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Original Article

Effects of cinnamon supplementation on antioxidant status and serum lipids in women with polycystic ovary syndrome

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ABSTRACT

Background: The objectives of study were to investigate the effects of cinnamon supplementation on antioxidant status and serum lipids in women with polycystic ovary syndrome (PCOS).
Methods: This double-blind randomized controlled clinical trial was conducted on 84 overweight or obese PCOS patients; aged 20–38 years. Subjects in cinnamon (n = 42) and placebo (n = 42) groups were given 3 cinnamon capsules (each one contained 500 mg cinnamon) or placebo daily for 8 weeks. Fasting blood samples, anthropometric measurements and dietary intake data were gathered at the beginning and at the end of the study. Independent t test, paired t test and analysis of covariance were used to analyze of data.
Results: Cinnamon significantly increased serum total antioxidant capacity (P = 0.005). Malondialdehyde was significantly decreased compared with placebo (P = 0.014). Cinnamon supplementation significantly improved serum level of total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol (all P < 0.05). No significant effect was detected on serum triglyceride level.
Conclusions: Cinnamon supplementation improved antioxidant status and serum lipid profile in women with PCOS and may be applicable for reducing PCOS risk factors.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common metabolic and reproductive condition in women with an estimated prevalence of 6% to as high as 26%.[1,2] This disorder is accompanied with irregular menstrual cycle, chronic anovulation and hyperandrogenism. PCOS is associated with complications in different health aspects, including obesity, insulin resistance, infertility, diabetes and atherosclerosis.[3] Oxidative stress (OS) as one of the main causes of molecular damage to cellular is increased in women with the PCOS. Obesity and insulin resistance play a vital role in the pathogenesis of PCOS and subsequently increased OS in these patients. In addition, the resultant oxidative stress induces an inflammatory environment furthering elevated insulin resistance and contributing to hyperandrogenism,[4] dyslipidemia, hypertension and etc.[5,6] Numerous investigations have revealed that oxidative stress level is significantly increased in patients with PCOS compared with the normal ones. Fenkci et al revealed that patients with PCOS had higher OS and increased OS is related to hyperandrogenism status.[7] In another study, Desai et al displayed that the OS is also present in non-obese women with PCOS.[8]

PCOS is a condition with a significant decrease in serum antioxidant. Therefore, antioxidant supplementation may be effective in these patients. Antioxidants are considered significant agents in the

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healthy body. Many studies have displayed that the use of antioxidants, as well as herbal agents, might help to reduce OS.[9] Furthermore, medicinal herbs are expected to have a similar degree of efficacy without the side effects related to conventional medication.

Cinnamomum zeylanicum, is an herbaceous plant, belonging to the Lauraceae family. It is one of the most important spices used by people all over the world. Different flavonoids and Polyphenols isolated from cinnamon have free-radical-scavenging activities and antioxidant properties.[10] These compounds have been revealed to decrease oxidative stress in a dose-dependent manner through the inhibition of 5-lipoxygenase.[11] Antihyperlipidemic and antioxidant activity of cinnamon has been proven in experimental studies.[12–17] In animal study, Shalaby et al indicated that consumption of cinnamon aqueous extract improved activity of tissue antioxidant enzymes in obese diabetic rat.[18] Additionally, in the study by Kim et al, cinnamon lowered total cholesterol and triglyceride levels in diabetic mice.[19] Roussel et al showed that supplementation of 250 mg/day of an aqueous extract of cinnamon increased the plasma levels of thiol group and decreased malondialdehyde compared to those of placebo in patients with impaired fasting blood glucose for 12 weeks.[20]

Although some studies have reported the effects of cinnamon on oxidative stress and lipids profile in several diseases,[5,6,21] Its possible effects on serum antioxidant status and lipids profile of women with PCOS have not been studied. Therefore, we initiated a study to assess the effects of cinnamon supplementation on oxidative stress including serum total antioxidant capacity (TAC), malondialdehyde (MDA) and lipids in women with PCOS.

2. Material and methods

2.1. Design study

A total of 84 women with PCOS aged 20–38 years with a BMI between 25–40 kg/m^2 were enrolled in this double-blind, randomized, controlled clinical trial from the Gynecology clinic, Mohheb Yas Hospital in Tehran, Iran from October 2015 to February 2016. The sample size was determined based on the information acquired from the study by Kort et al for IR.[22] Considering 95% confidence interval and 80% power, the sample size was computed to be 32 per group. This number was increased to 42 per group to accommodate the anticipated dropout rate.

The diagnosis of PCOS was established according to 2003 Rotterdam criteria, which require at least two of three features for diagnosis: chronic amenorrhea or oligo-amenorrhea, clinical and/or biochemical features of hyperandrogenism and polycystic ovaries by ultrasonography.[1] Study exclusion criteria included: thyroid disorders, hyperprolactinemia, diabetes mellitus, pregnancy and lactation, liver or kidney diseases, Cushing syndrome, cardiovascular diseases, seizure and cerebrovascular disorder, hypertension, the use of medications such as insulin sensitizers, insulin, B-blockers, cholesterol-lowering drugs and dietary supplements, smoking, current treatment of infertility, inhaled corticosteroid use, following a specific diet and regular exercise (>2 weeks) and allergy to cinnamon. The Ethical Committee of Tabriz University of Medical Science approved the study protocol and was registered on the Iranian Registry of Clinical Trials website (identifier: IRCT201508173664N14). Written informed consent was gained from each subject. The participants were randomly allocated into two groups using a block randomization procedure with matched subjects in each block based on age and BMI. Subjects were questioned to continue their usual dietary intakes and physical activity during the study.

A general questionnaire was completed for each patient. Body weight was measured using a scale (Seca, Hamburg, Germany), without shoes and wearing light clothing. Height was measured using a mounted tape without shoes. BMI was calculated as the weight in kilogram divided by the height in meters squared. Information about daily energy and macronutrient intakes were obtained by 24-h recall method for 3 d, including 2 d during the week and 1 during the weekend. A three day average for energy and macronutrient intakes of all subjects was analyzed by Nutritionist 4 software (First Databank Inc., San Bruno, CA).

Cinnamon bark was provided from the Iranian Institute of medicinal plants, Tehran, Iran. Cinnamon barks were grinded with a plant tissue grinder. Each capsule containing approximately of 500 mg cinnamon powder was manufactured on October 2015. Subjects in the treatment group received three capsules of cinnamon and control group subjects received three placebo capsules (wheat flour) that they were required to take daily for 8 weeks. The compliance of the volunteers with the study protocol was monitored via phone interviews once per week and also by counting returned capsules every 2 weeks.

2.2. Blood sampling and biochemical assays

Blood samples (5 ml) were collected after a 12-h overnight fasting, in the morning. The serum samples were separated from whole blood by centrifugation at 2606.8 $\times g$ for 10 min (Beckman Avanti J-25; Beckman Coulter, Brea, CA, USA). The serum samples were frozen immediately at −70 °C until assay. Serum total cholesterol (TC), triacylglycerol (TG) and high-density lipoprotein cholesterol (HDL-C) were measured using the standard enzymatic methods by Pars Azmun kit (Karaj, Iran). Low-density lipoprotein cholesterol (LDL-C) concentration was determined by the Friedewald formula: LDL − C = TC − (HDL − C + TG/5).[23] Measurement of TAC in serum was performed by using the colorimetric method with commercial kits (TAC, RANDOX kits; UK).[24–26] The serum MDA level was estimated by using a reaction with thiobarbituric acid as a thiobarbituric acid reactive substance to produce a pink colored complex. Next, its fluorescence intensity was measured at 547 nm with excitation at 525 nm by a spectrofluorimeter (model SFM 25 A; Kontron, Milan, Italy).[27] All anthropometric, dietary intakes, blood sampling and biochemical measurements were assessed again at the end of intervention period in both groups.

2.3. Statistical analyses

The collected data were analyzed using the statistical software SPSS, version 22. (SPSS Inc., Chicago, IL, USA) and the results are expressed as means ± SD. The normality of the distribution of variables was checked by Kurtosis–Skewness test. The baseline measurements and dietary intakes of subjects in two groups were compared using independent samples t test and chi-square test for quantitative and qualitative variables, respectively. Analysis of covariance (ANCOVA) was used to identify any differences between the two groups after intervention, adjusting for baseline measurements and confounders (BMI and energy changes during study). The changes in anthropometric measurements, energy and nutrient intakes and blood parameters of the participants between the beginning and end of the trial were compared by paired samples t test. The percentage of changes in variables after intervention was determined with the formula: [(after values − before values)/before values] × 100. Results with $P < 0.05$ were considered as statistically significant.

3. Results

All of the patients (42 patients in cinnamon group and 42 patients in placebo group) completed the study (Fig. 1). Compliance

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