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The effects of a novel combination of selenium and probiotic on weight loss, glycemic control and markers of cardio-metabolic risk in women with polycystic ovary syndrome

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ABSTRACT

Synergistic approach of selenium and probiotic co-supplementation may improve clinical symptoms of patients with polycystic ovary syndrome (PCOS) by improving their metabolic profiles. This investigation was carried out to evaluate the effects of selenium and probiotic co-supplementation on weight loss, glycemic control and markers of cardio-metabolic risk in women with PCOS. This randomized, double-blind, placebo-controlled trial was conducted among 60 women with PCOS. Participants were randomly divided into two groups to receive 200 μg/day selenium plus 8×10^9 CFU/day probiotic supplements (n = 30) or placebo (n = 30) for 12 weeks. Compared with the placebo, selenium and probiotic co-supplementation resulted in a significant reduction in weight (−0.7 ± 0.5 vs. +0.1 ± 1.1 kg), serum insulin levels (−2.8 ± 3.5 vs. +0.5 ± 3.9 μIU/mL) and homeostatic model of assessment for insulin resistance (−0.6 ± 0.8 vs. +0.1 ± 0.9), and a significant increase in the quantitative insulin sensitivity check index (+0.01 ± 0.02 vs. +0.001 ± 0.02). In addition, selenium and probiotic co-supplementation significantly decreased serum triglycerides (−12.1 ± 29.6 vs. +3.1 ± 12.2 mg/dL), total- (−17.9 ± 28.5 vs. +0.1 ± 28.8 mg/dL), LDL- (−14.7 ± 24.9 vs. +1.5 ± 26.6 mg/dL) and total-/HDL-cholesterol ratio (−0.3 ± 0.8 vs. +0.2 ± 0.8) compared with the placebo. Selenium and probiotic co-supplementation for 12 weeks to PCOS women had beneficial effects on weight loss and markers of cardio-metabolic risk.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine-metabolic disorder with a worldwide prevalence of 4–21% among reproductive-age women, depending on used diagnostic criteria (Brakta et al., 2017). PCOS is correlated with multiple cardiovascular risk factors including obesity, insulin resistance, dyslipidemia, hypertension, and obstructive sleep apnoea (Sartor & Dickey, 2005). Insulin resistance and impaired glucose tolerance occur in 60–80% and 31–35% of women with PCOS, respectively (Boudreaux, Talbott, Kip, Brooks, & Witchel, 2006; Colilla, Cox, & Ehrmann, 2001). Insulin resistance and hyperandrogenism in women with PCOS are associated with an elevated risk for the type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) (Velija-Asimi, Burekovic, Dujic, Dizdarevic-Bostandzic, & Semiz, 2016).

Earlier, the beneficial effects of single selenium (200 μg/day for 8 weeks) and probiotic (6×10^9 CFU/day for 12 weeks) supplementation on markers of insulin metabolism and few lipid profiles in women with PCOS were reported (Ahmadi et al., 2017; Jamilian et al., 2015). In another study, a 8-week probiotic supplementation to women with PCOS did not affect glucose homeostasis parameters (Shoaei et al., 2015). Previous studies have demonstrated that joint supplementation is much more efficient in influencing metabolic profiles that single selenium or probiotic supplementation. In a study by Nido et al. (2016), it was observed that selenium-enriched probiotics, compared with selenium and probiotic only, had a maximum effect in improving lipid profiles, antioxidative status, histopathological lesions, and gene expression related to metabolic profiles in mice fed a high-fat diet (HFD). In addition, selenium-enriched probiotics supplementation than sodium selenite or probiotics to piglets under high-temperature environments

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had a better effect on antioxidant status, immune function, and selenoprotein gene expression (Gan et al., 2014). Some studies have reported anti-diabetic, insulin-mimetic and anti-lipidemic effects of selenium and probiotic (Farrokhian et al., 2016; Pan, Pan, Chen, Zhang, & Zheng, 2017). However, a 12-week supplementation with selenium in diabetic patients did not influence insulin metabolism and lipid profiles, and even significantly increased fasting glucose levels (Faghihi et al., 2014). In another study, probiotic supplementation for 6 weeks to overweight men and women did not affect glucose homeostasis parameters (Ivey et al., 2014).

The beneficial effects of selenium and probiotic intake on glycemic control and lipid profiles may be due to their effects on inhibiting the expression of cyclooxygenase (COX)-2 and P-selectin (Li, Han, Jiang, & Wang, 2011), and decreasing systemic inflammation (Laitinen, Poussa, & Isolauri, 2009). Therefore, we hypothesized that selenium and probiotic co-supplementation might affect metabolic status in women with PCOS. This study aimed to investigate the effects of selenium and probiotic co-supplementation on weight loss and metabolic profiles of PCOS women.

2. Materials and methods

2.1. Trial design and subjects

The current randomized, double-blind, placebo-controlled trial, registered in the Iranian registry of clinical trials (http://www.irct.ir: IRCT2017082733941N11), was conducted at the Taleghani Hospital affiliated to Shahid Beheshti University of Medical Sciences (SUMS), Tehran, Iran between May 2017 to October 2017. Inclusion criteria were women with PCOS according to the Rotterdam criteria ("Revised consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome"2003, 2004), aged 18–40 years old. The study was approved by the research ethics committee of SUMS and written informed consent was taken from all participants prior to the intervention. We did not include women aged < 18 or > 40 years, individuals with neoplastic, hepatic, renal or CVD, malabsorptive disorders, current or previous (within the last 6 months) use of anti-diabetic, or anti-obesity medications, taking selenium, probiotics and synbiotics supplements within the past 3 months and pregnant women.

2.2. Study design

Sixty women with PCOS were randomized into two groups to take either 200 μg/day selenium as selenium yeast (Webber Naturals Company, Mississauga, Canada) plus 8×109 CFU/day probiotic (LactoCare®, Zisttakhmir Company, Tehran, Iran) containing *Lactobacillus acidophilus*, *Lactobacillus reuteri*, *Lactobacillus fermentum* and *Bifidobacterium bifidum* (2×10^9 CFU/g each) or placebo (n = 30 each group) for 12 weeks. Due to lack of evidence about the appropriate dosage of selenium plus probiotic for women with PCOS, we used the above-mentioned doses of selenium (Jamilian et al., 2015) and probiotic (Ahmadi et al., 2017) based on previous studies in women with PCOS. The placebos were matched in colour, shape, size, and packaging, smell and taste with selenium and probiotic supplements and were manufactured by Barij Essence Pharmaceuticals (Kashan, Iran). All participants completed 3-day food records and three physical activity records as metabolic equivalents (METs) at weeks 0, 3, 6, 9 and 12 of the treatment. To evaluate the compliance, subjects were asked to bring the medication container. In addition, to ensure adherence, participants received a short message on their cell phones to intake the supplements daily. Randomization assignment was conducted using computer-generated random numbers. Randomization and allocation were concealed from the investigators and participants until the final analyses were completed. The randomized allocation sequence, enrolling participants and allocating them to interventions were performed by a trained midwife at the gynecology clinic.

2.3. Assessment of outcomes

The primary outcomes were parameters of insulin metabolism. The secondary outcomes were markers of cardio-metabolic risk including lipid profiles, atherogenic index of plasma (AIP), atherogenic coefficient (AC) and cardiac risk ratio (CRR).

2.4. Biochemical assessment

Ten milliliter fasting blood samples were taken at weeks 0 and 12 of the intervention. To determine FPG, serum triglycerides, VLDL-, total-, LDL- and HDL-cholesterol concentrations, we used enzymatic kits (Pars Azmun, Tehran, Iran) with inter- and intra-assay coefficient variances (CVs) of lower than 5%. Serum insulin levels were assessed using the ELISA kit (Monobind, California, USA) with the intra- and inter-assay CVs of 3.4 and 4.6%, respectively. The homeostatic model of assessment for insulin resistance (HOMA-IR) and the quantitative insulin sensitivity check index (QUICKI) were determined according to suggested formulas (Pisprasert, Ingram, Lopez-Davila, Munoz, & Garvey, 2013). AIP, AC and CRR were calculated based on suggested formulas.

2.5. Statistical methods

To calculate the sample size, we used the standard formula suggested for clinical trials by considering type one error (α) of 0.05 and type two error (β) of 0.20 (power = 80%). Based on a previous study (Jamilian et al., 2015), we used 1.81 as SD and 1.45 as the difference in mean (d) of HOMA-IR as primary variable. Based on this, we needed 25 participants in each group. Considering a dropouts of 5 participants per group, we calculated to have 30 participants per group.

The Kolmogorov-Smirnov test was applied to control the normal distribution of variables. Independent sample *t*-test was used to determine changes in anthropometric measures, dietary intakes and metabolic profiles between the two groups. Adjustment for changes in baseline values of biochemical variables, age and baseline BMI was performed by analysis of covariance (ANCOVA). $P < 0.05$ were considered statistically significant. All statistical analyses conducted using the Statistical Package for Social Science version 18 (SPSS Inc., Chicago, Illinois, USA).

3. Results

From 68 subjects who were recruited in our study (8 subjects were excluded from the study because of not living in Tehran), 30 participants in each group completed the trial (Fig. 1). On average, higher than 90% of supplements were consumed in both groups throughout the study. No side effects were reported following the supplementation of selenium and probiotic capsules in PCOS women throughout the study.

Mean age, height, baseline weight and BMI of participants were not statistically different between both groups (Table 1). After the 12-week intervention, compared with the placebo, selenium and probiotic co-supplementation resulted in a significant reduction in weight (-0.7 ± 0.5 vs. $+0.1 \pm 1.1$ kg, P = 0.002) and BMI (-0.3 ± 0.2 vs. $+0.003 \pm 0.4$ kg/m^2, P = 0.001) compared with the placebo.

No statistically significant difference was observed between the two groups in terms of macro- and micro-nutrients intake throughout the study (Table 2).

After the 12-week intervention, compared with the placebo, selenium and probiotic co-supplementation resulted in a significant reduction in serum insulin levels (-2.8 ± 3.5 vs. $+0.5 \pm 3.9$ μIU/mL, P = 0.001) and HOMA-IR (-0.6 ± 0.8 vs. $+0.1 \pm 0.9$, P = 0.001), and a significant increase in QUICKI ($+0.01 \pm 0.02$ vs. $+0.001 \pm 0.02$, P = 0.04) (Table 3). In addition, selenium and probiotic co-supplementation significantly decreased serum triglycerides (-12.1 ± 29.6 vs. $+3.1 \pm 12.2$ mg/dL, P = 0.01), VLDL-cholesterol