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ORIGINAL ARTICLE

Metabolic response to selenium supplementation in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial

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Summary

Objective We are aware of no study examining the effects of selenium supplementation on metabolic profiles of patients with polycystic ovary syndrome (PCOS). This study was conducted to evaluate the effects of selenium supplementation on glucose homeostasis parameters and lipid concentrations in women with PCOS.

Design, patients and measurements This randomized, double-blind, placebo-controlled trial was conducted among 70 women diagnosed with PCOS and aged 18–40 years old. Participants were randomly divided into two groups to receive 200 μg per day selenium supplements ($N = 35$) or placebo ($N = 35$) for 8 weeks. Fasting blood samples were taken at baseline and after 8 weeks intervention to quantify glucose, insulin and lipid concentrations.

Results After 8 weeks of intervention, subjects who received selenium supplements had significantly decreased serum insulin levels ($-29{\cdot}83 \pm 47{\cdot}29$ *vs* $+9{\cdot}07 \pm 77{\cdot}12$ pmol/l, $P = 0{\cdot}013$), homeostasis model of assessment-insulin resistance (HOMA-IR) ($-1{\cdot}15 \pm 1{\cdot}81$ *vs* $+0{\cdot}42 \pm 3{\cdot}09$, $P = 0{\cdot}011$), homeostatic model assessment-beta-cell function (HOMA-B) ($-19{\cdot}06 \pm 30{\cdot}95$ *vs* $+4{\cdot}55 \pm 47{\cdot}99$, $P = 0{\cdot}017$) and increased quantitative insulin sensitivity check index (QUICKI) ($+0{\cdot}03 \pm 0{\cdot}04$ *vs* $+0{\cdot}0009 \pm 0{\cdot}05$, $P = 0{\cdot}032$) compared with placebo. In addition, supplementation with selenium resulted in a significant reduction in serum triglycerides ($-0{\cdot}14 \pm 0{\cdot}55$ *vs* $+0{\cdot}11 \pm 0{\cdot}30$ mmol/l, $P = 0{\cdot}025$) and VLDL-C concentrations ($-0{\cdot}03 \pm 0{\cdot}11$ *vs* $+0{\cdot}02 \pm 0{\cdot}06$ mmol/l, $P = 0{\cdot}025$) compared with placebo.

Conclusions In conclusion, 200 microgram per day selenium supplementation for 8 weeks among PCOS women had beneficial effects on insulin metabolism parameters, triglycerides and VLDL-C levels; however, it did not affect FPG and other lipid profiles.

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Introduction

The polycystic ovary syndrome (PCOS) is a common endocrine disorder associated with metabolic complications affecting 5–10% of reproductive-age women.[1] Women with PCOS usually have intrinsic insulin resistance (IR), increased risk of cardiovascular disease (CVD), hyperleptinemia and other metabolic disorders such as hypertension, gestational diabetes (GDM), type 2 diabetes mellitus (T2DM)[2] and dyslipidemia.[3] It is still under debate whether nonobese women with PCOS are insulin resistant. While there is no difference in insulin resistance between nonobese and obese patients in some studies,[4] others have not been able to demonstrate insulin resistance in lean PCOS women.[5] In addition, several studies have reported that the prevalence of CVD risk factors is higher in PCOS women compared with age-matched controls,[6] which in turn led to the assumption that PCOS female also run an increased risk of mortality, with most of the events predicted to occur during the postmenopausal years. In a study by Dahlgren *et al.*[7] was observed a sevenfold increased risk of myocardial infarction (MI) in PCOS women compared to age-matched referents.

Selenium is an essential micronutrient, which plays an important role in redox reactions including glutathione peroxidase and thioredoxin reductase.[8] More recently, evidence has also been presented that selenium could affect carbohydrate and fat metabolism. Induced selenium deficiency has resulted in an increase in plasma glucose levels in healthy rats and to further elevation of plasma glucose levels in diabetic rats.[9] *In vitro* and *in vivo* studies have shown that selenium possesses insulin-like actions.[10] In a study by Alizadeh *et al.*[11] demonstrated that the administration of 200 μg/day selenium supplements for 6 weeks resulted in a significant decrease in serum insulin levels and homeostatic model of assessment for insulin resistance (HOMA-IR) among women with central obesity. In addition, a significant decrease in total

cholesterol and triglyceride levels was observed in male New Zealand white rabbits after selenium intake.[12] However, a 3-month supplementation with 200 μg selenium supplements daily in diabetic patients did not influence serum insulin levels and led to increased fasting plasma glucose (FPG) levels.[13]

Beneficial effects of selenium supplementation on improved glucose homeostasis and lipid profiles might result from its effect on inhibiting the expression of cyclooxygenase (COX)-2 and P-selectin.[14] In addition, selenium may reduce insulin resistance through inhibiting the production of inflammatory cytokines including tumour necrosis factor-α (TNF- α) and IL-1.[15] Therefore, we hypothesized that selenium supplementation might affect metabolic status of women with PCOS. We are aware of no study that evaluated the effect of selenium supplementation on glucose homeostasis parameters and lipid profiles in patients with PCOS. This study aimed to investigate the effect of selenium supplementation on metabolic profile of PCOS women.

Subjects and methods

Participants

This study was a randomized, double-blind, placebo-controlled clinical trial that was performed from August 2014 to October 2014 among the women with PCOS (according to Rotterdam criteria) referred to the Research and Clinical Center for Infertility and Kossar Hospital, Arak, Iran. Individuals were eligible for participation if they were aged 18–40 years and met the Rotterdam criteria for PCOS. Diagnosis of PCOS was performed according to the Rotterdam criteria[16]: those with two of the following criteria were considered as having PCOS: oligo- and/or anovulation, hyperandrogenism and polycystic ovaries. Menstrual irregularity was assessed as the presence of chronic amenorrhoea or a menstrual cycle length of less than 21 days or more than 35 days, or more than 4 days variation between cycles. Biochemical hyperandrogenism was evaluated by increased levels of serum androgens (male hormones) including androstenedione and testosterone. Clinical hyperandrogenism was assessed as the self-reported degree of hirsutism using the modified Ferriman Gallwey (mF-G) scoring method based on a chart displaying degree of hair growth in nine regions[17] or acne. In this method, hair growth is rated from 0 (no growth of terminal hair) to 4 (extensive hair growth) in each of the nine locations. In addition, all individuals attending the centre were first examined by the study gynaecologist and after diagnosis of PCOS in all subjects; they were instructed to fill mF-G scoring form validated for the Iranian population.[18] The self-reported hirsutism was rechecked and confirmed by the study gynaecologist. Polycystic ovaries were diagnosed by ultrasonography (US) in participants with menstrual dysfunction and/or hirsutism. According to the Rotterdam criteria, 12 or more small follicles should be seen in an ovary on ultrasound examination. A total of 990 women attended gynaecology clinic, affiliated with Arak University of Medical Sciences (AUMS), were screened for PCOS. Subjects who reported menstrual irregularity and/or had a mF-G score of 8 or higher were invited for clinical examination. Those who did not meet these criteria were not further examined and were deemed not to have PCOS. Finally, 70 women met the inclusion criteria based on Rotterdam criteria and were enrolled in the study (Fig. 1). In this study, the primary outcome variable was HOMA-IR. For estimating sample size, we used the standard formula suggested for parallel 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,[11] we used 1·64 as SD and 1·20 as the difference in mean (d) of HOMA-IR as key variable. Based on this, we needed 30 subjects in each group. Considering 5 dropouts in each group, the final sample size was determined to be 35 patients per group. The women who were menopause, consumed selenium supplements and metformin in

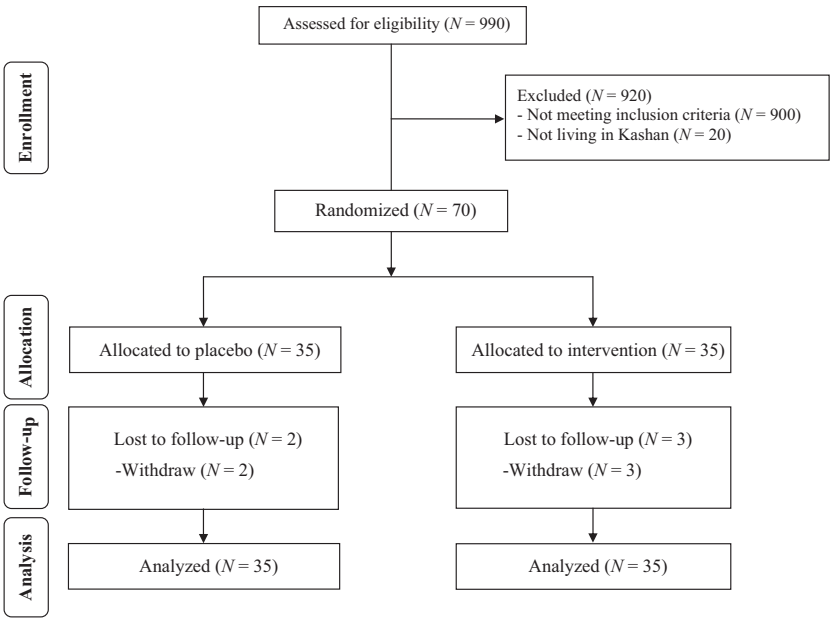

Fig. 1 Summary of patient flow diagram.

the last 3 months, used tobaccos, were diabetic or hypothyroidism, followed a special diet or consumed effective drugs on hormonal profile such as oral conceptive (OCP), and ovulation induction agents were excluded in this study. These variables may affect markers of insulin resistance or lipid profiles. This study was carried out according to the guidelines laid down in the Declaration of Helsinki. The ethical committee of AUMS approved the study, and informed written consent was obtained from all participants. The trial was registered in the Iranian website (www.irct.ir) for registration of clinical trials (IRCT code: IRCT201408155623N25).

Study design

At study baseline and after stratification for pre-intervention BMI (<25 and ≥25 kg/m^2) and age (<30 and ≥30 year), subjects were randomly divided into two groups to receive either 200 μg daily selenium supplements as tablet ($N = 35$) or placebo ($N = 35$) for 8 weeks. Selenium supplements and its placebos (cellulose) were manufactured by Nature Made Pharmaceutical Company (Los Angeles, CA, USA) and Barij Essence Pharmaceutical Company (Kashan, Iran), respectively. Supplements and placebos were in the same form of package, and the patients and researcher were not aware of the content of the pack until the end of analysis. Individuals were randomized, in a 1:1 ratio. Random assignment was performed by the use of computer-generated random numbers. Randomization and allocation were concealed from the researcher and participants until the main analyses were completed. A trained midwife at gynaecology clinic did the randomized allocation sequence, enrolled participants and assigned participants to interventions. At the start of the study, the individuals were asked to maintain their usual diet and level of physical activity throughout the study period as well as not to receive any lipid-lowering medications and medications that might affect their reproductive physiology during the 8-week intervention. The use of selenium supplements and placebos throughout the study was checked through asking participants to bring the medication containers. To increase the compliance, all patients were receiving short messages on their cell phones to take the supplements each day. All participants provided three dietary records (one weekend day and two weekdays) and three physical activity records to make sure that they maintained their usual diet and physical activity during intervention. Both dietary and physical activity records were obtained at week 2, 4 and 6 of intervention. The dietary records were based on estimated values in household measurements. To obtain nutrient intakes of participants based on these 3-day food diaries, we used Nutritionist IV software (First Databank, San Bruno, CA, USA) modified for Iranian foods.

Assessment of variables

Height and weight (Seca, Hamburg, Germany) were measured using standard protocols with subjects in light gown and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference was measured at the minimum circumference between the iliac crest and the last rib. Hip circumference was measured at the maximum protuberance of the buttocks. All measurements were taken by the same person to reduce subjective errors. Fasting blood samples (10 ml) were collected before and after 8-week intervention at Arak reference laboratory in an early morning after an overnight fast. Blood samples were immediately centrifuged (Hettich D-78532, Tuttlingen, Germany) at 1465 g for 10 min to separate serum. Then, the samples were stored at −80 °C before analysis at the AUMS reference laboratory.

Outcomes

As insulin resistance is the most important variable in PCOS patients, primary outcomes considered markers of insulin resistance in this study. Secondary outcomes were lipid profiles. Commercial kits were used to measure fasting plasma glucose (FPG), serum cholesterol, triglycerides, VLDL-C, LDL-C and HDL-C concentrations (Pars Azmun, Tehran, Iran). All inter- and intra-assay CVs for FPG and lipid profiles measurements were <5%. Serum insulin was assayed by ELISA kit (Monobind, CA, USA). The intra- and interassay CVs for serum insulin were 3·0% and 5·1%, respectively. HOMA-IR, homeostatic model assessment-beta-cell function (HOMA-B) and the quantitative insulin sensitivity check index (QUICKI) were calculated based on suggested formulas.[19] Measurements of glucose, lipid concentrations and insulin were taken in a blinded fashion, in duplicate, in pairs (before/after intervention) at the same time, in the same analytical run, and in random order to reduce systematic error and interassay variability.

Statistical methods

We used Kolmogorov–Smirnov test to examine the normal distribution of variables. The intention-to-treat (ITT) analysis of the primary study end-point was carried out for all the randomly allocated participants. Missing data from dropped out participants were imputed using the method of 'Last Observation Carried Forward'. To determine the effects of selenium supplementation on insulin metabolism parameters and lipid profiles, one-way repeated measures ANOVA was used to evaluate the between-group changes in variables during the study. In this analysis, the treatment was regarded as between-subject factor, and time with two time-points (baseline and week 8 of intervention) was considered as within-subject factor. To assess whether the magnitude of the change in dependent variables depended on the baseline values, age and baseline BMI, we controlled all analyses for baseline values, age and baseline BMI to avoid the potential bias that might have resulted. These analyses were also carried out using one-way repeated measures analysis of variance. A P-value <0·05 was considered statistically significant. All statistical analyses were carried out using the Statistical Package for Social Science version 17 (SPSS Inc., Chicago, IL, USA).

Results

In the present study, 70 women met the inclusion criteria based on Rotterdam criteria and were enrolled in the study. The groups were well-matched for age and BMI. Among individuals in the selenium group, three women [withdraw due to personal reasons ($N = 3$)] and in the placebo group, two women [withdraw due to personal reasons ($N = 2$)] did not complete the trial. However, as the analysis was carried out based on ITT, all 70 PCOS women were included in the final analysis. On average, the rate of compliance in our study was high, such that higher than 90% of tablets were taken throughout the study in both groups. No side effects were reported following the consumption of selenium supplements in patients with PCOS throughout the study.

Mean baseline BMI of study participants was 25·2 ± 3·9 kg/m^2 (range: 16·0–35·0 kg/m^2). Mean age and height of study participants were not statistically different between selenium and placebo groups. Baseline weight and BMI as well as their means before and after intervention were not significantly different comparing the two groups (Table 1).

Based on the 3-day dietary records obtained throughout the intervention, no statistically significant difference was seen between the two groups in terms of dietary intakes of energy, carbohydrates, proteins, fats, saturated fatty acids (SFA), polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA), cholesterol, total dietary fibre (TDF) and selenium (Table 2).

After 8 weeks of intervention, subjects who received selenium supplements had significantly decreased serum insulin levels (−29·83 ± 47·29 *vs* +9·07 ± 77·12 pmol/l, $P = 0·013$), HOMA-IR (−1·15 ± 1·81 *vs* +0·42 ± 3·09, $P = 0·011$), HOMA-B (−19·06 ± 30·95 *vs* +4·55 ± 47·99, $P = 0·017$) and increased QUICKI (+0·03 ± 0·04 *vs* +0·0009 ± 0·05, $P = 0·032$) compared with placebo (Table 3). In addition, supplementation with selenium resulted in a significant reduction in serum triglycerides (−0·14 ± 0·55 *vs* +0·11 ± 0·30 mmol/l, $P = 0·025$) and VLDL-C concentrations (−0·03 ± 0·11 *vs* +0·02 ± 0·06 mmol/l, $P = 0·025$) compared with placebo. We did not see any significant effects of selenium supplementation on FPG, other lipid profiles and waist and hip circumference. Within-group changes showed a significant reduction in serum insulin levels ($P = 0·001$), HOMA-IR ($P = 0·001$), HOMA-B ($P = 0·001$) and a significant rise in QUICKI ($P = 0·002$) in the selenium group. In addition, within-group changes revealed a significant increase in serum triglycerides ($P = 0·047$), VLDL-C ($P = 0·047$) and a significant reduction in LDL-C concentrations ($P = 0·023$) in the placebo group.

Baseline levels of FPG were significantly different between the two groups. Therefore, we controlled the analyses for the baseline levels. However, after this adjustment no significant changes in our findings occurred, except for FPG ($P = 0·009$) (Table 4). Additional adjustments for age and baseline BMI did not affect our findings, except for FPG ($P = 0·010$).

Table 1. General characteristics of study participants

	Placebo group ($N = 35$)	Selenium group ($N = 35$)	P*
Age (year)	25·7 ± 4·8	25·4 ± 5·1	0·80
Height (cm)	163·3 ± 6·5	163·1 ± 5·5	0·92
Weight at study baseline (kg)	67·1 ± 11·0	66·7 ± 10·0	0·87
Weight at end-of-trial (kg)	66·6 ± 10·8	65·9 ± 9·8	0·80
Weight change (kg)	−0·5 ± 1·4	−0·8 ± 0·8	0·45
BMI at study baseline (kg/m^2)	25·2 ± 4·1	25·0 ± 3·7	0·87
BMI at end-of-trial (kg/m^2)	25·0 ± 4·0	24·8 ± 3·6	0·81
BMI change (kg/m^2)	−0·2 ± 0·5	−0·2 ± 0·3	0·53

Data are means ± SD.
*Obtained from independent *t*-test.

Table 2. Dietary intakes of study participants throughout the study

	Placebo group ($N = 35$)	Selenium group ($N = 35$)	P*
Energy (kcal/day)	2402 ± 155	2364 ± 181	0·38
Carbohydrates (g/day)	325·7 ± 32·9	323·1 ± 42·6	0·79
Protein (g/day)	87·6 ± 9·2	84·8 ± 18·4	0·46
Fat (g/day)	87·1 ± 12·9	85·0 ± 18·0	0·60
SFA (g/day)	26·0 ± 5·8	24·0 ± 6·5	0·22
PUFA (g/day)	28·2 ± 7·1	28·1 ± 6·8	0·95
MUFA (g/day)	23·0 ± 4·8	23·5 ± 8·0	0·75
Cholesterol (mg/day)	225·1 ± 117·5	214·9 ± 139·9	0·76
TDF (g/day)	18·4 ± 4·7	17·9 ± 4·8	0·67
Selenium (μg/day)	58·5 ± 8·0	56·1 ± 10·5	0·33

Data are means ± SD.
SFA, saturated fatty acid; PUFA, poly unsaturated fatty acid; MUFA, mono unsaturated fatty acid; TDF, total dietary fibre.
*Obtained from independent *t*-test.

Discussion

The present study evaluated the effects of selenium supplementation on insulin metabolism parameters and lipid profiles among women with PCOS. The major finding was that selenium supplementation improved insulin function and decreased triglycerides and VLDL-C levels in PCOS subjects. To the best of our knowledge, this study is the first that reports the effect of selenium supplementation on metabolic status in women with PCOS. In the current study, no side effects were reported after selenium supplementation in patients with PCOS throughout the study. It must be considered that mean dietary plus supplemental selenium intake was lower in our study participants than upper limits (400 μg). However, data on the effects of selenium supplementation on health status even in subjects with high-dietary selenium intake are conflicting. For instance, in a study by Burk[20] was seen that intake of moderate (approximately 200 μg/day) to large (approximately 600 μg/day) selenium supplements as selenomethionine was safe among

Table 3. The effect of selenium supplementations on glucose metabolism and lipid profiles

	Placebo group ($N = 35$)			Selenium group ($N = 35$)			
	Wk0	Wk8	Change	Wk0	Wk8	Change	P†
FPG (mmol/l)	5·15 ± 0·39	5·14 ± 0·46	−0·01 ± 0·33	4·91 ± 0·52	4·68 ± 0·65	−0·23 ± 0·75	0·116
Insulin (pmol/l)	73·58 ± 59·50	82·65 ± 82·50	9·07 ± 77·12	80·69 ± 42·28	50·86 ± 32·83*	−29·83 ± 47·29	0·013
HOMA-IR	2·78 ± 2·25	3·20 ± 3·42	0·42 ± 3·09	3·00 ± 1·69	1·85 ± 1·22*	−1·15 ± 1·81	0·011
HOMA-B	44·87 ± 39·75	49·42 ± 49·74	4·55 ± 47·99	50·36 ± 26·67	31·30 ± 22·26*	−19·06 ± 30·95	0·017
QUICKI	0·34 ± 0·03	0·34 ± 0·04	0·0009 ± 0·05	0·33 ± 0·03	0·36 ± 0·03*	0·03 ± 0·04	0·032
Triglycerides (mmol/l)	1·30 ± 0·59	1·41 ± 0·70*	0·11 ± 0·30	1·26 ± 0·73	1·12 ± 0·48	−0·14 ± 0·55	0·025
VLDL-C (mmol/l)	0·26 ± 0·11	0·28 ± 0·14*	0·02 ± 0·06	0·25 ± 0·14	0·22 ± 0·09	−0·03 ± 0·11	0·025
Total cholesterol (mmol/l)	4·40 ± 0·76	4·25 ± 0·76	−0·15 ± 0·62	4·08 ± 0·94	3·93 ± 0·87	−0·15 ± 0·62	0·993
LDL-C (mmol/l)	2·28 ± 0·62	2·03 ± 0·68*	−0·25 ± 0·63	1·95 ± 0·70	1·92 ± 0·56	−0·03 ± 0·75	0·168
HDL-C (mmol/l)	1·51 ± 0·24	1·57 ± 0·38	0·06 ± 0·32	1·54 ± 0·27	1·48 ± 0·34	−0·06 ± 0·25	0·091
Waist circumference (cm)	80·25 ± 10·12	79·60 ± 10·47	−0·65 ± 1·57	77·00 ± 8·85	76·14 ± 8·88	−0·86 ± 0·90	0·516
Hip circumference (cm)	96·77 ± 9·96	96·25 ± 10·20	−0·51 ± 1·70	93·82 ± 8·64	93·01 ± 8·41	−0·81 ± 1·82	0·479

All values are means ± SD.

FPG, fasting plasma glucose; HOMA-IR, homeostasis model of assessment-insulin resistance; HOMA-B, homeostatic model assessment-beta-cell function; QUICKI, quantitative insulin sensitivity check index; VLDL-C, very low-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

*Significant difference from baseline.

†Obtained from repeated measures ANOVA test (time × group interaction).

volunteers ages ≥18 years for 16 weeks. However, some studies have reported hair loss and dermatitis as the adverse effects of selenium supplementation.[21] Nonetheless, further studies are required about potential toxicity/teratogenicity of long-term increased selenium intake.

Patients with PCOS are susceptible to insulin resistance-related condition including hirsutism, increased inflammatory factors, hypertension, increased lipid profiles and increased risk of CVD.[22] The current study demonstrated that taking selenium supplements for 8 weeks in women with PCOS resulted in a significant decrease in serum insulin levels, HOMA-IR, HOMA-B and a significant rise in QUICKI compared with placebo, but did not influence FPG levels. Few studies have examined the effects of selenium supplementation on insulin metabolism parameters. In line with our study, in a study by Alizadeh *et al.*[11] was seen a significant decrease in serum insulin levels and HOMA-IR score following the administration of 200 μg per day selenium supplements among women with central obesity for 6 weeks. In addition, oral selenate administration for 9 weeks in diabetic *db/db* mice significantly increased plasma insulin concentrations.[23] Campbell *et al.*[24] demonstrated that selenium stimulated pancreatic beta-cell gene expression and enhanced islet function in cell culture. In contrast to our findings, some studies did not observe such favourable effect of selenium supplementation on insulin function. For instance, in a study by Faghihi *et al.*[13] found no significant difference in serum insulin levels following the intake of selenium supplements among diabetic patients for 3 months. Hyperinsulinism and insulin resistance are frequent findings in PCOS patients, and these traits have cause–consequence relationships with increased risk of CVD,[25] GDM and T2DM[2] as well as dyslipidemia.[3] A previous meta-analysis has reported that selenium concentrations were inversely associated with coronary heart disease risk in observational studies.[26] Other randomized trials which have examined the effect of selenium supplements in combination with other vitamins or minerals on CVD end-points have yielded inconclusive findings.[27,28] Beneficial effects of selenium supplementation on improved insulin metabolism parameters in the present study might have been resulted from its effect on inhibiting the expression of COX-2 and P-selectin.[14] In addition, selenium has insulin-like properties and may act as a potential antidiabetic agent.[10] Selenium can also improve insulin function through the inhibition of inflammatory cytokines including TNF-α and IL-1.[15]

Findings from the current study revealed that taking selenium supplements in patients with PCOS has resulted in a significant decrease in serum triglycerides and VLDL-C levels compared with placebo, but did not affect other lipid profiles. In line with our findings, a significant decrease in serum triglycerides levels after intake of 200 μg per day selenium supplements among women with central obesity for 6 weeks, but did not affect other lipid profiles.[11] Furthermore, selenium supplementation led to a significant decrease in triglyceride levels in male New Zealand white rabbits[12] and male mongrel rabbits.[29] Specifically, selenium supplementation was reported to decrease the level of triglycerides in Sprague-Dawley rats after 4 months.[30] However, Cheung *et al.*[31] showed that vitamins E and C, beta-carotene and selenium supplementation tended to increase levels of serum very low-density lipoproteins (TG-rich lipoproteins) among coronary artery disease (CAD) patients for 12 months. In addition, 100 μg daily selenium supplementation in pregnant women did not affect cord-blood total LDL-C and HDL-C levels and led to increased serum triglycerides.[32] Different study designs, different dosages of selenium used, lack of considering

Table 4. Adjusted changes in metabolic variables in PCOS patients

	Placebo group ($N = 35$)	Selenium group ($N = 35$)	P*
FPG (mmol/l)			
Model 1†	0·05 ± 0·08	−0·29 ± 0·08	0·009
Model 2‡	0·05 ± 0·09	−0·29 ± 0·09	0·010
Insulin (pmol/l)			
Model 1	7·19 ± 9·86	−27·95 ± 9·86	0·014
Model 2	7·32 ± 9·73	−28·09 ± 9·73	0·012
HOMA-IR			
Model 1	0·37 ± 0·40	−1·10 ± 0·40	0·011
Model 2	0·38 ± 0·39	−1·11 ± 0·39	0·010
HOMA-B			
Model 1	2·99 ± 6·07	−17·51 ± 6·07	0·020
Model 2	3·06 ± 5·97	−17·59 ± 5·97	0·017
QUICKI			
Model 1	0·003 ± 0·007	0·02 ± 0·007	0·040
Model 2	0·003 ± 0·007	0·02 ± 0·007	0·039
Triglycerides (mmol/l)			
Model 1	0·11 ± 0·06	−0·14 ± 0·06	0·009
Model 2	0·11 ± 0·06	−0·14 ± 0·06	0·009
VLDL-C (mmol/l)			
Model 1	0·02 ± 0·01	−0·02 ± 0·01	0·009
Model 2	0·02 ± 0·01	−0·02 ± 0·01	0·009
Total cholesterol (mmol/l)			
Model 1	−0·06 ± 0·12	−0·22 ± 0·11	0·371
Model 2	−0·07 ± 0·12	−0·22 ± 0·12	0·382
LDL-C (mmol/l)			
Model 1	−0·15 ± 0·09	−0·12 ± 0·09	0·851
Model 2	−0·15 ± 0·09	−0·12 ± 0·09	0·885
HDL-C (mmol/l)			
Model 1	0·05 ± 0·04	−0·05 ± 0·04	0·107
Model 2	0·05 ± 0·04	−0·05 ± 0·04	0·111

All values are means ± SE.
FPG, fasting plasma glucose; HOMA-IR, homeostasis model of assessment-insulin resistance; HOMA-B, homeostatic model assessment-beta-cell function; QUICKI, quantitative insulin sensitivity check index; VLDL-C, very low-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.
*Obtained from repeated measure analysis of variance (time × group interaction).
†Obtained from repeated measure ANOVA adjusted for baseline values.
‡Obtained from repeated measure ANOVA adjusted for baseline values, age and baseline BMI.

baseline levels of dependent variables along with characteristics of study participants might provide some reasons for discrepant findings. Increased expression of very long chain dehydrogenase (VLCAD), medium chain acyl-CoA dehydrogenase (MCAD) and β-oxidation gene expression after selenium intake may result in increased lipid metabolism.[33] In addition, in the present study, within-group changes revealed a significant increase in serum triglycerides and VLDL-C levels in the placebo group. This may result from increased follicular fluid (FF) leptin and visfatin levels.[34] In addition, the stability in their diet and weight, and short duration of the study, this seems unexpected, may influence lipid profiles. However, further research is required in this area to confirm our findings.

Some limitations must be considered in the interpretation of our findings. Due to limited funding, we did not examine the effects of selenium supplementation on plasma or urine selenium, inflammatory factors and PCOS relevant androgen levels. Furthermore, our study was relatively of short duration of intervention. Long-term interventions might result in greater changes in circulating levels of lipid profiles. In addition, the beneficial effects of selenium supplementation on the postprandial glycaemia and triglycerideamia would be of interest, and it is suggested for a future study.

Taken together, 200 micrograms per day selenium supplementation for 8 weeks among PCOS women had beneficial effects on insulin metabolism parameters, triglycerides and VLDL-C levels; however, it did not affect FPG and other lipid profiles.

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Competing interests/financial disclosure

Nothing to declare.

Authors' contributions

Z.A. contributed in conception, design, statistical analysis and drafting of the manuscript. M.J., M.R, Z.F., Y.Gh. and T.B. contributed in data collection and manuscript drafting. Z.A. supervised the study. All authors approved the final version for submission.

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