Original Article

Comparison of Green Tea and Metformin Effects on Anthropometric Indicators in Women with Polycystic Ovarian Syndrome: A Clinical Trial Study

Abstract

Background: Polycystic ovary syndrome (PCOS), as a complex reproductive and endocrinological disorder, affects up to one in five women. Treatment for obesity in women with this syndrome is necessary due to the occurrence of various complications, especially infertility. Recently, green tea with many health benefits, as a natural herbal medicine, has been widely considered in treating various diseases. **Objective:** This clinical study was planned to compare the effect of green tea and metformin treatment on the anthropometric indices of women with PCOS. **Materials and Methods:** In this double-blind, randomized clinical trial, 45 women among 18–35 years of age with PCOS referring to the endometriosis center of Fatemieh Hospital of Hamadan, Iran, who had the eligibility criteria for entering the study, were randomized into three study groups: the green tea, the metformin group, and the control group. Weight, body mass index (BMI), waist circumference, hip circumference, and waist-to-hip ratio, before, 1 month later, and 3 months after intervention in each group were measured. Data were statistically analyzed using Statistical Package for the Social Sciences (SPSS) statistical software, version 23.0. **Results:** No statistically significant difference was observed between the three groups during the study period. A significant reduction of anthropometric indices, such as weight, BMI, waist, and hip circumference, was observed in the green tea group. **Conclusion:** The use of green tea for patients with PCOS is recommended as a complementary therapy that can have potential effects on obesity.

Keywords: *Anthropometric indices, green tea, metformin, polycystic ovary syndrome, randomized controlled trials*

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Introduction

Polycystic ovary syndrome (PCOS), as a complex reproductive and hormonal disorder, affects up to one in five women.[1,2] It is diagnosed by the presence of ovarian cysts, oligo-ovulation or anovulation, and hyperandrogenemia.[3] This syndrome can affect multiple systems in the body and hence can cause different health implications including reproductive (irregular menstrual cycles, ovulatory infertility, pregnancy, miscarriage, and neonatal complications), metabolic abnormalities (obesity, dyslipidemia, cardiovascular, and type two diabetes disease), hyperandrogenic features (hirsutism, scalp hair loss, and acne), and psychological comorbidities (stress, depression, and anxiety).[4,5] It is one of the major health problems for women and societies, which imposes high costs on the public health system.[6] Treatment of this

syndrome is necessary due to the occurrence of various complications, especially infertility. The desired goal of PCOS treatment is to attempt ovulation induction in women and increase the likelihood of becoming pregnant.[7]

Insulin resistance plays a major role in the pathogenesis of PCOS,[8] thus insulin sensitizing agents such as metformin can be used in PCOS management.[9] Metformin, an oral antihyperglycemic agent, is a first-line drug in the treatment of type 2 diabetes.[10] Metformin can provide ovulatory menstrual cycles, improve dyslipidemia, increase the insulin sensitivity, promote weight loss, and increase the rate and frequency of ovulations.[11] Insulin resistance, and more importantly, waist-to-hip ratio are the main clinical predictors for the efficacy of metformin therapy.[12]

Studies have shown that women with PCOS are more obese than controls, and over the past few years, obesity has increased among women with PCOS.[13] The significance of

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this point is that overweight causes clinical manifestations of women who are prone to this syndrome.[14] In fact, lean women with PCOS have a higher mean body fat percentage and average waist-to-hip ratio compared to normal controls with similar body mass index (BMI). Visceral fats produce inflammatory cytokines and are involved in insulin resistance and ovulation reduction in these women.[15] This effect on ovulation is due to insulin resistance, which in turn causes hyperinsulinemia and stimulates the production of a lot of androgens from the ovaries. Intraovarian androgen enhancement inhibits follicular maturation.[16]

Recently, natural herbal medicines have been widely considered in treating various diseases, and among them, green tea has been widely studied.[17,18] Green tea comprises a mixture of polyphenolic flavonoids (catechin) and caffeine, which are very useful for weight loss and weight maintenance.[19] Besides beneficial effects on fat metabolism, green tea is also effective on glucose tolerance and insulin resistance.[20] Some of the beneficial effects of green tea on health include relaxation, antioxidant, cardiovascular disease protective effect, anti-inflammatory, anticancer, antihyperlipidemic potentials, and enhancement of immune system function.[21] Green tea consumption has a significant effect on fasting insulin levels in obese and overweight patients with PCOS.[22]

The aim of this study was to compare the effect of green tea and metformin treatment on the anthropometric indices of women with PCOS.

Materials and Methods

In this double-blind, randomized clinical trial, 45 women among 18–35 years of age with PCOS, referred to the endometriosis center of Fatemieh Hospital of Hamadan (west of Iran), were included. This trial was registered with Clinical Trials Registration Code: IRCT201703029014N148. It is noted that, this study was a part of a clinical trial in which the evaluation of morphological indices as a secondary goal has been studied.

The PCOS diagnosis was certified by a gynecologist based on the Rotterdam criteria.[23] At the beginning of the study, a study and methodology was described for each participant, and they provided written consent. Demographic data were recorded and completed by filling in a questionnaire. History and physical examination were performed. The block randomization method was also randomly categorized based on age and BMI. This process was carried out by a person who did not know the research project by randomly assigning the patients to the three groups of 15 recipients of green tea, metformin, and control recipient. To measure the weight, the fasting individuals, without shoe and minimal clothing, were weighed between 8 am and 9 am in the morning, they were placed on a digital scale at a precision of 0.1 kg and their weight was measured and recorded in kilograms.

To measure the height, the patient was placed beside the wall without shoes, with the heel, hips, and shoulders, sticking to the wall and head in the direction of the body, and looking

direct and forward, and then measuring their height with the height gauge in centimeter. Waist-to-hip ratio was determined from the waist circumference at the midpoint between the last gear and the bone ridge and hip circumference at the hip circumference. Weight, BMI, waist circumference, hip circumference, and waist-to-hip ratio, before, 1 month later, and 3 months after intervention in each group were measured. To prevent side effects of metformin, the first 3 days one tablet, three second day two tablets, and 3 days later, three tablets were given daily for patients.

Inclusion criteria

PCOS diagnosis is based on the following criteria:

- *Clinical findings*: Periodic disorders (oligomenorrhea/amenorrhea), hirsutism, infertility, acne, and oily skin
- *Laboratory findings*: High levels of androgen, increased Luteinizing hormone, and increased LH/follicle-stimulating hormone ratio
- *Ultrasound findings*: Large ovaries and 2–10 mm follicles in excess of 10 in one or both ovaries
- Non-ovulation as menstrual disorders, 35-day cycles, negative pregnancy test, and absence of adult follicles on day 14 of menstrual cycle in ultrasound
- Normal thyroid function and prolactin levels
- Normal hysterosalpingography

Exclusion criteria

- Liver failure, kidney, or cardiovascular disease
- The presence of diabetes mellitus according to the American Diabetic Association
- Taking effective medications for secretion and insulin action
- The use of warfarin and also an antidepressant drug of propranolol

To apply the criteria for including and excluding a person, all patients referred to the study were evaluated for renal, hepatic, cardiovascular, and cardiovascular problems.

All the women with PCOS who met eligibility criteria were randomized to three study groups: the green tea group was treated by green tea tablets 500 mg (three times a day for 12 weeks), the metformin group was treated by metformin tablets 500 mg (three times a day for 12 weeks), and the control group received only placebo. The green tea capsule was the same green tea pill that was poured into the capsule cover. Metformin capsule was the same as metformin pill, which was powdered and was poured into the capsule cover, and placebo was wheat flour that was filled in the capsule. It should be noted that none of these women took medication due to infertility or hirsutism during the observation period. Patients with a 30-day interval (three times during the course of the trial) were referred to receive medicine and checked for morphometric measurements. All measures were assessed at each time point: baseline, 1, 2, and 3 months (endpoint). The consolidated standards of reporting trials flow diagram of trial is presented in Figure 1.
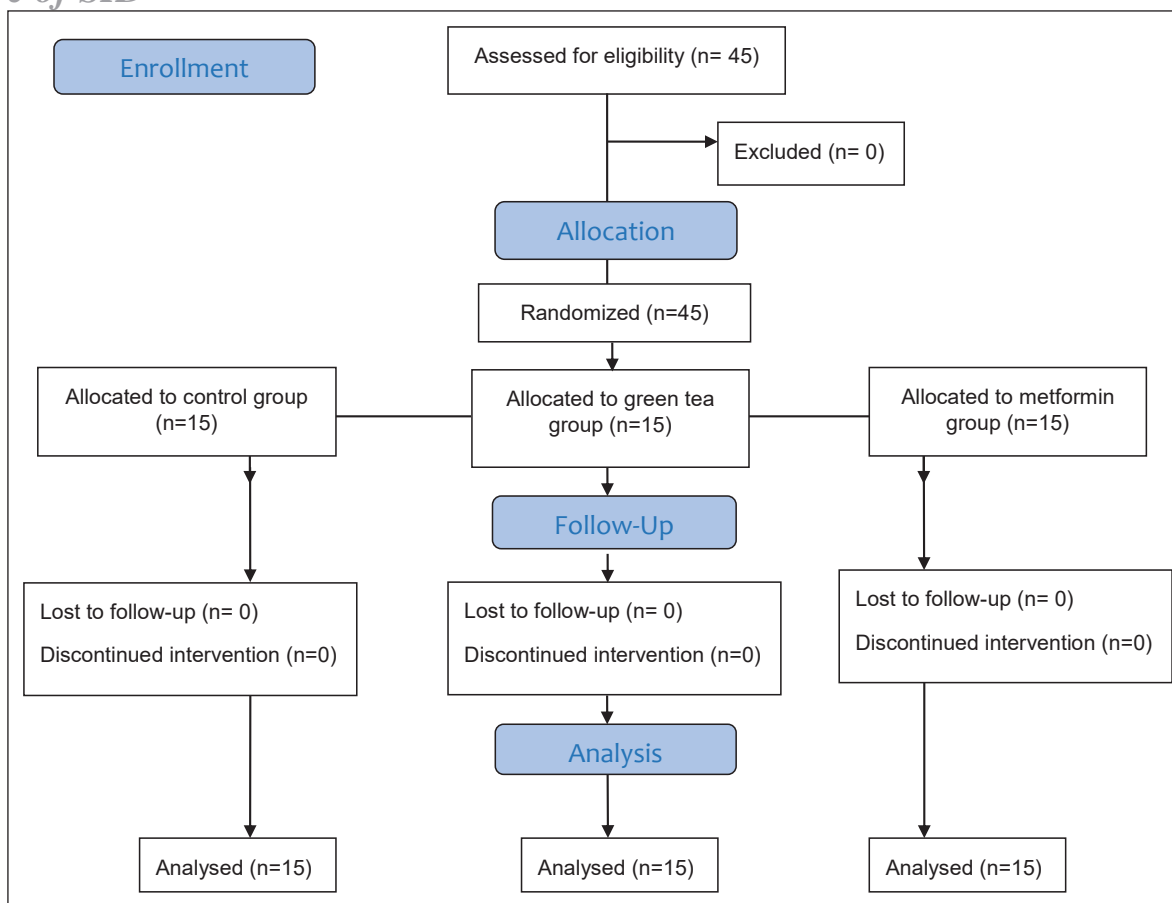
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Figure 1: CONSORT flow diagram

Statistical analysis

Statistical analyses and calculations were conducted using Statistical Package for the Social Sciences (SPSS) statistical software, version 23.0 (SPSS, Chicago, Illinois). The data were presented using the mean ± standard deviation (SD). The normal distribution of the variables was examined by using the Kolmogorov–Smirnov test. Between group comparisons in each time point were performed using analysis of variance (ANOVA) test. Repeated measure ANOVA test was used to compare the data between the three groups in three measurement point times. For all statistical analyses, the level of significance was considered as $P < 0.05$. Mauchly's test was used to check the sphericity assumption and Greenhouse–Geisser correction for violation of sphericity.

Results

The results related to the comparison of changes in weight, BMI, waist circumference, hip circumference, and waist-to-hip ratio are presented in Table 1. Also, the comparison of the changes in these variables during the study periods is presented in Figures 2–6.

The results of the ANOVA test for the comparison between the groups at baseline, 1, 2, and 3 months indicate that the mean

of the variables between the three studied groups in terms of baseline measurement was not significantly different. Also, at 1, 2, and 3 months, no significant difference was observed between the groups in relation to all variables.

The results of the repeated measure ANOVA to compare each of the variables over baseline, 1, 2, and 3 months' time intervals among the considered groups also indicate that there was no significant difference between the mean of the variables in the studied groups over time.

The results of the repeated measure ANOVA for intragroup comparison of each of the variables over baseline, 1, 2, and 3 months' time indicate that the average of all variables except for waist-to-hip ratio was significantly reduced in the group receiving green tea. For example, in the group receiving green tea, the mean value of weight decreased from 75.33 ± 6.47 kg in the baseline, to 75.00 ± 6.24 kg in 1 month, 73.53 ± 6.10 kg in 2 months, and finally to 72.81 ± 5.96 kg in 3 months, and this reduction trend in the mean value of weight was statistically significant. In the case of waist-to-hip ratio, although it decreased from 0.837 ± 0.039 in the baseline, to 0.825 ± 0.051 in 3 months, this decrease was not statistically significant.

In the metformin group, a slight and insignificant decrease in the mean value of BMI and weight was observed. There was also a

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Table 1: Changes in anthropometric indices measurement over time according to the group

Weight (kg)	Green Tea Mean ± SD	Control Mean ± SD	Metformin Mean ± SD	ANOVA	RM-ANOVA
Baseline	75.33 ± 6.47	74.46 ± 7.59	74.93 ± 11.47	0.964	0.969
1 Month	75.00 ± 6.24	74.41 ± 7.54	75.20 ± 11.17	0.967	
2 Months	73.53 ± 6.10	74.78 ± 7.76	75.27 ± 10.63	0.844	
3 Months	72.81 ± 5.96	74.84 ± 8.19	74.40 ± 10.68	0.791	
RM-ANOVA	<0.001	0.423	0.139		
BMI	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**ANOVA**	**RM-ANOVA**
Baseline	29.32 ± 4.31	28.45 ± 2.64	29.06 ± 4.11	0.812	0.926
1 Month	29.00 ± 4.05	28.47 ± 2.68	29.14 ± 3.90	0.867	
2 Months	28.28 ± 3.76	28.60 ± 2.85	29.11 ± 3.92	0.813	
3 Months	28.02 ± 3.49	28.69 ± 2.90	28.83 ± 3.47	0.776	
RM-ANOVA	0.001	0.187	0.307		
Waist	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**ANOVA**	**RM-ANOVA**
Baseline	88.86 ± 7.60	86.40 ± 7.78	88.60 ± 7.24	0.620	0.494
1 Month	87.40 ± 7.44	86.20 ± 7.54	89.33 ± 6.23	0.481	
2 Months	86.33 ± 7.07	86.93 ± 7.87	90.20 ± 6.47	0.292	
3 Months	85.60 ± 7.13	87.60 ± 8.87	90.40 ± 6.47	0.229	
RM-ANOVA	<0.001	0.128	0.102		
Hip	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**ANOVA**	**RM-ANOVA**
Baseline	106.27 ± 9.07	106.67 ± 6.48	107.53 ± 6.16	0.890	0.460
1 Month	105.47 ± 8.63	106.00 ± 6.52	108.27 ± 5.64	0.518	
2 Months	104.73 ± 8.02	107.00 ± 6.93	108.33 ± 5.08	0.349	
3 Months	103.87 ± 7.38	107.53 ± 7.22	108.53 ± 4.72	0.134	
RM-ANOVA	0.042	0.124	0.495		
Waist/hip	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**ANOVA**	**RM-ANOVA**
Baseline	0.837 ± 0.039	0.809 ± 0.041	0.823 ± 0.035	0.156	0.953
1 Month	0.829 ± 0.044	0.813 ± 0.044	0.826 ± 0.047	0.574	
2 Months	0.825 ± 0.045	0.812 ± 0.044	0.833 ± 0.047	0.456	
3 Months	0.825 ± 0.051	0.814 ± 0.047	0.833 ± 0.046	0.556	
RM-ANOVA	0.237	0.778	0.477		

SD = standard deviation, ANOVA = analysis of variance, RM-ANOVA = Repeated Measure ANOVA
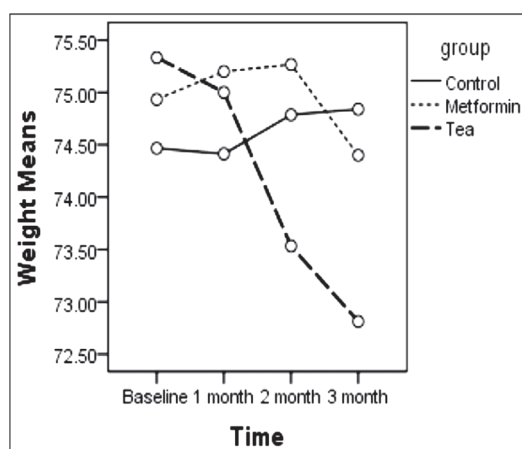

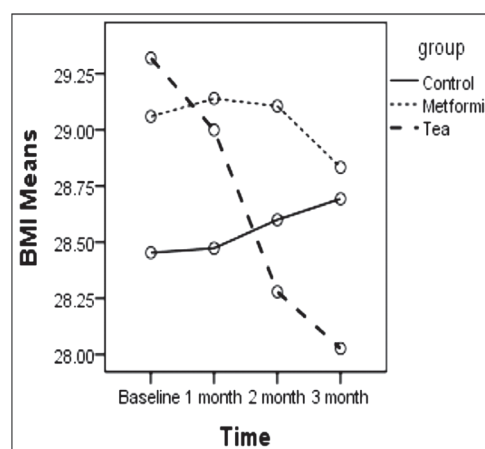Figure 2: Changes in weight over time by study groups

Figure 3: Changes in body mass index over time by study groups

slight and insignificant increase in the mean value of waist and hip circumference and waist-to-hip ratio. In the control group, a slight increase was observed in all of the variables under study.

Discussion

This observational study was a randomized double-blind clinical trial in which 45 women diagnosed with PCOS consumed capsules of metformin, green tea, or placebo during 3 months. The effects of green tea and metformin supplementation on weight, BMI, and waist-to-hip ratio in women with PCOS were evaluated and compared. The results showed that the average of all variables except for waist-to-hip ratio was significantly reduced in the group receiving herbal medicine (green tea), and this reduction trend was statistically significant.
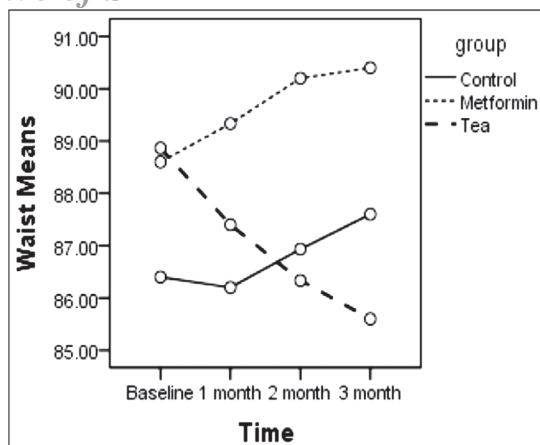
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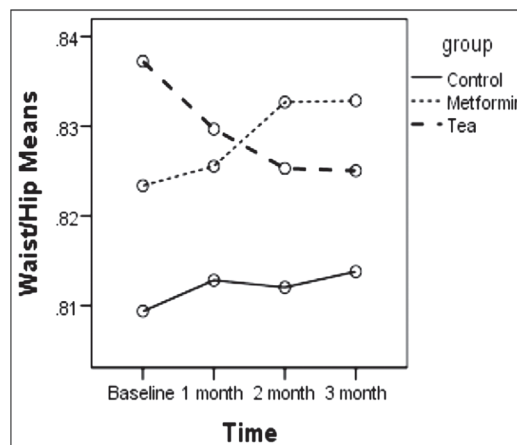Figure 4: Changes in waist over time by study groups

Figure 6: Changes in waist-to-hip ratio over time by study groups
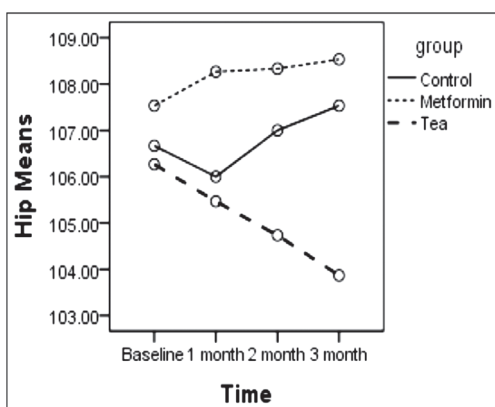

Figure 5: Changes in hip over time by study groups

It is known that green tea includes active ingredients, that is, caffeine and catechins, and it promotes sympathetic activation, causes high increase in fat oxidation and effective promoters of thermogenesis, leading to an increase in energy expenditure.[16] Also green tea influences obese people through desensitizing insulin-resistant muscles and increasing adiponectin levels.[20]

Today medicinal plants are one of the most commonly used treatments for any type of illness, because in addition to cost-effectiveness, they have fewer side effects than chemical drugs. According to studies by the World Health Organization (WHO), medicinal herbs are the best source for obtaining various medications. Therefore, medicinal herbs should be further investigated for better understanding regarding their efficacy, safety, and specificity. Owing to the resistance of microorganisms to chemical drugs and their unwanted side effects, the use of herbal extracts has been considered in recent years.[24,25]

Some studies confirmed that green tea consumption for 12 weeks has led to weight loss by increasing calorie intake and fat oxidation.[26] Also, green tea consumption has a significant effect on reduction of fasting insulin levels in obese and overweight patients with PCOS.[22] Some researchers have shown the potential role of green tea in controlling weight.[27]

The effect of green tea through reduction of intestinal glucose absorption and control of blood glucose on weight loss has been studied.[28] Green tea improves blood insulin levels and decreases the amount of glucose, fatty acid, and triglyceride, and is effective in treating type 2 diabetes.[29]

Weight loss has many benefits in the overall health of women with PCOS.[30] In women with PCOS, increasing daily physical activity and participating in a regular exercise program is essential for the treatment and prevention of insulin resistance and helping to reduce weight.[31] Weight loss needed to achieve clinical and biochemical benefits, including increased pregnancy rates, is 5% of the initial body weight.[32] Although this weight loss may seem low, it is accompanied with approximately 30% reduction in visceral fat content, which is sufficient for significant improvement in insulin resistance and insulin level.[33] Obesity makes insulin resistance worse. Losing weight can lower insulin and androgen levels and may return ovulation to its original state. Accordingly, diet control is one of the most principled therapies for this disease.[34]

Insulin resistance, and more importantly, the waist-to-hip ratio are the main clinical predictors in the measurement of response to metformin.[9] In obese populations, higher doses of metformin are needed to achieve clinical benefits, and these values, if tolerated, are more effective than lower doses to start weight loss. Most published articles, in which metformin was used in women with PCOS, reported a significant decrease in endogenous levels in lean subjects.[35]

On the basis of the results obtained from this study, it is recommended to consider the following notes in further studies: Investigating the antioxidant effects of green tea pills in patients with PCOS. In this study, the effects of green tea pills on anthropometric measurement were evaluated. However, it is suggested that the antioxidant effects of green tea pills in patients with PCOS should be specifically investigated. Also, the effect of green tea pills on the expression of genes should be investigated.

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Conclusion

The results of this study showed that green tea consumption has a significant effect on the reduction of anthropometric indices such as weight, BMI, and waist and hip circumference. Therefore, the use of green tea for patients with PCOS is recommended as a complementary therapy that can have potential effects on obesity.

Conflicts of interest

There are no conflicts of interest.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Hamadan University of Medical Sciences (number: IR.UMSHA. REC.1395.580).

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