resistance was estimated using the homeostasis model assessment of insulin resistance (HOMA-IR) index, which is defined as fasting plasma insulin (mU/l) times fasting plasma glucose (mmol/l) divided by 22.5 [17]. Serum hs-CRP (pg/ml) concentration was measured by using enzyme-linked immunosorbent assay (ELISA) kit (Diagnostics Biochem Canada Inc., Ontario, Canada). The intra assay coefficient of

variations of all assays was < 5%.

2.5. Statistical Methods

The sample size was calculated to detect a difference among groups in serum hs-CRP with 95% CI and 90% power; sample size with regard to the possible loss of the samples was calculated as 20 patients in each group. Statistical analysis was performed with SPSS (version 16.0; SPSS, Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to test for a normal distribution. Differences between the 2 groups at baseline were tested with student's t-test. Paired t test was used to compare baseline and 6-week values in each group. P values < 0.05 were considered significant.

3. Results

Of forty-one randomized patients, 36 completed the study [group A, n=20 and group B, n=16] and were included in the analysis. Baseline characteristics of study participants are shown in Table 1. The mean age of participants was 50±10 and 52±9 y, and duration of diabetes was 7.6±5.5 and 7.4±4.4 y, in groups A and B respectively. There were no significant differences between the groups for age, duration of diabetes and other anthropometrics and clinical measurements at baseline.

Table 1. Baseline characteristics of participants¹

	Baseline values	
	Tahini (n=20)	Control (n=16)
Age, y	50 ± 10	52 ± 9
Sex, M/F	4/16	4/12
Duration of diabetes, y	7.6 ± 5.5	7.4 ± 4.4
Weight, kg	72.3 ± 9.6	74.8 ± 9.7
Body mass index, kg/m ²	28.5 ± 3.1	29.9 ± 3.4
Waist circumference, cm	93 ± 6.9	98 ± 8.2
Systolic blood pressure, mmHg	116 ± 18	125 ± 15
Diastolic blood pressure, mmHg	78 ± 10	81 ± 8

¹ Data are mean ± SD (No significant differences were observed between the groups using the independent sample t-test.

A regular breakfast meal for most patients, before the study, was bread and cheese; this pattern changed to bread and Tahini for the intervention group, and remained unchanged for controls during the study. Breakfast patterns in both groups had similar energy content of approximately 270 kcal. Nutritional composition of Tahini is presented in Table 2. Energy content of 28 g Tahini was approximately 172 kcal; carbohydrate, protein and total fat also were 5.1 g, 5.07 g, and 16 g, respectively. The nutrients content of both breakfast patterns (calculated using the Nutritionist Software version 4) is shown in Table 3. As compared to control pattern, Tahini consumption increased fat (total fat, mono-unsaturated fat, and poly-unsaturated fat) and fiber, and decreased saturated

fat content of breakfast meal in group A. Based on the patient reports, lifestyle and medication status remained unchanged during the study period. Subject compliance was over 88% for 92% for Tahini (based on remaining weight of Tahini at the end of treatment period) and control groups, respectively. None of the patients in group A reported any adverse effects from consumption of Tahini.

Table 2. Nutritional composition of Tahini (paste of ground un-hulled sesame seeds)

Nutritional composition	Tahini (28 g)
Energy, kcal	172
Carbohydrate, g	5.1
Protein, g	5.07
Total fat, g	16
Saturated fat, g	2.24
Mono-unsaturated fat, g	6.04
Poly-unsaturated fat, g	7.01
Dietary fiber, g	2.6

Table 3. Comparison of the nutritional composition of the breakfast meal patterns in intervention and control group

	Baseline values	
	Intervention (n=20)	Control (n=16)
Wheat bread, g	30	60
Cheese, g	-	30
Ardeh*, g	28	-
Tea, cup	1	1
Sugar, g	5	5
Energy, kcal	271	269
Carbohydrate, g	29.06	42.5
Protein, g	7.54	9.8
Total fat, g	15.24	6.7
Saturated fat, g	2.24	4.47
Mono-unsaturated fat, g	6.04	1.38
Poly-unsaturated fat, g	7.01	0.18
Dietary fiber, g	3.21	1.3

* Ardeh; paste of ground un-hulled sesame seeds

Nutritional composition of both breakfast meal was determined using the Nutritionist software, version 4.

Comparison between serum levels of fasting glucose, insulin, hs-CRP and glucose homeostasis parameters, before and after intervention in both groups group are shown in Table 4. After 6 weeks, there was a significant 21.1% decrease in serum hs-CRP levels in group A. More slightly but non-significant decrease in fasting serum glucose, serum insulin, insulin sensitivity index and HOMA-IR also were observed during Tahini supplementation. Anthropometric measures and blood pressure were unchanged throughout the study period in both groups (data are not shown).

Table 4. Serum levels of fasting glucose, insulin, hs-CRP and glucose homeostasis parameters in intervention and control group ¹

	Intervention (n=20)				Control (n=16)			
	Baseline		6 Weeks		Baseline		6 Weeks	
Fasting glucose, mmol/l	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fasting serum insulin, mU/l	8.56	2.83	7.68	2.87	8.39	2.89	8.72	2.82
Insulin sensitivity index	10.22	6.89	9.69	4.50	8.85	2.73	9.22	7.55
HOMA-IR	1.24	0.91	1.01	0.60	1.01	0.41	1.31	0.74
hs-CRP, µg/ml	3.82	3.60	3.13	1.43	3.39	1.75	3.43	2.34
	4.76	2.35	3.48 ²	2.21	3.01	2.73	3.04	2.42

¹ Data are mean ± SD

² Significantly different from baseline (paired t test; $P < 0.05$)

HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, High-sensitive C reactive protein.

4. Discussion

The results from this randomized clinical trial showed that replacement of 28g/d Tahini in breakfast meal, for 6 weeks, led to significant decrease in serum levels of hs-CRP, as a sensitive marker of sub-clinical systemic inflammation, in type 2 diabetic patients. Since the attenuation of inflammatory processes in diabetic patients is considered as a key therapeutic approach to prevent progression of undesirable complications, so this favorable capacity of sesame seeds may be clinically valuable.

There are limited and inconsistent studies investigated the anti-inflammatory capacity of sesame seed and its by products; five weeks supplementation of overweight and obese men with 25 g/d sesame (~50 mg/d sesame lignan) had not beneficial effects on systemic inflammatory markers including C-reactive protein, interleukin-6, tumor necrosis factor- α [13]. Recently, Kratzi et al reported that consumption of 35 g/d sesame oil had not favorable postprandial and long-term effects on serum CRP levels [14]; however previously anti-inflammatory potential of sesame had been reported in animal models [11,12]. It seems that anti-inflammatory properties of sesame seeds and its by products are mainly associated with bioactive components including lignans; Sesamin and sesamol, main sesame lignans, could reduce activity of p38 mitogen-activated protein kinase (MAPK) and nuclear factor (NF)-kappaB [18]; enhanced activity of p38 MAPK and NF- κ B have key roles in the development of inflammation in diabetes, and inhibitors of these pathways could interact with production of inflammatory mediators including IL-1, TNF- α and IL-6 and prevent diabetes development and its long-term complications [19,20]. Another mechanism could explain anti-inflammatory properties of sesame seed is that sesame lignans act as natural ligands for peroxisome proliferator-activated receptor gamma (PPAR- γ) [21]; treatment with PPAR- γ agonist has lead to substantial reduction of hs-CRP and other cardiovascular risk markers [22].

In this study we did not observed significant improvement in glucose homeostasis parameters after supplementation with Tahini in type 2 diabetic patients; however beneficial effects of sesame seeds and sesame oil on glycemic control have been previously reported by some studies. In one

controlled and open-label clinical trial, treatment of type 2 diabetic women with defatted sesame flour was accompanied with better glycemic control [23]; administration of 35 g/d sesame oil for 45 days led to significant decrease of blood glucose and hemoglobin A1c in diabetic patients [24]. In streptozotocin-induced diabetic rats, supplementation of a commercial diet with 6% sesame oil for 42 days significantly reduced blood glucose and serum levels of glycated hemoglobin [25].

To our knowledge this was a first study indicated the effects of Tahini on insulin resistance and inflammation in type 2 diabetic patients; however like other studies this clinical trial had few limitations including sample size was small, study duration was short and only one sample was obtained following the intervention. Further studies with longer duration and various doses may shed more light on the importance of the anti-inflammatory therapeutic effects of Tahini in diabetic patients. In the present study, the effects of Tahini, as a traditional and unique functional food, on glucose homeostasis parameters and serum hs-CRP in type 2 diabetic patients were investigated; the results showed that replacing a part of regular diet with Tahini could have favorable effects on modulation of inflammation in these patients.

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