Original Article

Examining the Effect of Chamomile on Clinical Symptoms and Hormonal Parameters Among Patients With Polycystic Ovarian Syndrome

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Abstract

Objective: Polycystic ovarian syndrome is the most common cause of infertility and endocrine disorder among women due to anovulation. The aim of the present study is to investigate the effect of chamomile on oligomenorrhea and hirsutism symptoms as well as hormonal parameters among patients suffering from polycystic ovarian syndrome.

Materials and methods: The present study is a randomized clinical trial performed on 70 patients with diagnosis of polycystic ovarian syndrome according to Rotterdam criteria referring to the infertility clinic of a university hospital. The patients were randomly assigned into intervention and control groups, with the former receiving two chamomile capsules 500 mg for three months, and the latter receiving two placebo capsules for 3 months. Both groups were evaluated in terms of laboratory parameters (FBS, LDL, and testosterone) on the third day of first and third cycles. The collected data were analyzed by SPSS 20.

Results: The mean age, body mass index, marital status, history of infertility, and pregnancy rate showed no significant difference between the two groups. In the chamomile group, clinical symptoms of hirsutism ($p<0.001$) and oligomenorrhea ($p=0.048$) decreased following the treatment, but significant difference was found between the two groups only in hirsutism symptoms ($p=0.028$). Regarding the parameters of FBS ($p=0.06$), HDL ($p=0.224$), cholesterol ($p=0.99$), triglyceride ($p=0.106$), testosterone ($p=0.894$), and LDL ($p=0.61$), no significant difference was observed between the two groups. Nevertheless, following the treatment, testosterone decreased in both placebo ($p=0.005$) and chamomile ($p=0.001$) groups.

Conclusion: overall, the chamomile therapeutic regimen has relatively been able to mitigate the clinical symptoms and testosterone levels in patients suffering from polycystic ovarian syndrome. Use of chamomile plant as a simple, inexpensive, and effective measure can be suggested for improving and treating patients with PCOS after confirmation by further studies.

Keywords: Chamomile; Clinical Symptom; Hormonal Parameters; Polycystic Ovarian Syndrome

Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders in reproductive age women, with 10-15% of women developing it in their lifetime (1). The Rotterdam diagnostic criteria

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syndrome for PCOS include menstruation disorders (amenorrhea, oligomenorrhea), clinical or biochemical hyperandrogenism. Alternatively, sonography symptoms of PCOS, after ruling out other diseases causing a phenotype similar to PCOS include adrenal congenital hyperplasia, adrenal and ovarian neoplasm, Cushing's syndrome, hypo or hypergonadotropic disorders, hyperprolactinemia, and thyroid disease (2).

In PCOS, the pituitary gland may secrete high levels of luteinizing hormone, and the ovaries produce high levels of androgens. This impairs the menstruation cycle and can cause infertility, hirsutism, and acne (3). Various factors underlie incidence of PCOS including diet, environmental factors, physical activity, genetic factors, and neuroendocrine factors (4). There are various treatment methods for PCOS such as changing lifestyle (5), weight loss, exercise (6), daily regular jogging, surgery, as well as taking drugs. The treatment methods and drugs include contraceptive drugs, medroxyprogesterone acetate, gonadotropin releasing hormone agonists, glucocorticoids, ketoconazole, spironolactone, cyproterone acetate, flutamide, cimetidine, finasteride, and insulin sensitizers (7).

Herbal plants are one of the selected choices for improving the symptoms of PCOS. Recently, extensive studies have dealt with examining the effect of different types of herbs on PCOS (8-10). Chamomile plant with the scientific name of chamomilla matricaria belongs to the family of chicory, and its extract contains flavonoid and antioxidant compounds including gallic acid, chamazulene, farnesene, matricin, coumarin derivatives, apigenin, and colin, which has anti-inflammatory properties (11). Other properties of chamomile include antidiabetic (12) and menstruation regulating effects (13). Chamomile has shown antidiabetic effects in female rats. Chamomile flowers contain Anthemine oil extract, tannin, phytosterol as well as a bitter compound called Anthemique acid (14).

There are various drugs for treating this disease, with each having their own side effects. Chamomile is an herb with anti-estrogenic and menstruation cycle regulating effects. So far, no study has been performed regarding the effect of chamomile on PCOS. Given the inexpensiveness of this plant and since it grows easily in most parts of Iran and is easily available and eventually does not have the side effects of chemical products, in this research we intended to compare the effect of chamomile against placebo on oligomenorrhea and hirsutism symptoms as well as changes in hormonal parameters including the levels of testosterone hormone and metabolism including glucose and lipid in PCOS

Materials and methods

This randomized clinical control trial has been performed on 70 patients with PCOS. It has been approved on 6 November 2017 in the organizational/regional ethics committee of the faculty at Mashhad University of medical sciences with the code of IR.MUMS.fm.REC.1396.444. This study was approved on 16 June 2018 with the code of IRCT20170315033085N3 in clinical trial centers. The sample size in the initial study, since so far no study has used chamomile for treating PCOS, was obtained 31 in each group, with the initial assumption that chamomile may have 20% effect in the intervention group over the control, and while considering α=0.05 and β=0.2 using PASS software. According to possible attrition of 10%, eventually 35 was the final number considered in each group.

The sampling method was available sampling, whereby the studied individuals were chosen from among clients referring to special clinic of educational hospitals of Mashhad in case they fulfilled the inclusion criteria and signed written informed consent form. The inclusion criteria were having PCOS according to the criteria of normal history of maturity, thyroid test within the normal range (0.5-5), having dysmenorrhea, patient age 18-35 years, no recent history of surgery for PCOS and treatment for PCOS, nonuse of sexual steroids (such as contraceptive pills, hormone therapy, androgenic drugs), nonuse of chemical or herbal drugs and no smoking.

Initially, other disorders that would mimic PCOS phenotype including hyperprolactinemia, thyroid functional disorders, Cushing's syndrome, adrenal congenital hyperplasia, and androgen secreting ovarian tumors were ruled out by a gynecologist. Next, based on Rotterdam criteria, PCOS was diagnosed. Based on this criterion, having at least two out of three criteria (Rotterdam criteria) is essential: 1) anovulation which usually presents as oligomenorrhea, amenorrhea, and polymenorrhea, 2) elevated levels of androgens in the bloodstream, hirsutism and FSH/LH ratio of 2, and 3) polycystic ovaries that would be observed in ultrasonography.

After explaining the study objectives, observing the ethical considerations according to Helsinki declaration as well as information confidentiality, first written informed consent form was taken from

all participants in the test. Also, they could refuse to participate in the test if they were not willing. Next, a questionnaire capturing demographic variables was completed for the participants. The patients were asked to refer to the clinic of Imam Reza educational hospital in case they experienced menstruation on days 3-5, and in the patients with amenorrhea, after bleeding (following daily prescription of 10 mg/dL of progesterone for 7 days) in order to undergo transvaginal sonography.

The patients with their sonography and biochemical tests results referred to the gynecology clinic of educational hospitals, and in case of confirmation of PCOS, they would be included in the study.

Next the patients would be randomly assigned into intervention and control groups based on the prepared software, and the drugs would be provided to the patients through the researcher based on the checklist. The first group were 35 individuals who received two chamomile capsules 500 mg for three months, and the second group were 35 subjects who received two placebo capsules for three months. The drugs were placed inside the packet and numbered by a person not related to the research. Indeed, the chamomile and placebo tablets which were absolutely similar to each other in appearance were placed inside packets A and B by a colleague, and for each patient, selection of packet would be randomized through the site. The executives of the plan and researchers were unaware of the packet content. As such, it could be stated that the study was performed as double-blind. For the control group, again a similar capsule (with the same color, shape, and size) was given which contained starch. Further, on day 12 of the third cycle, and in case of amenorrhea, at the end of day 90, the subjects were refered for transvaginal sonography in order to evaluate the effect of drug on the volume and follicles of ovaries.

Statistical methods: The recorded data were analyzed by SPSS 23. The characteristics of the studied individuals were presented through descriptive statistical methods including central, dispersion, and frequency distribution indices in the form of proper tables and diagrams. In order to compare quantitative variables between the two groups, in case of normal data distribution, t-test, and otherwise Mann-Whitney test were applied. For comparing the qualitative variables between the two groups, chi-square test and if required Fisher's exact test were employed. In all calculations, $p<0.05$ was considered significant.

Results

CONSORT Flow Diagram was showed in Figure 1. The mean age (p=0.076), body mass index (p=0.831), marital status (p=0.436), history of infertility (p=0.99), and pregnancy (p=0.898) showed no significant difference between the two groups (table 1).

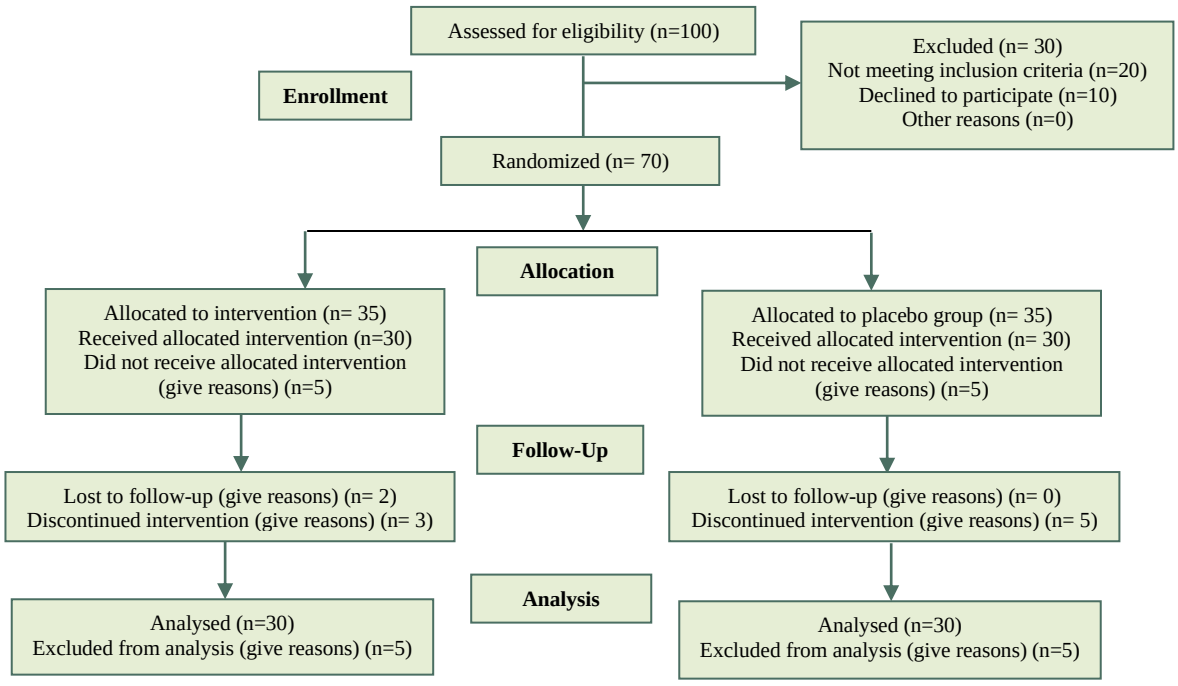

Figure 1: CONSORT Flow Diagram

Table 1: Pretreatment characteristics in two groups

	Placebo group (n = 30)	Intervention group (n = 30)	P
Age	28.06 ± 5.71	25.43 ± 5.58	0.076*
Pre-treatment BMI	25.58 ± 5.98	25.28 ± 4.98	0.831*
Marital status			
Married	15 (50%)	18 (60%)	0.436**
Single	15 (50%)	12 (40%)	
History of pregnancy	7 (46.7%)	8 (44.4%)	0.898***
History of infertility	2 (13.3%)	3 (16.7%)	> 0.99***

*Independent Samples Test, **Chi-Square, ***Fisher's Exact Test

Comparison of clinical symptoms in the placebo and chamomile groups indicated that in the chamomile group, hirsutism (p<0.001) and oligomenorrhea (p=0.048) increased post treatment, but the significant difference was only observed between the two groups regarding hirsutism symptoms (p=0.028) (table 2).

The tests in the placebo and chamomile groups were investigated, whereby no significant difference was observed between them regarding the following parameters: FBS (p=0.06), HDL (p=0.224), cholesterol (p=0.99), triglyceride (p=0.106), testosterone (p=0.894), and LDL (p=0.61). Nevertheless, posttreatment, testosterone decreased in both placebo (p=0.005) and chamomile (p=0.001) Groups (table 3).

In the intervention group, two subjects due to digestive side effects and three due to incomplete drug consumption, and in the placebo group five subjects due to incomplete drug consumption were excluded. Eventually, the collected information from 60 patients including 30 in the intervention and 30 in the placebo groups was analyzed.

Discussion

Overall, there are various treatment methods for treating PCOS including modifying lifestyle, surgery, and pharmacotherapy. Currently, the most well-known treatment method is use of drugs such as clomiphene citrate, metformin, letrozole, and tamoxifen (15). Considering the side effects resulting from these drugs, identifying and preparing alternative drugs are important. Herbal medicine is the oldest form of therapy known by human and has traditionally been used for many years. Usage of this treatment method can be found in all civilizations and is considered an important component in progression of medicine. One of these herbs is chamomile. In the study by Johari et al. entitled investigating the hydroalcoholic extract of chamomile on hypothalamus - pituitary- ovary axis of rats, chamomile caused significant reduction in the level of estrogen and significant elevation in progesterone. It also resulted in significant decline in the number of graph and primary follicles (16). Thus, chamomile is a phytoestrogen with antiestrogenic properties (lowering estrogen levels). This plant can function as a selective estrogen receptor, and this property can be harnessed in regulating endogenous estrogens in individuals with PCOS who have high estrogen levels. Chamomile has also progesterone effects which is effective in treating PCOS.

The present study investigated the effect of chamomile on induction of ovulation as well as hormonal parameters in patients with PCOS. Hirsutism and oligomenorrhea decreased significantly posttreatment in the chamomile group, though only hirsutism had diminished significantly between the two groups.

Table 2: Pre- and post-treatment clinical symptoms in two groups

	Placebo group (n = 30)	Intervention group (n = 30)	P
Pre-treatment hirsutism	3 (10%)	23 (76.7%)	< 0.001
Pot-treatment hirsutism	3 (10%)	10 (33.3%)	0.028
Intragroup P value	< 0.001	< 0.001	
Pre-treatment oligomenorrhea			
More than 35 days	18 (60%)	19 (63.3%)	0.071
Post-treatment oligomenorrhea			
More than 35 days	17 (56.7%)	10 (33.3%)	0.069
Intragroup P value	> 0.99	0.049	

*Chi-Square

Table 3: Lab test results before and after treatment in two groups

	Placebo group (n = 30)	Intervention group (n = 30)	Between-group P
Pre-treatment FBS	92.966± 8.40	89.86± 8.82	0.169*
Post-treatment FBS	91.90± 9.41	87.73±7.75	0.066*
Intragroup P value	0.214	0.193	***
Pre-treatment cholesterol	146.37±53.73	151.8±41.8	0.66*
Post-treatment cholesterol	147.5±45.5	147.4±37.4	0.993*
Intragroup P value	0.776	0.354	***
Pre-treatment triglyceride	127.30±39.11	111.93±49.7	0.189*
Post-treatment triglyceride	121.73±38.01	104.40±43.4	0.106*
Intragroup P value	0.1	0.125	***
Pre-treatment HDL	43.966±8.93	47.23±12.8	0.257*
Post-treatment HDL	43.066±7.44	45.86±9.99	0.224*
Intragroup P value	0.388	0.524	***
Pre-treatment LDL	99.166±32.3	102.43±30.1	0.687*
Post-treatment LDL	97.13±28.3	93.80±21.72	0.611*
Intragroup P value	0.465	0.068	***
Pre-treatment testosterone	(64-20)17	(110.58-25)30	0.346**
Post-treatment testosterone	(62-20)8.5	(57.89-25)16.5	0.894**
Intragroup P value	0.005	0.001	****

*Independent Samples Test, **Mann-Whitney U, ***Paired T-Test, ****Wilcoxon signed ranks test

Cholesterol, triglyceride, HDL, LDL, and testosterone had no significant difference at the beginning and end of study, but testosterone had diminished in both groups. The mean FBS in the chamomile group had decreased as borderline compared to the control group.

A review study by Arentz et al. with the aim of examining the effects of PCOS management and treatment using herbs showed regulation of ovulation, improvements in metabolic hormones as well as rate of fertility, oligomenorrhea, amenorrhea, and hyperandrogenism in PCOS patients (17).

Further, the study by Karampoor et al. (2014) on fennel extract among rats with PCOS indicated that fennel could elevate the serum level of FSH and reduce LH (fennel plant with estrogenic properties behaves similar to chamomile). In that study, reduction of testosterone was observed in both groups though it was not statistically significant (18).

Elsewhere, a study was performed by Heidary et al. (2018) on 80 women (40 in the placebo group and 40 in the chamomile capsule group) on reproductive age women with PCOS. The control group received capsule 370 mg chamomile (three times per day for three months). The results indicated that the testosterone level decreased considerably in the control group. In the present study, testosterone reduction was significant (19). Heidary et al. investigated the effect of capsule 370 mg of chamomile on 80 women with PCOS. The levels of hormones, LDL, HDL, cholesterol, triglyceride, and DHEA.S showed reduction, and HDL was elevated but this change was not significant (19). In our study again we observed reduction of mean FBS, triglyceride, and LDL at the end of study, but this reduction was not significant.

The study by Zafari et al. (2010) (20) dealt with examining the effect of chamomile on clinical and biochemical parameters among PCOS patients. They examined 30 virgin mice, and in the control group the mice with PCOS underwent treatment with intraperitoneal injection of three doses as 25, 50, and 75 ny/kg. The results indicated morphological improvement of ovaries and endometriosis both macroscopically and microscopically. Also, the cysts were eliminated considerably and the number of follicles increased. The levels of estradiol hormones diminished post-injection. Two major limitations in the present study were small sample size and failure to control genetic differences as well as variations in diet.

Conclusion

Overall, chamomile therapeutic regimen could relatively be effective in improving the hormonal parameters as well as oligomenorrhea and hirsutism in patients suffering from PCOS. Thus, based on the results of the present study, use of chamomile plant as a simple, inexpensive, and effective measure could be proposed for improving and treating patients with PCOS after confirmation by further studies with larger sample sizes.

Conflict of Interests

Authors have no conflict of interests.

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