Efficacy of Topical Application of Plant Extract Based Natural Oils in Management of Polycystic Ovarian Syndrome: a Two-Arm Parallel Group Randomised Double-Blind Placebo-Controlled Clinical Study

Amul S Bahl*

Yogic Naturals, God's Own Store LLP, Delhi, India

*Corresponding author:
Amul S Bahl

✉ pcos@yogicnaturals.com

Tell: +09250090027

Yogic Naturals, God's Own Store LLP, Delhi, India

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Abstract

Background: Literature indicates current treatments of PCOS are designed to manage individual symptoms and not the syndrome itself. Pharmacological treatments may have side effects in long-term. Whereas, the studies to measure effectiveness of complementary and alternative medicine (CAM) are done on rat models. Thus, there are also no human clinical trials to establish CAM efficacy to manage PCOS.

Objective: This study objective is to scientifically establish the clinical efficacy of topical application of 100% plant extract based natural oil-blend on PCOS management by addressing the subjective (viz., irregular menstruation, menstrual cycle duration, bleeding quantity, pain during menses) and objective (viz., hirsutism, ovarian volume, number of follicular cysts, number of mature follicles) PCOS symptoms.

Method: In a two-arm parallel group, prospective, randomized, double-blind, placebo-controlled study with adult female participants diagnosed with PCOS and fulfilling inclusion criteria; 100 participants were allocated between two study arms (test and placebo) in the ratio of 1:1 using a randomisation list.

Findings: After treatment, compared to placebo, test group showed significant decrease ($p<0.01$) in the average composite score for subjective symptoms. Test oil resulted in significant decrease in hirsutism, in ovarian volume in both right and left ovaries, and in number of follicular cysts on both the ovaries. Mature follicles in test group increased resulting in 17 incidences of conception out of 46 after 6 months post-study follow-up. No adverse events were reported.

Conclusion: The test oil-blend effectively managed eight studied symptoms of PCOS rather than working on isolated symptoms of PCOS.

Keywords: Polycystic ovarian syndrome; Natural oil-blend; Topical application; Mensuration-related symptoms; Mature follicles; Ovarian volume

Introduction

Polycystic ovarian syndrome (PCOS), also referred to as Stein–Leventhal syndrome [1], is a highly prevalent endocrine system disorder that affect women in their reproductive age and is a major cause of anovulatory infertility [2-6]. Described since 1935 by Stein and Leventhal [7], it represents a condition in which an estimate of 10 small cysts of a diameter ranging between 2 and 9 mm develop on one or both ovaries and/or the ovarian volume in at least one ovary exceeds 10 ml [8]. Previously regarded as a disorder of adult women, PCOS is now considered as a lifelong syndrome that can manifest at pre-natal age, amplify by adolescence and affect multiple aspects of women's health well beyond the reproductive age [4-6,9-10]. Based on different

epidemiologic studies [2,3,11-17] prevalence of PCOS in adult women worldwide ranges from 4% to 21%; the prevalence rate varied depending on the study population and diagnostic criteria used.

The economic burden of PCOS is significantly huge. Around 4 billion dollars are spent annually in the United States whereas the Australian health system spends more than 800 million dollars every year to screen for the disease and treat its various morbidities, including hirsutism (means abnormal growth of hair on a woman's face and body), infertility, and diabetes mellitus [18]. Patients with PCOS are twice more likely to be admitted to hospital [19].

Although the aetiology of PCOS is not completely understood yet, PCOS is considered a multifactorial disorder influenced by various genetic, metabolic, endocrine and environmental factors [20]. Similar to its aetiology, it is likely that pathophysiology of PCOS is multifaceted involving hormonal imbalance, ovarian dysfunction, aberrant insulin signalling, excessive oxidative stress and genetic/ environmental factors [4-6]. Hyperandrogenemia or increase in androgen is the most typical hormonal alteration of PCOS; it causes premature atresia of ovarian follicles, forming multiple cysts and anovulation [6].

The treatment regimen for PCOS depends on the symptoms presented by patients. The symptoms can be broadly categorized as menstruation related disorders; androgen-related symptoms (hirsutism and acne being the most common); and infertility (including anovulation) [21]. Oral contraceptive pills (OCP) are most commonly recommended [22] for the long-term treatment of women with PCOS as first-line of pharmacological treatment for management of androgen-related symptoms [23] and menstrual cycle irregularities [24]. The primary treatment recommended for PCOS-related menstrual abnormalities is low dose of combine hormonal contraception [25]. Ovulation induction with gonadotropins and laparoscopic ovarian drilling are second line therapies whereas, *in-vitro* fertilization (IVF) is recommended as third-line therapy for the management of infertility [26]. Despite their widespread popularity, current treatments for PCOS are only moderately effective at controlling symptoms and preventing complications [21,27]. There are also concerns about the adverse effects of medications in long-term. For example, OCP has negative effects on cardiovascular profile of females with PCOS [28].

Existing studies suggest that several complementary and alternative medicines (CAMs) could be beneficial as an adjunct to conventional medical management of PCOS. They are considered safer than their pharmacological counterparts and in certain cases, have been found clinically effective in reducing the severity of PCOS and its endocrine, cardiometabolic, and reproductive complications [27,29]. Essential oils can be used in different ways, including massage, bathing, and inhalation. Different oils are thought to act on the body in different ways, having a relaxing, energizing, calming, or uplifting effect. It is theorized that when massaged, the oils are absorbed by the skin, allowing them to act fast [30].

Some of the essential oils that have been scientifically linked for treatment of PCOS are spearmint oil (of *Mentha spicata*) [31], chamomile oil [32], dill oil (of *Anethumgraveolens L.*) [33], white cedar oil (of *Thuja occidentalis L.*) [34], and cinnamon oil (of *Cinnamomum cassia*) [35]. Other essential oils such as ylangylang, geranium, lavender and clary sage, also claim to be beneficial in treatment of PCOS, but have not been scientifically researched [36].

Herbal medicines, 100% natural plant extract based formulations, have demonstrated positive effects in management of PCOS, similar to their pharmacological counterparts [27,29]. Several herbal medicines, ayurvedic products and essential oils are available in the markets that claim to have a beneficial effect in patients of PCOS, but only few claims have been validated through laboratory and clinical evidences and most studies are small, nonrandomized, or uncontrolled [29]. Till date, role of essential oil in management of PCOS has mainly been studied on rat models [32,35,36] and there are no clinical trials proving beneficial effect of topical application of essential oil and its safety in treatment of PCOS.

The test product, a therapeutic blend of oils, is prepared using traditional principles of Ayurveda by blending plants extracts with volatile oils. This blend helps support the body's intrinsic healing processes. The proprietary composition of the oil blend is given in **Table 1**. The placebo oil used is a blend of oils soyabean, sunflower and musturd.

Given the absence of any clinical study on the use of volatile essential oils in the management of PCOS, the objective of this study is to scientifically establish and validate the clinical efficacy of plant extract based natural oil-blend (referred as test product/ test oil) on management of PCOS by addressing the subjective (viz., irregular menstruation, menstrual cycle duration, bleeding quantity, pain during menses) and objective (viz., hirsutism, ovarian volume, number of follicular cysts, number of mature follicles) PCOS symptoms. It is aimed to provide a safe, cost-effective, non-surgical treatment for PCOS management.

Methods

Study design and participants

This is a two-arm parallel group, prospective, randomized, double-blind, placebo-controlled study at a single centre with participants diagnosed with PCOS. This study was conducted at a medical centre which is a multi-specialty ISO certified hospital and included in the list of National Health Portal, Government of India. The required pre-approvals were reviewed and approved by the investigational centres' Independent Ethics Committee and Institutional Review Board. This study was conducted in accordance with ethical principles in the Declaration of Helsinki (2013). EC notifications were made as per Good Clinical Practice Guidelines issued by Central Drug Standard Control Organization and Ethical Guidelines for Biomedical Research on Human Subjects issued by Indian Council of Medical Research. This trial was performed in accordance with 'Guidelines for Clinical Trials on Pharmaceutical Products in India - GCP guidelines' issued by the Central Drugs Standard Control Organization, Ministry of Health, Government of India. The clinical trial was

Table 1 Plant names used for the test oil preparation.

Plant Extracts from			Base Oil		
English Name	**Latin Name**	**%Age**	**English Name**	**Latin Name**	**%Age**
Oregano	*Origanum vulgare* var.Carvacrol		Almond	*Prunus dulcis*	
Sandalwood	*Santalum album*		Olive	*Olea europaea*	
Myrrh	*Commiphora myrrha*		Coconut	*Cocos nucifera*	
Basil	*Ocimum basilicum* var. Linalool		Til	*Sesamum indicum* L.	Total 92%
Geranium	*Pelargonium graveolens*		Apricot	*Prunus armeniaca*	
Grapeseed	*Citrus paradisii*		Sunflower	*Helianthus annuus*	
Clary Sage	*Salvia sclarea*		Castor	*Ricinus communis*	
Cedarwood	*Cedrus atlantica*				
Peppermint	*Mentha piperita*	Total 8%			
Ylang Ylang	*Cananga odorata* var.Genuana				
Rose	*Rosa damascene*				
Cypress	*Cupressus sempervirens*				
Fennel	*Foeniculum vulgare*				
Myrtle	*Myrtus communis*				
Avacado	*Persea americana*				
Thyme	*Thymus vulgaris* var. Linalool				

registered with the Clinical Trial Registry of India (CTRI) number CTRI/2018/04/013334.

The study population included adult females diagnosed with PCOS. 100 volunteer participants (including anticipated dropout of about 10%) were recruited at the specified investigation centre, without bias. The sample size was assessed at the confidence level 95% and test power 80%. The PCOS participants were informed about the study. Married female participants diagnosed with PCOS were eligible for inclusion if aged between 18-40 years and suffering from primary infertility, irregular/scanty menses due to anovulatory cycles and increased luteinizing hormone (LH) levels in blood. Participants had LH:FSH ratio>3 (FSH=Follicular Stimulating Hormone) confirmed by haematological examinations; had clinical or biochemical evidence of hyperandrogenism; had a negative pregnancy test. Participants who were unmarried; pregnant or lactating mothers; currently on hormone replacement therapy (HRT) or having taken any herbal medications in the last 30 days were excluded from the study. Participants were excluded if diagnosed with cervical tumour, polyp or cervical cancer; diagnosed with uterine fibroid, congenital anomalies in genital tract, tubercular endometritis, congenital adrenal hyperplasia; who were HIV/VDRL/HbsAg positive; and were with evidence or history of significant systemic, immunological, gynaecological disorder. Participants with hypothyroidism who were on adequate and stable thyroid replacement were not excluded.

The participants were to be excluded if absent for the follow-up visit. They were to be excluded on the follow-up visit if initiated HRT or any allopathic, herbal or any other medical treatment for the disorder without prior information to the investigator. Participants were informed that they were free to withdraw from the study at any time without stating the reason. The investigator could withdraw a participant from the study due to any serious adverse event (AE); protocol violation; consent withdrawal not due to an AE; migration from the study site; lost to follow-up; and for any other appropriate reason. The participant was followed up by the investigator after withdrawal; the cause of which was recorded in the 'Study Completion page' and AE if any was recorded in the AE section of case report form. Participants withdrawn from the study were not replaced.

Randomisation and masking

The study was double-blind with both the participants and the physician with supporting investigator not knowing the study arm to which a participant has been allocated. 100 eligible participants were allocated to one of the two study arms (test or placebo) in the ratio of 1:1 using a randomisation list. The randomisation list was prepared by a biostatistician, and the group list was passed on to the study liaison. The details of randomisation list were not revealed to the study liaison. Study Liaison has provided the bottles with sequential numbers and did not share any allocation information with the participants, physician and investigator. It was reported by investigator at the end of the study that blinding process was successful as no participant was able to assess who received test oil or placebo as well as there was no disclosure to the physician and the investigator.

Procedures

The participants were informed about the study. If agreed, they signed the informed consent form, and were screened for applicable enrolment criteria. The informed consent process of individual participants, including the procedure of providing information to the participants and her understanding on such consent, were maintained by the investigator for record. The participants were refrained from taking any other medications for treatment of PCOS, irregular menses and infertility including HRT from the outset of the study until final evaluation (if participant insisted to take above said medicine, participant was dropped from the study).

Participants were screened in baseline interview (day 0) and were randomised into two groups to be treated either with the test oil or the placebo. The baseline interview collected demographics; viz. age, height, weight, body mass index, time since diagnosis, number of cycles in past 12 years, smoking/non-smoking as well as menstrual cycle characteristics. Participants were individually evaluated for grading (mild to severe) and scoring (0 to 3) by a physician at day0 and day60 for the subjective parameters; viz. irregular menstruation, duration of menstruation bleeding, quantity of bleeding and pain during menstrual period/menses. **Table 2** presents the grades and scores for the four subjective parameters. Irregular menstruation is calculated by intermediate days between menses, duration of menstrual bleeding was measured in number of days of bleeding, amount of bleeding is measured by pads used per cycle, and the level of menstrual pain was evaluated by Visual Analog Score (VAS). A composite score was calculated by adding all scores for each of the subjective parameters investigated (higher score indicated severity of the disease) before and after the given treatment in both groups. Change in grade or decrease in composite or individual parameter score as compared to the placebo were used to assess efficacy of the treatment.

Objective parameters indicating the symptoms of PCOS, viz. ovarian volume, number of mature follicles and number of follicular cysts were measured by USG of pelvic and abdomen for each treatment group. Hirsutism is another assessed objective parameter.

Enrolled participants received the test oil or the placebo with instructions on how and when to apply. There was only a topical application of test oil and placebo oil. Oils had to be applied locally over the lower back area, lower abdominal and pelvic area and massaged lightly into the skin till oil is absorbed. It was required to apply 8-10 drops each time for three times a day. Participants were evaluated for change, if any, in menstrual cycle characteristics as well as objective parameters during follow-up visit at Day 60. AE analyses was done at each follow-up visit, if any. The use of any incidental medication (e.g. thyroid medication, antipyretic medication etc.) was recorded. The study was conducted between 28-04-2018 to 29-09-2018 and then a six-month follow-up was done with test oil participants to know incidence of pregnancy.

The test oil as well as the placebo oil was packed in similar bottles with the same appearance like colour, shape, and size by the study liaison, who was the only one to identify the intervention according to the number given on each bottle.

An AE is defined as any unfavourable and unintended sign, symptom or disease, whatever their nature, severity, seriousness, and the supposed role (causality) of the product administered or the experimental procedure. Vital examination (axillary temperature, heart rate and respiratory rate) and clinical examination (including general physical and systemic examination) were done on each visit day and on any unsolicited follow up visit or at any time during the conduct of study, if deemed necessary. Incidences of local and systemic solicited and unsolicited AEs occurring were noted, if any.

Before proceeding on the study, a safety and skin toxicology study was conducted at an NABL (National Accreditation Board of Testing and Calibration of Laboratories) certified laboratory. It was reported that the test oil is safe to use for topical application free from steroids, heavy metals and any other toxic elements/impurities. The test reports are identified with numbers DTRLAF-260617034 and DTRLAF-260617042.

Outcomes

Test oil was to be considered effective if the studied subjective and objective symptoms of PCOS were alleviated significantly on application of the test oil as compared to the placebo. Efficacy of the test oil is measured with an increase in total number of participants with a lower score, indicative of reduction in severity of the disease, for a given subjective parameter; and change in results for heuristics, reduction in number of cysts as well as ovarian volume and increased mature follicles by pelvic USG examination at day60. In a 6-month post-study follow-up, incidence of pregnancy was checked with test oil participants.

Statistical analysis

Demographic and baseline characteristics for both treatment groups were compared with mean and standard deviation (SD). Only smoking characteristic was compared in percentage. For subjective and objective parameters indicating symptoms of PCOS, the data is represented as mean $\pm$ standard deviation (SD) and/or in numbers. The statistical analysis for before versus after treatment in each group was done by Fisher's exact t-test and for data analysis between test and placebo group, before and after treatment, 2-way ANOVA was applied. Hirsutism was established by Ferriman-Gallway scale between the two groups before and after treatment. All p-values reported are based on 2-sided tests and p-values <0.05 were considered to be significant.

Table 2 Grades and Scores with assessment criteria for measuring the four subjective parameters.

Grade	Nil	Mild	Moderate	Severe
Score	0	1	2	3
Parameters	Assessment criteria to grade and score for the given parameter			
Irregular menstruation	28 days	28-45 days	45-60 days	Above 60 days
Menstrual Cycle duration	3-5 days	1-2/6-7 days	1/8-9 days	Spotting >9 days
Bleeding quantity (no. of pads per cycle)	<15	15-19	20-25	>25
Pain during menses	No pain	Painful but daily activities are not affected, no need for analgesic	Daily activities are affected, need to take analgesic	Daily activities are inhibited, pain continue after taking analgesic

Results

The two treatment groups had comparable demographic characteristics (**Table 3**) at the time of baseline investigations indicating similarity in test group and placebo group. After baseline assessment, four participants in test group and three participants in placebo group did not continue the study on their own will. Thus 46 participants in test group and 47 in placebo group were examined further. For the results of four subjective parameters refer to **Table 4**.

Irregular menstruation

Menstruation irregularity was measured by recording the time between two menstrual cycles. Numbers of participants experiencing different level of irregularity were comparable between groups before treatment. In the test group, number of participants with regular menses increased (nil group) significantly (before: 5/50; after: 22/46, $p<0.05$). It was observed that number of participants in test group whose menstrual cycle was 45-60 days (moderate irregularity; before: 25/50 and after: 5/46) and >60 days (severe irregularity; before: 10/50 and after: 0/46) significantly declined. The effect of the treatment was most evident in the moderate group, where the number of participants significantly decreased subsequent to test treatment (before: 25/50 and after: 5/46) as compared to placebo (before: 27/50 and after: 27/47; $p<0.0026$). The average score calculated between the test group (1.8 ± 0.88) and the placebo group (1.98 0.769) was comparable before treatment. After treatment, the test group showed significant decrease in the average score (0.63 ± 0.67) as compared to the placebo group (1.76 ± 0.75) which indicates that the participants in the test group experienced a significant decline ($p<0.05$) in the level of irregularity of their menstrual cycles (**Table 4**).

Duration of bleeding/menstrual cycle

Number of participants in different grades of duration of bleeding and also, the average score calculated for the test group (1.8 ± 0.94) and the placebo group (1.6 ± 0.968) were comparable between groups before treatment. In the test group, number of participants with optimal duration of menstruation (3-5 days; nil) increased significantly subsequent to treatment with test product (5/50 versus 17/46); this effect was also found to be statistically significant when compared to placebo group ($p<0.01$). Similarly, number of participants with longer duration of bleeding (mild, moderate and severe) showed improvement after test oil treatment; this improvement was significant ($p<0.01$) in comparison to placebo group for moderate and severe conditions. After treatment, the test group showed significant decrease in the average score (0.67 ± 0.56) as compared to the placebo (1.78 ± 0.858) which indicates that the participants in the test group experienced a significant improvement in regulating the duration of the bleeding cycle ($p<0.05$).

Quantity of menstrual bleeding

Amount of menstrual bleeding was estimated by evaluating number of saturated pads used per cycle by an individual participant. No significant difference was observed in number of participants experiencing different level of menstrual flow between both groups before treatment. Also, the average score between the test group (1.6 ± 0.88) and the placebo group (1.84 ± 1.01) was comparable before treatment. Subsequent to treatment, number of participants experiencing regular menstrual flow (<15 pads; nil) significantly increased in test group (before: 8/50; after: 28/46) versus a decrease in number of participants with regular menstrual flow in placebo group (before: 9/50; after: 4/47) and was found statistically significant ($p<0.01$). Number of participants with moderate menstrual bleeding showed significant improvement ($p<0.01$) after test oil treatment though same results were recorded for severe condition in both test and placebo groups. After treatment, the average score for test group showed significant decrease (0.5 ± 0.69) as compared to placebo group (1.66 ± 0.81) indicating a statistically significant improvement in regulating the amount of menstrual bleeding ($p<0.05$) in test group.

Pain during menses

Numbers of participants experiencing different level of menstrual pain based on VAS were comparable between groups before treatment. The average VAS-pain score of the test (1.86 ± 0.639) and placebo (1.8 ± 0.728) group was also comparable before treatment. Subsequent to treatment, number of participants

Table 3 Summary of Demographics of two treatment groups.

Parameter	Placebo (n=50)	Test Oil (n=50)
Age (year)	29.65 ± 7.06	28.20 ± 7.49
Height (m)	1.63 ± 0.14	1.63 ± 0.12
Weight (Kg)	78.92 ± 20.37	78.31 ± 17.16
Body mass index (kg/m^2)	29.72 ± 6.22	29.52 ± 5.94
Time from diagnosis (year)	5.47 ± 3.13	5.43 ± 3.36
No. of cycles in past 12 months	8.33 ± 1.81	8.02 ± 1.57
Smoking (%)	13.73%	9.80%

Table 4 Individual and mean composite scores of the subjective parameters between the test and placebo groups before and after treatment.

Subjective Parameter	Test group		Placebo group	
	Before treatment (n = 50)	After treatment (n = 46)	Before treatment (n= 50)	After treatment (n =47)
Irregular menstruation	1.8±0.88	0.63 ± 0.67	1.98 ± 0.769	1.76±0.75
Duration of bleeding	1.8±0.94	0.67 ± 0.56	1.6 ± 0.968	1.78 ± 0.858
Quantity of bleeding	1.6 ± 0.88	0.5 ± 0.69	1.84± 1.01	1.65 ±0.81
Pain during menses	1.86 ± 0.63	0.54 ± 0.78	1.8 ± 0.728	2 ± 0.69
Mean Composite Score	7.06 ± 1.73	2.34 ± 1.32	7.22 ± 1.96	7.2 ± 1.35

experiencing no pain (nil) significantly increased in test group (before: 10/50; after: 28/46; p<0.05); this effect was not measurable in placebo group due to no participant in nil grade. A smaller, albeit significant increase in the number of participants experiencing mild menstrual pain was observed only in the test group after the treatment (before: 4/50; after: 12/46). Further, number of participants experiencing increased level of menstrual pain (moderate and severe) showed significant decrease after test oil treatment; no such difference was observed after placebo treatment. Comparison of average VAS-pain scores indicated that test group showed significant decrease (p<0.05) in the average score (0.54 ± 0.78) subsequent to treatment whereas the average VAS-pain remained almost unchanged before and after treatment in placebo group (2 ± 0.69).

The average composite score between test group (7.06 ± 1.73) and placebo group (7.22 ± 1.96) was comparable before treatment. After treatment, test group showed significant decrease (p<0.01) in the average composite score (2.34 ± 1.32) whereas no difference was observed in placebo group (7.2 ± 1.35). This indicates that the participants in test group experienced a significant improvement in regulating all the four subjective symptoms associated with PCOS.

Hirsutism

Treatment with the test oil resulted in significant decrease (before: 10.06 ± 3.45; after: 8.30 ± 3.36) in hirsutism (p<0.05) in comparison to placebo group (before: 9.48 ± 3.29; after: 9.36 ± 2.95).

Ovarian volume

Prior to treatment, the ovarian volume of the right ovary in test group (18.13 ± 1.6) and that of placebo group (19.52 ± 1.54) was comparable. Similarly, the ovarian volume of the left ovary in test group (14.95 ± 1.4) and that of placebo group (18.88 ± 1.52) was found comparable. Subsequent to treatment with test oil, ovarian volume significantly (p<0.05) decreased in both right (12.44 ± 1.2) and left (9.52 ± 1.03) ovaries. However, in placebo group the ovarian volume increased (right: 20.73 ± 1.3, left: 20.33 ± 1.8). Test oil treatment was found to be significant than placebo (p<0.05) in reducing the size of the ovary (both left and right) in the participants.

Number of follicular cysts

follicle>3cm found on both the ovaries were significantly reduced subsequent to treatment with test oil (before: 21 cysts; after: 4 cysts; p<0.05) as compared to placebo treatment (before:36 cysts; after:30 cysts). The effect of the test oil was specific and significant as compared to placebo group (p<0.01).

Number of maturing follicles

In test group increased significantly in right ovary (before: 34 to after: 43) and slightly decreased in left ovary (before: 45 to after: 43). However, in placebo group it decreased both in right (before: 31 to after: 28) and left ovary (before: 33 to after: 28). In a 6-month post-study follow-up, it was observed that out of 46 participants who were using test oil, 17 patients had successfully conceived, suggesting that the test oil may help in treating PCOS induced anovulatory infertility.

During the study, no AE was reported. No participant was withdrawn due to any AE.

Discussion

PCOS represented by various symptoms needs to be managed in a comprehensive way rather than answering only a few symptoms. Besides traditional medicine, CAM may provide a more sustainable solution to PCOS. The studies to measure effectiveness of CAM are majorly done on rat models [32,35,36]. Mentha spicata is found effective in reinstatement of follicular development in rat ovarian tissues [32]. T. occidentalis essential oil is identified to reduce ovarian cysts in rats without inducing osteoporosis [35]. Similarly, role of Chamomile extract is studied to reduce signs of PCOS in rat ovarian tissue [36]. One study with 15 PCOS women sample identified the role of Cinnamon extract on menstrual cycle through reduction in insulin resistance [37]. Thus, there are almost no human clinical trials to establish CAM efficacy to manage PCOS as a syndrome with multiple symptoms.

This study is the one to study the effect of natural oil-blend on PCOS symptoms including both subjective and objective ones. The test group experienced 1. a significant decline in the level of irregularity of their menstrual cycles, 2. a significant improvement for severe and moderate duration of bleeding cycle, 3. a shift from heavier to regular menstrual bleeding, 4. a significant shift in experiencing severe menstrual pain to mild or no pain as compared to placebo. Overall, it can be inferred that test oil has positive impact in managing subjective symptoms of PCOS. With respect to objective parameters, there was a significant decrease in hirsutism symptom. The USG results after test oil treatment have shown significant reduction in ovarian volume as well as reduction is follicular cysts of both right and left ovaries. A significant increase in maturing follicles indicates increased chances of ovulation which may lead to improved fertility in women suffering from PCOS. In a 6-month follow up nearly 38% patients had successfully conceived.

The promising results indicate that the test oil can be considered for PCOS management. Nonetheless, the results can't be generalized considering various physiological parameters with patients and may be further explored.

Conclusion

This study is the one to assess the effectiveness of topical application of 100% plant-extract based natural oil-blend on the management of PCOS. There is nothing to ingest and only topical application is required. The test oil-blend is found effective to manage the syndrome by and large and effectively managed a number of symptoms of PCOS rather than working on isolated symptoms of PCOS. The cost effectiveness is not directly measured in the study but significant cost effectiveness is evident considering the cost of hospitalization, medicines among others plus huge cost of physical and psychological discomfort to patients suffering from PCOS.

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