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Randomized double blind clinical trial evaluating the Ellagic acid effects on insulin resistance, oxidative stress and sex hormones levels in women with polycystic ovarian syndrome

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Abstract

Objective: The design of this study was due to the report of the antioxidant properties of Ellagic acid (EA) for its evaluation on the Insulin resistance (IR), oxidative stress and sex hormones levels in women with polycystic ovarian syndrome (PCOS).

Methods: In this randomized, double-blind, placebo-controlled clinical trial, 60 patients were recruited. Patients were randomly allocated consumed a capsule containing 200 mg of EA per day ($n = 30$) or placebo ($n = 30$) for 8 weeks. The fasting blood sugar (FBS), insulin, IR, total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), total antioxidant capacity (TAC), Malondialdehyde (MDA), C-reactive protein (CRP), Tumor necrosis factor-alpha (TNF- α), sex hormones and anti-mullerian hormone (AMH) were measured at the beginning and end of the study.

Result: At the end of the study, the mean of FBS, insulin, IR, TC, TG, LDL, MDA, CRP, TNF- α , total testosterone, prolactin and AMH were significantly decreased in the intervention group compared to the placebo group ($P < 0.05$). Also, there was a significant increase in the mean of TAC after supplementation with EA ($P < 0.05$). At the end of the study, no significant changes were observed in the mean of anthropometric factors, physical activity and food intake ($P > 0.05$).

Conclusion: EA supplementation can be helpful as a diet supplement in women with PCOS through improvement in insulin resistance. This supplement may be used to reduce metabolic disorders in women.

Trial registration: This study was retrospectively (07–07–2019) registered in the Iranian website (www.irct.ir) for registration of clinical trials (IRCT20141025019669N12).

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and ultimately reducing sex hormones and lowering AMH [39]. One of the most effective factors in reducing IR is the use of plant polyphenols. So far, no clinical studies have examined the effects of EA polyphenol on mentioned factors, but some micronutrients have been studied with antioxidant properties. The results of Shokrpour et al. [40]. study indicated that receiving CoQ10 in women with PCOS significantly decreased the level of AMH. In this clinical trial, 30 women with PCOS consumed CoQ10 pills 100 mg daily for 3 months. Also, in AbdulameerYahya et al. [41]. study, taking the vitamin D and CoQ10 oral supplement in PCOS patients ameliorated the hormonal profile, oxidative marker, and ovulation outcome. Their results showed that these antioxidants significantly decreased the LH and AMH after eight weeks. Also, studies that have examined the effects of IR-reducing drugs such as metformin in women with this syndrome have also reported a significant reduction in sex hormones such as LH, testosterone and AMH at the end of the study [42]. This clinical study, like other studies, can have strengths and weaknesses. One of the strengths of this study is that for the first time the effect of pure supplement of EA was investigated in women with PCOS. Also, the design of this study as a double-blind randomized clinical trial that had parallel groups, making the results of this study remarkable. It is also important to control confounder factors such as weight, physical activity, and food intake in studies that conducted on metabolic diseases, which was done in this research. However, due to the low budget and the limited number of participants and the duration of the intervention, the results of this study have been statistically analyzed, it should be noted that in order to draw clinical conclusions and examine the clinical effects, it is necessary to conduct studies with a larger number of participants and intervention period.

Conclusion

In conclusion, the results of this study indicated that 8 weeks of supplementation with EA, 200 mg/day, reduced the levels of blood sugar, blood lipids and IR in PCOS patients. Also, with the ameliorating in the status of oxidative stress and inflammatory status, at the end of the study, we saw a significant decrease in the amount of AMH in these patients. These results provide evidence to support the view that polyphenol antioxidant group with reducing the biochemical factors, can play an important role in helping to control the condition of this syndrome. Nevertheless, further studies are needed to provide additional evidences.

Abbreviations

AGEs: Advanced glycation end products; AMH: Anti-mullerian hormone; BMI: Body Mass Index; COX-2: Cyclooxygenase 2; CRP: C-reactive protein; EA: Ellagic acid; ELISA: Enzyme-Linked Immunosorbent Assay; FBS: Fasting Blood Glucose; FSH: Follicle-stimulating hormone; Glut2: Glucose transporter 2; GSH-Px: Glutathione Peroxidase; HDL: High density lipoprotein; HMG-CoA: Hydroxymethyl-glutaryl-CoA; IPAQ: International Physical Activity Questionnaire; IR: Insulin resistance; LDL-C: Low density lipoprotein; LH: Luteinizing hormone; MDA: Malondialdehyde; NO: Nitric oxide; PCOS: Polycystic ovary syndrome; PGE2: Prostaglandin E2; PPAR γ : Peroxisome proliferator-activated receptor-gamma; PRL: Prolactin; ROS: Reactive Oxygen Species; TAC: Total antioxidant capacity; TC: Total Cholesterol; TG: Triacylglycerol; TNF- α : Tumor Necrosis Factor Alpha.

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Authors' contributions

Conceptualization: [Mahnaz Kazemi], [Fateme Lalooha], [Maria Kavianpour] and [Hossein Khadem Haghighian]; Methodology: [Mohamadreza Rashidi Nooshabadi], [Mahnaz Kazemi] and [Fariba Dashti]; Formal analysis and investigation: [Maria Kavianpour] and [Hossein Khadem Haghighian]; Writing—original draft preparation: [Hossein Khadem Haghighian] and [Maria Kavianpour]; Writing—review and editing: [Hossein Khadem Haghighian]; Funding acquisition: [Hossein Khadem Haghighian], ...; Resources: [Mohamadreza Rashidi Nooshabadi], [Fariba Dashti] and [Fateme Lalooha]; Supervision: [Hossein Khadem Haghighian]. The authors read and approved the final manuscript.

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Availability of data and materials

We make sure that all data and materials support our published claims and comply with field standards.

Declarations

Ethics approval and consent to participate

The protocol of the study after approving with the ethic committee of Qazvin University of Medical Sciences (ethic code: IR.QUMS.REC.1398.033), Qazvin, Iran, was registered in the Iranian Registry of Clinical Trials website by the IRCT20141025019669N12 code. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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