

Original Article



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Conflict of Interest

The authors declare that they have no
competing interests.

The Effect of Soluble Fiber Supplementation on Metabolic Syndrome Profile among Newly Diagnosed Type 2 Diabetes Patients

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ABSTRACT

Diets with high fiber content improve most metabolic syndrome (MetS) profile in non-diabetic individuals, but there is scarce information about the role of fiber intake in patients with the MetS and diabetes. The objective of this study is to determine whether soluble fiber supplementation improve MetS profile for 8 weeks of intervention in newly diagnosed type 2 diabetes (T2D) adult patients. After one week of dietary stabilization phase, 36 newly diagnosed T2D patients were stratified to different strata according to sex, age, fasting blood sugar (FBS), and waist circumference (WC). Then they were randomly allocated into 2 groups. The psyllium group (n = 18) received 10.5 g of psyllium daily for 8 weeks. The control group (n = 18) maintained their regular diet for 8 weeks. Soluble fiber supplementation showed significant reduction in the majority of MetS profile; FBS (43.55 mg/dL, $p < 0.001$), triglyceride (37.89 mg/dL, $p < 0.001$), total cholesterol (20.32 mg/dL, $p < 0.001$), systolic blood pressure (7.50 mmHg, $p < 0.001$), diastolic blood pressure (2.78 mmHg, $p = 0.013$), and WC (2.54 cm, $p < 0.001$) in the intervention group compared with the control group after 8 weeks of intervention. The high-density lipoprotein cholesterol was reduced in both groups, but this reduction was insignificant. The improvement in the MetS profile was enhanced by combining psyllium to the normal diet. Consumption of foods containing moderate amounts of these fibers may improve MetS profile in newly diagnosed T2D patients. This study was registered in Current Controlled Trials (PHRC/HC/28/15).

Keywords: Metabolic syndrome; Type 2 diabetes; Fiber

INTRODUCTION

Metabolic syndrome (MetS) is a group of risk factors that raises the risk of a lot of health problems. Diagnosed patients with MetS must have at least three of the following metabolic risk factors; abdominal obesity (waist circumference [WC] > 102 centimeters [cm] in men, > 88 cm in women), high triglyceride [TAG] level > 150 mg/dL, low high-density lipoprotein cholesterol (HDL-C) (< 40 mg/dL in men, < 50 mg/dL in women), high blood pressure ($\geq 130/85$ millimeters of mercury [mm Hg]), and high fasting blood sugar (FBS) ≥ 110 mg/dL [1].

Having MetS can increase the risk of developing type 2 diabetes (T2D) because of excess weight, which can lead to insulin resistance [2]. The greater the number of MetS

components, the greater the frequency of coronary artery disease and microvascular chronic complications due to the buildup of plaques in the arteries, and these plaques can narrow and harden cardiac arteries, which can lead to a heart attack or stroke [3].

MetS increased at an alarming rate in Middle East region [4]. Therefore, it demands urgent therapeutic attention and interventional approaches. On the other hand, MetS profiles are modifiable risk factors that can be modified by diet, physical activity and life style changes.

There is a debate about the reduction degree of MetS parameters by soluble fiber supplementation. Some studies described that soluble fibers improve FBS, TAG, total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), systolic blood pressure (SBP), diastolic blood pressure (DBP), and WC [5-8]. While other studies indicated that soluble fiber does not improve FBS, TAG, TC, HDL-C [9] and LDL-C, SBP, DBP, and WC [10-12]. Indeed, the reasons for these variations may include different sample sizes, different doses of supplemented fibers, different background diets, concurrent changes in body weight, varying dietary control, and different types of subjects. It is also possible that certain soluble fibers lower MetS profiles more effectively than others.

The purpose of this study was to investigate the effects of adding psyllium to the normal daily diet on MetS profile for eight weeks of intervention among newly diagnosed T2D patients.

MATERIALS AND METHODS

The present trial is part of a comprehensive study of master thesis, in which we assessed the impact of soluble fiber from psyllium on insulin sensitivity and other metabolic controls among newly diagnosed T2D patients.

Subjects

A total of 40 males and females newly diagnosed T2D patients were recruited in this study. After one-week of dietary stabilization phase, 4 respondents dropped out during the study period, and 36 respondents have completed the trial successfully. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human patients were approved by the deanship of the Faculty of Pharmacy at Al-Azhar University-Gaza. Written informed consent was obtained from all patients. The present trial was registered at clinicaltrials.gov as PHRC/HC/28/15.

The inclusion criteria include; patients with T2D of both genders, over 35 years old were selected based on the following criteria: FBS level more than 110 mg/dL, newly diagnosed T2D (maximum 1 year) controlled by anti-diabetes medication (i.e., metformin), non-smoking, and agree to participant in the trial and sign the consent form. While the exclusion criteria include; diagnosed with current major illness (renal disease, significant cardiovascular disease [CVD], severe liver disease, gastrointestinal disorders, cancer, or other significant disorder, for which the doctor of the patients did not agree his or her participation), participants of other food supplements and clinical trials, on antihypertensive medication any type, on anti-lipid medication any type, pregnant women, and patients controlled by insulin injection.

Study design

This study utilized an experimental design, called clinical randomized controlled trial. This study procedure started with one-week dietary stabilization phase, followed by 8 weeks of intervention program. After dietary stabilization phase, subjects were randomly stratified to homogeneous strata according to sex, age, FBS, and WC, and randomly allocated into 2 groups using simple random method. In the control group, 18 participants (9 males and 9 females) did not receive any food supplements throughout the intervention period, and instead continued with their regular diets. In the intervention group, 18 participants (9 males and 9 females) were on soluble fiber supplementation (psyllium 10.5 g daily) for 8 weeks beside their regular diet.

Intervention protocol

During the dietary stabilization phase, the subjects in both groups were instructed to follow a prescribed diet plan for one week to stabilize the serum glucose level ($\leq 30\%$ of total energy from fat, $\leq 10\%$ of energy from saturated fat, and $\geq 55\%$ of energy from carbohydrate-focused on complex carbohydrate).

During intervention phase, psyllium was provided to the intervention group in this study and both groups remained on their regular diet, medications and lifestyle. The intervention protocol was designed in a way that 7.0 g of psyllium was given to the intervention group 15 minutes before lunch and 3.5 g of psyllium 15 minutes before dinner with 150 mL of water with each dose.

To ensure subjects' compliance to the intervention program, subjects in both groups were contacted by phone 3 times weekly, fill up the compliance checklists to record daily consumption of the soluble fiber doses, and subjects visits every week.

Measurements

All parameters were measured at the baseline and after 8 weeks of intervention. Blood pressure was measured by electronic trusted device after 15 minutes from non-dominant hand while the subject lying-down on the bed, and the average of 3 measurements was recorded. The measured biochemical includes FBS, TAG, TC, and HDL-C levels in the plasma. LDL-C was calculated according to the following formula [13]: $LDL-C = TC - HDL-C - (TAG/5.0)$ (mg/dL). WC was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a stretch resistant tape that provides a constant 100 g tension [14]. The average of 3 measurements was recorded.

Kits and devices

The device used for chemistry analysis (FBS, TC, TAG, and HDL-C) was semi-auto chemistry analyzer BA-88A (S.N WR-04002031; Mindray, Shenzhen, China), and the kits used in this device were for; FBS (Glucose L.S, normal level in the plasma 60–110 mg/dL, and sensitivity: 0.4 mg/dL; Biomed Diagnostics Inc., White City, OR, USA), TC (cholesterol total-L AMS, reference value: less than 200 mg/dL recommended, 200–239 mg/dL upper limit, more than 240 mg/dL high value, sensitivity: 4 mg/dL), TAG (triglyceride glycerol-3-phosphate-oxidase [GPO]-peroxidase [POD], reference value: less than 150 mg/dL desirable, 150–200 upper limit, more than 200 mg/dL high, sensitivity 1 mg/dL), HDL-C (BioMaxima HDL precipitating, reference range: 30–65 mg/dL normal, more than 60 mg/dL desired, less than 35 mg/dL high risk for coronary artery disease, sensitivity: 2.76 mA \times dL/mg).

Statistical analysis

All measurements and indicators of the 2 groups were compared at the baseline and after 8 weeks of intervention to evaluate the impact of the intervention. To compare the changes between the groups, one-way repeated measure analysis of variance was used. Data analysis was performed using statistical package for social sciences (SPSS) version 20 (IBM Corp., Chicago, IL, USA), data base for windows. The level of significance was set at p values < 0.05 .

Ethics approval and consent to participate

We confirm our responsibility to deliver the research project in accordance with Al-Azhar University policies and procedures, which include the University's Financial Regulations, Good Research Practice Standards and the Ethics Policy Governing Research Involving Human Participants, Personal Data and Human Tissue, approval from Deanship of the Faculty of Pharmacy, Graduate Studies, and Helsinki Committee. There is no potential material interest that may or may appear to impair the independence and objectivity. Subject to the research being approved.

RESULTS

Out of the 40 respondents who entered the dietary stabilization phase, 36 of them were stratified and allocated into 2 groups (18 in the intervention group and 18 in the control group). Baseline characteristics among adult patients with T2D and MetS for both intervention and control groups were presented in **Table 1**. The baseline FBS and WC were not significantly different between groups. The mean WC, TAG, and FBS were above normal level in both groups.

Table 2 summarized the changes of the MetS profiles for both groups after 8 weeks of intervention. There were significant differences between the groups in all MetS profiles after 8 weeks of psyllium supplementations except in HDL-C. As noted by the mean differences, changes in the positive side indicating that MetS profiles were improved, while changes in the negative side indicating that MetS profiles were become worse.

Table 1. Baseline characteristics among adult patients with T2D and MetS

Variables	Control group (n = 18)	Intervention group (n = 18)	p value*
Age, yr	47.50 (4.2)	47.05 (3.6)	-
Sex (male:female)	9:9	9:9	-
WC, cm	107.5 (7.1)	106.2 (7.7)	0.406
Male	110.0 (5.4)	108.7 (9.0)	
Female	104.9 (7.9)	103.6 (5.5)	
SBP, mmHg	129.5 (5.9)	133.9 (8.8)	0.111
DBP, mmHg	77.5 (6.0)	80.3 (7.4)	0.389
Cholesterol, mg/dL	161.7 (23.7)	175.8 (34.3)	0.279
LDL-C, mg/dL	70.4 (19.5)	93.9 (39.4)	0.047
HDL-C, mg/dL	49.4 (9.5)	41.7 (9.9)	0.027
TAG, mg/dL	209.3 (47.6)	201.1 (48.7)	0.696
FBS, mg/dL	156.4 (18.3)	163.1 (18.3)	0.323

Values are presented as mean (standard deviation).

T2D, type 2 diabetes; MetS, metabolic syndrome; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TAG, triglyceride; FBS, fasting blood sugar.

*Mann-Whitney U test for 2 independent nonparametric data. The level of significance is < 0.05 .

Table 2. Comparison of MetS profile among adult patients with T2D and MetS

Measurements	Control group (n = 18)	Intervention group (n = 18)	p value
WC, cm	-0.41 (-1.0007, 0.196)	2.54 (1.8, 3.434)*	< 0.001
TAG, mg/dL	-11.44 (-27.010, 4.121)	37.89 (25.711, 50.078)*	< 0.001
Cholesterol, mg/dL	-10.53 (-19.457, -1.603)*	20.32 (12.019, 28.615)*	< 0.001
HDL-C, mg/dL	3.33 (0.428, 6.239)*	2.28 (-1.912, 6.470)	0.665
LDL-C, mg/dL	-11.57 (-20.639, -2.509)*	10.46 (1.139, 19.779)*	0.001
SBP, mmHg	-1.34 (3.604, 0.916)	7.50 (3.662, 11.338) [†]	< 0.001
DBP, mmHg	-2.78 (-5.505, 0.051)*	2.78 (-0.761, 6.317)	0.013
FBS, mg/dL	2.78 (-3.518, 13.851)	43.55 (31.474, 55.637)*	< 0.001

Values are presented as mean difference (95% confidence interval). One-way repeated measures analysis of variance between and within the groups analyses were applied, followed by pairwise comparison with confidence interval adjustment. Mean difference have calculated follow as: value at baseline – value after 8 weeks of intervention.

MetS, metabolic syndrome; T2D, type 2 diabetes; WC, waist circumference; TAG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar.

Asterisk significantly different by paired t-test between baseline and 8th week in the same intervention group,

*p < 0.05; [†]p < 0.01; *p < 0.001.

DISCUSSION

The present trial showed significant changes from baseline between the groups. Psyllium group showed improved MetS profiles compared with the control group.

Obesity and overweight, in particular abdominal obesity, are an important risk factor of insulin resistance and T2D [15]. The uncontrolled anthropometric measurements, especially WC at baseline level, may explain why MetS profiles were not controlled before this study. Our results are consistent with those of Dall'Alba et al.'s study [11], in which the WC was significantly improved even though other studies show the opposite [12].

Soluble fiber was found to enhance satiety by stimulation and enhancement of satiety hormones such as cholecystokinin, glucagon-like peptide-1, and peptide YY [16,17], increase of the viscosity in the gastrointestinal tract and gastric distension [18], and slowing the absorption of macronutrients [19]. The enhancing satiety may decrease energy consumption, therefore resulting in reduction of body compartment. In addition, the calories from soluble fiber equal to zero, and processed more slowly than other nutrients [20].

Result of this study shows that there is a significant reduction in TC, LDL-C, and TAG. Anderson and his colleague proved that psyllium supplementation significantly improved LDL-C [21]. One clinical trial revealed that psyllium supplementation significantly improved TAG level in the plasma [9] without significant effect on other lipoproteins. Another study indicated that soluble fiber supplementation improved TAG, TC, and LDL-C [7]. On the other hand, one study indicated that soluble fiber did not improve TC, LDL-C, and TAG levels in the plasma [11]. One clinical trial study demonstrated that psyllium supplementation increased HDL-C from 34.61 to 36.77 mg/dL after intervention [22]. This study indicated that there is no significant reduction in HDL-C level in the plasma, equal to 2.28 mg/dL before and after psyllium supplementation. Other studies stated that HDL-C level remained unaffected after consumption of a diet containing psyllium [9,23,24]. This insignificant reduction may be due to small sample size.

Viscous soluble fibers from psyllium improved blood lipids by several mechanisms including reducing emulsification of dietary lipids [25], decreasing cholesterol absorption

[26], altering bile acid metabolism and hepatic cholesterol synthesis, and short chain fatty acids (SCFAs) production, increasing excretion of neutral steroids and bile acids [27,28], binding bile acids and cholesterol, increasing fecal excretion of bile salts, and reducing cholesterol synthesis via production of SCFAs [29]. It is well known that increased viscosity of intestinal contents would decrease the diffusion in the intestine, which results in reduced absorption of cholesterol and bile acid [30]. It is also possible that cholesterol synthesis would be directly inhibited by SCFAs produced by large bowel bacterial fermentation [31]. Intake of soluble fibers increase SCFAs production by colonic bacteria, which increases serum concentrations of propionate and to a lesser extent, acetate, propionate was shown to inhibit acetate incorporation to serum lipids [32]. It was reported that viscous fibers interfere with lipid absorption by disrupting micelle formation [33].

Findings of this study showed that there was a significant reduction of SBP and DBP in intervention group when compared with control group after 8 weeks of intervention. One clinical trial proved that soluble fiber supplementation significantly reduced both SBP and DBP [34]. Another study revealed that soluble fiber supplementation improved SBP alone [7], while other studies indicated that there was no significant impact of soluble fiber on blood pressure [11]. A lot of literature points to the association between T2D patients and the increased incidence of atherosclerotic CVD and increased blood pressure [35-37] might be related to dyslipidemia [38].

Soluble fiber may have a beneficial physiological activity of reducing blood pressure [34,39,40]. The possible mechanisms are reduction of the glycemic index of foods and the attenuation of insulin response [41], while insulin itself plays an important role in regulating blood pressure [42], increasing absorption of calcium, magnesium, and potassium by several mechanisms [43], and reducing the lipid profile and the risk of atherosclerosis [44]. In this study, desirable improvement of the lipid profile was achieved and in particular LDL-C level.

Results of this study showed significant reduction in FBS in the intervention group after 8 weeks of soluble fiber from psyllium supplementation. These results were in line with Anderson et al.'s study [21]. While other studies indicated that, there is no significant effect of soluble fiber supplementation on the level of FBS [11].

This reduction in FBS might be achieved by several proposed mechanisms; rapid feeling of fullness by delay intestinal transit time [45], which leads to reduction in extra energy consumption, decreasing glucose absorption in the gut [46] by slowing and longer-lasting release and absorption of macronutrients due to increased intraluminal viscosity [18,45], and enhancement of gut peptide responses, especially ghrelin and peptide YY release [45].

In conclusion, in patients with T2D and the MetS, the inclusion of soluble fiber to the usual diet improved the MetS profile and factors associated with cardiovascular risk. It seems that soluble fiber deserves attention as the potential natural dietary supplements for use in nutritional rehabilitation of MetS profile and T2D, as it is inexpensive and shows positive results within a short span of time.

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