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Effects of psyllium vs. placebo on constipation, weight, glycemia, and lipids: A randomized trial in patients with type 2 diabetes and chronic constipation

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ABSTRACT

Objective: To compare the effects of baked psyllium supplementation versus those who received a placebo on constipation symptoms, body weight, glycemic and lipids control in patients with type 2 diabetes (T2D) and chronic constipation.

Methods: In a single-blinded, randomized controlled trial, 51 patients with T2D and chronic constipation with body mass index (BMI) 20–47 kg/m^2 received either 10 g of psyllium pre-mixed in cookies twice per day or placebo cookies for 12 weeks. Constipation symptoms, body mass index (BMI), fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), and lipid profile were determined at the beginning and end of 4, 8, and 12-week period. Constipation was evaluated with a stool diary (ROME III).

Results: The psyllium group showed improvement in constipation symptoms, body weight, glucose and lipid values compared with the baseline and the placebo group. Body weight and FPG decreased from baseline in the psyllium group ($P < 0.001$ and $P = 0.056$, respectively). The differences (95% CI) of absolute change of body weight (−2.0 (−3.0, −1.0) kg; $P < 0.001$), FPG (−13.6 (−24.3, −2.9) mg/dl; P = .040), and HbA1c (−1.7 (−2.9, −0.5)); $P = 0.002$) between the groups were statistically significant. Cholesterol (−21.5 (−25.6, −14.4); $P < 0.001$), triglycerides (−20.0 (−32.3, −7.7); $P = 0.021$) and constipation symptoms (1.5 (0.4, 2.3); $P < 0.001$) decreased in the psyllium group. The compliance was good and no adverse effects were observed.

Conclusion: In patients with T2D and chronic constipation, psyllium supplementation decreased constipation symptoms, body weight, glycemic, cholesterol, and increased HDLC levels.

1. Introduction

Type 2 diabetes (T2D) is an increasingly prevalent chronic disease and places a huge burden on public health that has been expected to continue far into the future.[1] Constipation is more common in people with T2D and estimated that around 60 percent of people with long-standing T2D deal with constipation.[2] Although constipation is a predictable complication of T2D, inadequate management of constipation is common and may have profound implications.[3,4] Its treatment remains challenging because most of the patients are not satisfied with current therapies due to lack of efficacy or safety or availability.[5] Although previous studies have been evaluated the health benefits of psyllium in patients with T2D and indicate that it may improve glycemic and lipid control,[6–14] body weight,[15] and bowel movement,[16–18] no data is available for constipated patients with T2D. Therefore, it is reasonable to examine evidence of clinically meaningful health benefit before selecting or recommending a psyllium supplement to patients being treated for T2D and chronic constipation.

Psyllium or Indian Plantago Seed consists of the ground husk of psyllium seed (psyllium plantago or plantago ovata),[19] a mixture of polysaccharides containing pentoses, hexoses, anduronic acids, is a soluble, viscous, gel forming non-fermented fiber supplement and is marked as a bulk fiber laxative, whose mechanism of action has remained elusive.

This single-blinded, randomized, placebo-controlled trial aims to test the hypothesis that 10 g psyllium supplementation per day, as compared to a placebo, would improve constipation symptoms and reduce body weight, the glycemic and lipid levels in patients with T2D and chronic constipation. The objective of this trial was to assess the beneficial effects of adding psyllium to the normal diet for 12 weeks of intervention among patients with T2D and chronic constipation.

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2. Patients and methods

The study was approved by the Isfahan University of Medical Sciences ethics committee (approval no. IR.MUI.REC.1396.3.464), and was conducted in accordance with Good Clinical practice. The study protocol was registered at irct.ir as IRCT20110416006202N2.

2.1. Patients and trial design

This is a single-blinded, parallel-design, randomized, placebo-controlled trial of 51 consecutive patients with T2D and symptoms of chronic constipation (Rome III)[20] attending outpatient clinics in Isfahan Endocrine and Metabolism Research Center affiliated to the Isfahan University of Medical Sciences, Iran from Jan. to Oct. 2017. A one-week baseline placebo phase, where patients were not allowed any laxative treatment, preceded a 12-week treatment phase, and followed by 4-week no treatment phase. Patients were included if they had a bowel movement frequency of < 3/week during the past three months[20]; age ≥30 years, and diabetes duration > 3 year. Patients were excluded from the study if they had type 1 diabetes, weight loss, use of lipid-lowering drugs, fiber supplementation, anorectal problems, abdominal pain, and history of opioid use in the last 48 h, any other factors which would interfere with constipation assessment and management, or pre-existing severe cardiac, endocrinological, hematological, hepatic, renal, metabolic, neurological or psychiatric disorders. Pregnant or nursing women were excluded. Women of childbearing potential were required to use effective birth control during the study. Non-adherent patients during baseline or treatment phases as evaluated by taking < 75% of either cookie during a one-week period throughout the course of the study and unable to provide informed consent were excluded from the patient data analysis. After they had provided written informed consent, participants were counselled at the initial visit to maintain their usual lifestyle, diet, physical activity, and diabetic treatment throughout the study. Participants were instructed to take 2 cookies (placebo cookies or psyllium cookies) with a glass of water or tea twice a day at 10 a.m. and 4 pm as a snack. The formulation of the psyllium cookie was such that each cookie contained about 2.5 g of psyllium. Thus, the 4 cookies per day consumed by each participant containing about 10 g of psyllium. The stool diary was used to provide a stool accounting system and to obtain a subjective measure of efficacy. The participants were contacted at the end of week 1 to evaluate compliance to intervention. The clinician examined patients at baseline and each month after the start of therapy to evaluate the possible appearance of side effects of the interventions, and efficacy parameters.

The ROME III[20] definition was used for the chronic constipation by the presence of two or more of the following six complaints with at least 25% of bowel movements: straining, feeling of incomplete evacuation, hard or lumpy stool, feeling of anorectal obstruction/blockage, use of manual maneuvers, and less than 3 bowel movements/week.

2.2. Randomization scheme

A total of 60 consecutive patients were recruited. Four patients declined participation, and 2 patients did not meet our study criteria. The 54 participants (10 (18.5%) men, 44 (81.5%) women) were assigned randomly and equally to one of two treatment groups. Of those randomized, 3 patients in the psyllium group lost to follow-up and were not evaluated (Fig. 1). Patients were randomized according to a pre-existing list produced by a computer program that differed from a random number generator only in that it assigned equal numbers of patients to each treatment group, and the group assignments were concealed in an opaque sealed envelope.

2.3. Intervention

Participants in the control group received sugar-free orange-flavored maltodextrin cookies twice per day for 12 weeks as placebo. The psyllium group received 10 g psyllium pre-mixed in a sugar-free orange-flavored maltodextrin cookies twice per day for 12 weeks. Each placebo cookie contained ~56.4 kcal and each psyllium cookie contained ~55.5 kcal (Table 1). Participants were instructed to consume two cookies two times per day for a period of 12 weeks. A regimen of 4 cookies/ day was packed in individually labeled packs and provided to the individuals on a weekly basis. Cookie packs were labeled as cookie A and B. The study cookies described above was prepared by the Kamvar Co., Isfahan, Iran who was not involved in patient care.

In order to assess the durability of psyllium, constipation symptoms, glycemic, and lipid profile were assessed for another four weeks after stopping intervention, and the data from baseline, after 12 weeks of intervention, and the post-intervention periods were compared.

2.4. Evaluation

The trial was designed as double blinded in that both patients and physician were blind to the treatment. But during study period a physician who assessed the outcomes became un-blinded. Masking of the two treatments was preserved by creating cookies that looked, tasted, and textured identically. The differences in taste were minimal because the prominent flavor was that of the orange-flavor in which the cookies was mixed. The data were extracted and analyzed by one investigator (MJ) who was not involved with the study conduct. Only one author (NS) was not blinded to subject allocation and did not participate in data analysis.

Measurements: All participants were 12-h overnight fast and data on age, gender, body size, fasting plasma glucose (FPG) (measured using the glucose oxidase method), glycosylated hemoglobin (HbA1c) (measured by ion-exchange chromatography), total cholesterol, high-density lipoprotein cholesterol (HDLC), triglyceride (measured using standardized procedures), and low-density lipoprotein cholesterol (LDLC) (using the Friedewald equation[21]), were collected at baseline and at follow-ups. Height (assessed at baseline only) and weight (assessed at baseline and after 12 week) were measured with subjects in light clothes and without shoes using standard apparatus. Weight was measured to the nearest 0.1 kg on a calibrated beam scale. Height was measured to the nearest 0.5 cm with a measuring tape. Body mass index (BMI) (kg/m^2) was considered as weight (kg) divided by the squared of height (m^2). The physician defined T2D (as defined by the American Diabetes Association) and all participants were under anti-diabetes medication for more than 3 years.

Participants in both groups maintained a constipation symptom diary for 12 weeks of intervention and for 1 week run-in phase and a 4-week without treatment. Constipation was assessed with a 5-point Likert Scale included bowel movement frequency, feelings of complete evacuation, use of digital maneuvers, stool consistency (Bristol Stool Form Scale), straining during bowel movement, pain during bowel movement, and overall feeling of constipation by a previously validated stool and symptom diary.[22] In addition, at the end of 4, 8, 12 and 16 week, patients were asked to fill out a global constipation symptom score. This validated Rome III outcome measure rated current constipation-related symptoms on a seven-point Likert scale (-3 = markedly worse, -2 = somewhat worse, -1 = a little bit worse, 0 = no change, +1 = a little better, +2 = somewhat better, +3 = markedly better) when compared to baseline symptoms. Participants were asked about any gastrointestinal disturbances or physiological changes. At the end of 12-week treatment period, patients were also asked to rate the looks, taste, and texture of the cookies that they had consumed on a visual analogue scale (0 = worst, 10 = best).

2.5. Statistical analysis

Primary outcome measures included analysis of numerical values of constipation intensity according to global constipation symptom score