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RESEARCH ARTICLE

Clinical Efficacy of Ayurvedic Formulations *Rajahpravartini Vati*, *Varunadi Kashaya* and *Kanchanar Guggulu* in the Management of Polycystic Ovary Syndrome: A Prospective, Open-label, Multicenter Study

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is characterized by oligo-anovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries. It is a metabolic disorder and around 4 to 9% of women of reproductive age are affected by it.

Objective: To evaluate the clinical usefulness of *Rajahpravartini Vati*, *Varunadi Kashaya*, and *Kanchanar Guggulu* in the management of PCOS and changes in the quality of life (QOL) of PCOS women.

Materials and methods: It was a multicenter single-arm prospective study. Sixty women aged between 18 and 40 years with PCOS confirmed as per Rotterdam criteria 2003, i.e., hyperandrogenism clinically (hirsutism)/or biochemically (elevated serum testosterone concentrations), anovulation/or oligomenorrhea, or amenorrhea after negative screening pregnancy test and/or polycystic ovary were included in the study. Ayurvedic regimen comprising *Rajahpravartini Vati* (250 mg), *Kanchanar Guggulu* (500 mg), and *Varunadi Kashaya* (20 mL) was administered with lukewarm water twice daily for 180 days. The outcome measures were attainment of normal menstrual cycle length, changes on acne score, hirsutism (Ferriman–Gallwey score), and improvement in QOL of women with PCOS.

Results: The trial drugs have statistically significant effect ($p<0.001$) on the signs and symptoms, i.e., oligomenorrhea, presence of body hair. The drugs have significant effects on reducing the number of cysts in both the ovaries (p-value <0.001) and also improvement in QOL of the women studied. There was no adverse event reported during the study period and all laboratory safety parameters were within the normal range.

Conclusion: *Rajahpravartini Vati*, *Varunadi Kashaya*, and *Kanchanar Guggulu* have shown a positive role for the treatment of PCOS and to improve the QOL of the subjects and clinically safe to use.

Keywords: *Kanchanar Guggulu*, Menstrual cycle, Polycystic ovary syndrome, Quality of life, *Rajahpravartini Vati*, *Varunadi Kashaya*.

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INTRODUCTION

Polycystic ovary syndrome is characterized by any of oligo-anovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries.[1,2] The syndrome affects around 4 to 9% of women of reproductive age.[3] Insulin resistance (IR) accompanied by compensatory hyperinsulinemia constitutes another major biochemical feature of PCOS, which leads to early luteinizing hormone (LH) sensitivity of the follicle and to stimulation of both ovarian and adrenal androgen production.[4-8]

Oligo-anovulation due to ovarian dysfunction continues to be the pivotal feature that makes this syndrome the major cause of anovulatory infertility in developed countries.[9]

The European Society for Human Reproduction and the American Society of Reproductive Medicine or Rotterdam criteria 2003 are the agreed international diagnostic criteria for PCOS. Hyperandrogenism clinically (hirsutism)/or biochemically (elevated serum testosterone concentrations), anovulation/or oligomenorrhea (cycles of 35 days

or longer), or amenorrhea (no menses in the last 6 months) after negative screening pregnancy test and/or polycystic ovary are the three main diagnostic criteria, and two out of these three confirm the diagnosis, with exclusion of other androgen excess etiologies.

The conditions like thyroid dysfunction and hyperprolactinemia are to be excluded biochemically, while rarer conditions (congenital adrenal hyperplasia, Cushing's syndrome, virilizing tumors, etc.) should be excluded clinically as well as biochemically to confirm the diagnosis of PCOS.[10]

Polycystic ovary syndrome is the most common cause of anovulatory infertility affecting 90 to 95% of women, attending infertility clinics. Hirsutism and hyperandrogenism in PCOS occur in 60% of women and result from increased synthesis and release of ovarian androgens. Insulin resistance occurs in 50 to 80% of PCOS women, primarily in those who are overweight. Lean women appear to have less severe IR. Due to the high prevalence of IR, PCOS shares components of metabolic syndrome: Abdominal obesity, impaired glucose tolerance, gestational and type II diabetes, abnormalities in lipid profile, hypertension, endothelial dysfunction, and probably cardiovascular disease. Women with PCOS also have an increased risk of endometrial carcinoma because of longstanding unopposed estrogen stimulation.[11]

The features of PCOS may be correlated with "*Puspaghnee Jataharinee*" described in Ayurvedic classics (*Kashyap Samhita, Kalpasthana*) having the clinical features, viz. *Vrutha Pushpa* (may be correlated with amenorrhea/anovulatory cycle), *Sthula lomasha Ganda,* i.e., obese cheeks with hairs (may be correlated with hirsutism/hyperandrogenism).[12] But there is no treatment principle/treatment available in the said classic. But to regulate the menstruation and ovulation, weight reduction, and assisting fertility, many effective Ayurvedic regimens are described, namely *Rajahpravartini Vati, Dasamularista/Kwatha, Ashokarista, Kumaryasava, Phalaghrita, Rajadoshahara vati, Vyoshadi Guggulu, Kanchanar Guggulu*, etc.

The investigational agents were three classical Ayurvedic formulations, i.e., *Rajapravartini Vati* [Ayurvedic Formulary of India (AFI), Part-1 12:25],[13] *Kanchanar Guggulu* (AFI, Part-1, 5:1),[13] *Varunadi Kashaya (Sahasra Yoga, Prathama Prakarana, Kashaya Yoga/472)*[14] selected according to their therapeutic uses reported in the classics, i.e., *Rajapravartini Vati* is a herbo-mineral formulation used for oligomenorrhea/amenorrhea and dysmenorrhea. It is known to regularize the menstruation. *Kanchanar Guggulu* is an herbal compound used for the treatment of cysts. It is also used for the reduction of weight in the obesity as it contains *Guggulu*. *Varunadi Kashaya* is also a herbal compound indicated in the treatment of cysts. All the drugs are mentioned in Ayurvedic literatures for aforesaid therapeutic uses.

OBJECTIVES

The primary objective of this study was to assess the therapeutic efficacy of *Rajahpravartini Vati, Kanchanar Guggulu*, and *Varunadi Kashaya* on clinical features of PCOS, viz., irregular menstrual cycles, and regression of ovarian cysts.

Secondary objectives of the study were to determine the effect of trial interventions on hirsutism and acne. Furthermore, to assess the changes in the QOL of the study participants and to generate evidence on the clinical safety of trial drugs.

MATERIALS AND METHODS

Study Site

This was a multicenter, prospective, single-arm study. The women with PCOS were recruited between September 2013 and February 2015 from two institutes of Council for Research in Ayurvedic Sciences, viz., Regional Ayurveda Research Institute for Life Style Related Disorders, Poojapura, Thiruvananthapuram, Kerala, India and Central Ayurveda Research Institute for Respiratory Disorders, Moti Bagh Road, Patiala, Punjab, India.

Selection of Study Subject

Inclusion Criteria

Women of 18 to 40 years with PCOS as defined by Rotterdam 2003 criteria hyperandrogenism clinically (hirsutism)/or biochemically (elevated serum testosterone concentrations), anovulation/or oligomenorrhea (cycles of 35 days or longer), or amenorrhea (no menses in the last 6 months) after negative screening pregnancy test, polycystic ovary (more than 10 follicles in a ovary/or one cyst more than 10 mm in size), and those were able and willing to provide signed informed consent were included in the study.

Exclusion Criteria

Women having the history of primary amenorrhea; secondary amenorrhea due to lactation; pregnancy/planned pregnancy during the treatment period; not associated with any organic reproductive system abnormalities (excluded clinically and radiologically), pelvic inflammatory disease, hydrosalpinx, endometriosis, adenomyosis, fibroid uterus, carcinoma of reproductive organ, and the subjects with metabolic and endocrinal disorders like diabetes mellitus, chronic liver disease, renal disorder, high

blood pressure, hypo and hyperthyroidism were excluded from the study. Furthermore, the women in use of oral contraceptives (current or within the last 3 months), glucocorticoids, antiandrogens, ovulation induction agents, antiobesity drugs, or other hormonal drugs, and ingestion of any investigational drug within 4 weeks prior to the recruitment in the study were excluded from the study. As the laboratory screening of hormonal parameters have to be performed on day 2/3 of the menstrual cycle, those were having no uterine bleeding in progesterone challenge test for induction of cycle were also excluded.

Interventions

Three Ayurvedic classical formulations, viz., *Rajahpravartini Vati, Kanchanar Guggulu,* and *Varunadi Kashaya*, were prepared as per the standard procedures mentioned in Ayurvedic Pharmacopoeia of India and were tested for quality and safety parameters, viz., heavy metals, aflatoxin, microbial load, and pesticide residue, which were within the permissible limit. It was administered in a dose of 250 mg, 500 mg, and 20 mL with 40 mL lukewarm water respectively twice a day in the morning and evening after food for 180 days. There is no classical reference for the said dose and ratio of the water for *Varunadi Kashaya*. It was procured from the Aushadhi Pharmaceutical, Kerala, India. As per their practice, the Pharma usually manufacturing the Kashaya in concentrate form for better stability as the shelf life of the Kashaya is very short. The dose of the Kashaya is two palas (50–60 mL approx.). So, said dose of Kashaya and water was decided by the Pharma to make the appropriate therapeutic dose of *Varunadi Kashaya*.

Outcome Measures

The primary outcome measures were changes in menstrual cycle length (21–35 days) from baseline at the end of the treatment, obesity as per ratio of waist and hip circumference, and basal metabolic index, in metabolic parameters (i.e., blood sugar and lipid profile), changes in hormone level, such as serum follicular stimulating hormone (FSH), LH, prolactin, testosterone, dehydroepiandrosterone sulfate (DHEAS), and 17-hydroxyprogesterone (OHP). The secondary outcome measures were changes in the degree of hirsutism, acne score, and improvement in QOL by using PCOS-QOL questionnaire. It contains 27 items for assessment of five health domains, such as emotion, body hair, weight, infertility, and menstrual problems.

Study Procedures

The study was conducted after getting the approval from the Institutional Ethics Committee of each participating center and complied with the Declaration of Helsinki and existing good clinical practice guidelines of the country. All subjects were screened properly based on the exclusion and inclusion criteria and a signed consent were taken from them prior to their enrollment in the study. All investigators were trained in the protocol before initiation of the trial. The study has also been registered in Clinical Trial Registry of India No. CTRI/2015/03/005649.

After screening, laboratory parameters, viz., fasting serum concentration of FSH, LH, prolactin, testosterone, DHEAS, estradiol, 17-OHP, insulin, and blood sugar were assessed on day 2/3 of menstrual period of a spontaneous or progestin-induced cycle and the values entered in the specified Case Record Forms (CRFs) on first day of enrollment, i.e., baseline, subject's demographic profile, medical history, family history, menstrual history, and ultrasonography (USG) findings were noted in the CRFs. Clinical manifestation of hyperandrogenism, i.e., the degree of hirsutism was assessed by using modified Ferriman–Gallwey score[15] and increased acne score[16] in 1 to 4 grade scale and also noted in the CRFs. Body mass index (BMI) was calculated using the formula "weight (kg)/height (m^2)."

Hematological and other biochemical parameters for assessment of clinical efficacy and safety of trial drugs were also assessed at baseline, 90th, and 180th day of treatment. Quality of life was assessed by using PCOS-QOL questionnaire[17] at baseline and at the end of the treatment period (180th day). This questionnaire has 26 questions and 5 domains, viz., emotion (8 items), body hair (5 items), body weight (5 items), infertility (4 items), and menstrual problems (4 items). Each item has 7-point scale in which 7 represents the highest function and 1 represents the lowest function.

At the enrollment day and each follow-up visit, i.e., at baseline, 30th, 60th, 90th, 120th, and 150th day (interventional period), trial medication were dispensed and menstrual diary were filled for menstrual history. The interim and final assessment of changes in ovary in USG, hormonal and biochemical parameters were carried out on 90th day and assessed at the end of the treatment, i.e., 180th day. For the assessment of clinical safety, lab parameters were assessed at 90th day and the end of the intervention period, i.e., 180th day. Patient compliance was monitored by keeping a regular follow-up of the subjects by personal contact, telephonic/electronic communication. The investigators were used to check the medicine packing for its exhaustion at each visit.

Statistical Analysis

The data of the enrolled subjects who had taken the medicine at least up to 90th day after baseline were

analyzed. The data of last visit was considered as the data of subsequent visit up to the end of the treatment period by "last observation carry forward method" under modified intention-to-treat analysis for missing data. The obtained data were entered and analyzed using the Statistical Package for the Social Sciences version 15. Descriptive statistics frequencies and percentages for categorical variables, means and standard deviation (SD) for continuous variables were used to describe the total study cohort. Pairwise comparison and within-subject effect of outcome measures were done by using repeated measures analysis of variance. Paired t-test was carried out for assessing the difference in QOL from baseline to 180th day. In all the analysis, p-value of the pairwise comparison is <0.005 and Bonferroni adjusted. McNemar test was used to know the improvement status of the subjects.

RESULTS

Totally, 75 subjects were screened according to inclusion and exclusion criteria of the study. The flow of the study subjects is summarized in Flow Chart 1.

Table 1 summarized the baseline value of different variables, viz., age, marital status and other demographic profiles, anthropometric measurements, menstrual history, etc.

Effect of the Trial Drugs on Anthropometric Parameters

The effects of the trial drugs on various anthropometric parameters are presented in Graph 1. There are no significant changes observed in the body weight, hip circumference, waste/hip ratio, and BMI at the end of the 90th and 180th day of treatment in comparison to baseline.

Effect of the Drugs on Chief Complaints of the Enrolled Subjects

The effect of trial drugs was assessed on the chief complaints of the subjects at baseline, at the end of the 90th day and 180th day of treatment. It is observed that subjects got statistically significant relief on oligomenorrhea, body hair, acne over face and back, and blackening of neck region. But the relief observed in excessive sweating was statistically not significant. The status of study subjects as relieved/static/worse at mid of the treatment and at the end of the treatment (McNemar test) is presented in Table 2. The data show statistically significant changes ($p < 0.001$).

Flow Chart 1: Status of screened and enrolled subjects in the study

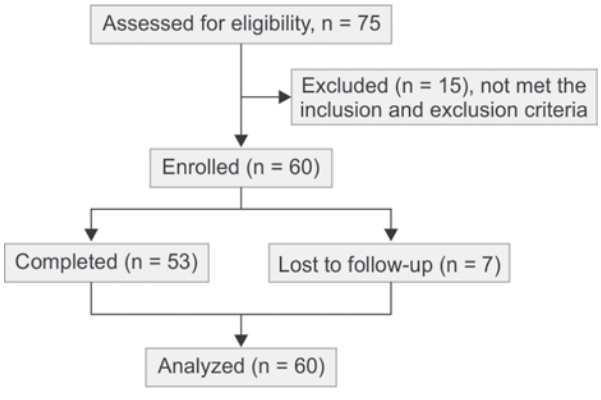
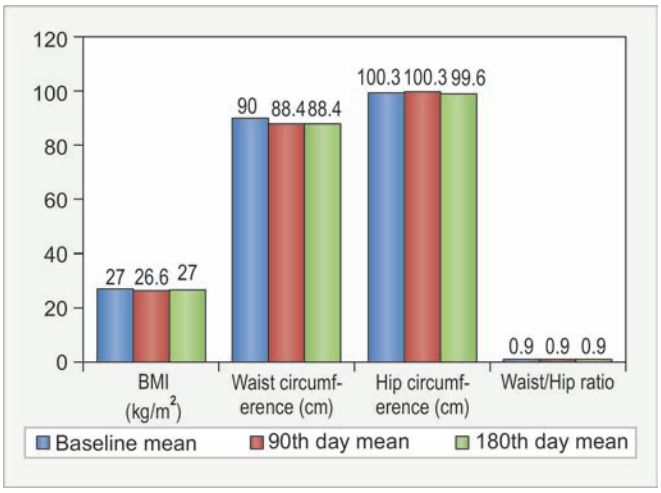
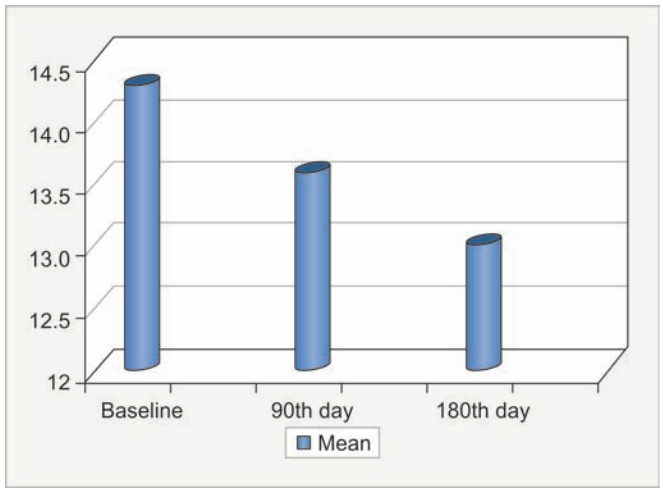


Table 1: Baseline characteristics of study participants (n = 60)

Variables	*n (%)*	*Mean ± SD*
Age (in years)		
18–24	39 (65)	
25–30	15 (25)	
31–36	5 (8.3)	
37–40	1 (1.7)	
Marital status		
Married	17 (28.3)	
Unmarried	43 (71.7)	
Education		
Up to primary	1 (1.7)	
Up to middle	6 (10.0)	
Up to 10 + 2	11 (8.3)	
College and above	47 (78.3)	
Occupation		
Housewife	9 (16.4)	
Field work	1 (1.8)	
Desk work	12 (21.8)	
Student	33 (60.1)	
Nature of diet		
Vegetarian	22 (36.7)	
Nonvegetarian	38 (63.3)	
Body weight (kg)		**65.84 ± 14.5**
Height (m)		**155.56 ± 6.2**
BMI		**27.2 ± 5.5**
Waist circumference (cm)		**90.1 ± 1.3**
Hip circumference (cm)		**100.3 ± 11.9**
Blood pressure		
Systolic (mm Hg)		114.7 ± 11.1
Diastolic (mm Hg)		75.07 ± 6.8
Sharirik prakriti		
Vata-Kaphaja	2 (3.3)	
Vata-Pittaja	19 (31.7)	
Pitta-Kaphaja	35 (58.3)	
Pittaja	1 (1.7)	
Sannipataja	3 (5.0)	
Menstrual history		
Age of menarche		13.05 ±1.6
Duration of menstrual flow		4.97 ± 2.6
Amount of bleeding (in no. pads)		2.98 ± 1.65
Excessive	16 (26.7)	
Scanty	14 (23.3)	
Normal	19 (31.7)	
Prolonged	8 (13.3)	
Midcycle spotting	3 (5.0)	
Length of menstrual cycle (in days)		73.8 ± 47.7
Pain during cycle	26 (43.3)	



Graph 1: Effect of trial drugs on anthropometric parameters



Graph 2: Effect of the drugs on hirsutism (Ferriman–Gallwey score)

Effect of the Trial Drugs on Menstrual Cycle

From the result, it is observed that at baseline, six (10%) women had five menstrual cycles in 6 months of period, but after 180 days of the treatment, total 12 (20%) attained the five menstrual cycles. Further, at baseline only five women were having six/seven cycles, but three more women, i.e., total eight women, were having six/seven cycles at the end of the treatment. Overall, it is observed that the trial drugs have not shown significant effect on attainment of required number of cycles. Further, it is observed that average interval between two cycles was 73.8 days at baseline, which was gradually shorten and was 53.7 days after the treatment. The mean duration of the menstrual bleeding at baseline and at the end of the treatment was almost the same and in normal range. The details are given in Tables 3 and 4.

Effect of the Trial Drugs on Hirsutism

The severity of hair growth (hirsutism) on the body was assessed by Ferriman–Gallwey score and that statistically significant reduction has been observed at the end of 90th day and at the end of the treatment, i.e., 180th day, with the p-value of 0.01 and <0.005 respectively. The result is depicted in Graph 2.

Effect of the Drugs on Acne Score

A Wilcoxon signed-rank test showed that a treatment course for the period of 180th day did not elicit a statistically significant change in acne score in the study participant with PCOS with existing acne score ($Z = -1.7$, $p = 0.09$ at 90th day and $Z = -2.14$, $p = 0.03$ at 180th day). The detail is presented in Table 5.

Table 2: Effect of the drugs on chief complaints of study participants

		90th day n (%)				*180th day n (%)*		
Variables	*Relieved*	*Static*	*Worse*	*p-value*	*Relieved*	*Static*	*Worse*	*p-value*
Oligomenorrhea	13 (21.7)	45 (75)	2 (3.3)	0.007	18 (30)	40 (66.7)	2 (3.3)	<0.001
Presence of body hair	5 (8.3)	55 (91.7)	0 (0)	0.06	22 (36.7)	38 (63.3)	0 (0)	<0.001
Presence of acne over face, back	17 (28.3)	42 (70)	1 (1.7)	<0.001	22 (36.7)	38 (63.3)	0 (0)	<0.001
Blackening of neck region	10 (16.7)	49 (81.7)	1 (1.7)	<0.01	16 (26.7)	42 (44.4)	2 (3.3)	<0.001
Excessive sweating	13 (21.7)	40 (66.7)	7 (11.7)	0.26	14 (23.3)	39 (65)	7 (11.7)	0.2

Table 3: Effect of the trial drugs on number of menstrual cycles during last 6 months

Number of cycles in last 6 months	*Baseline n (%)*	*End of the treatment period, i.e., 180 days n (%)*
No cycle	0	5 (8.3)
One	4 (6.7)	5 (8.3)
Two	16 (26.7)	9 (15)
Three	18 (30)	11 (18.3)
Four	11 (18.3)	10 (16.7)
Five	6 (10)	12 (20)
Six/seven	5 (8.3)	8 (13.3)

Table 4: Effect of the trial drugs on nature of menstrual cycle

Assessment stage	*Duration (in days) (Mean ± SD)*	*Interval (in days) (Mean ± SD)*	*Pain n (%)*
Baseline	4.9 ± 2.6	73.8 ± 47.7	26 (43.3)
30th day	4.7 ± 2.1	30.03 ± 7.96	16 (55.2)
60th day	4.3 ± 2.2	39.5 ± 13.1	14 (46.7)
90th day	5.90 ± 8.9	52.1 ± 25.9	22 (52.4)
120th day	5.4 ± 2.6	43.1 ± 23.6	12 (41.4)
150th day	4.8 ± 2.1	47.03 ± 22.5	13 (37.1)
180th day	4.9 ± 2.2	53.7 ± 46.1	17 (47.2)

Table 5: Effect of the drugs on acne score (n = 60)

Acne score	*90th day*	*180th day*
Z-value	−1.7	−2.14
p-value	0.09	0.032

Effect of the Drugs on Hormonal Profile

The level of hormones like LH, FSH, LH/FSH ratio, prolactin, testosterone, DHEAS, OHP, and estradiol were assessed at baseline, 90th day, and 180th day of treatment. But there is no significant changes observed in all the hormones level. The details are presented in Table 6.

Effect of the Drugs on Ovarian Cysts

From the result it is observed that there is a negligible reduction in the mean score of the size of the cysts (vol. in cc) in right ovary on 90th day, i.e., 11.14 and 10.27 at 180th day, which is statistically insignificant. But in the left ovary no changes observed. But significant effects have been observed in reducing the number of cysts in both the ovaries (p-value < 0.001) (Graph 3).

Effect of the Drugs on Laboratory Parameters for Safety Evaluation

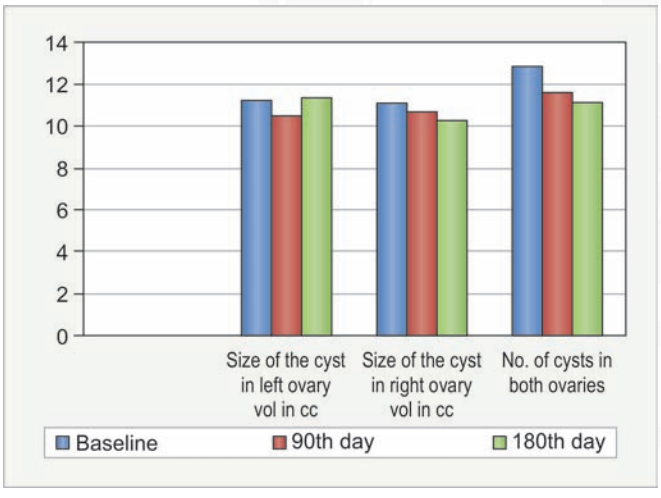
The safety laboratory parameters, i.e., liver and renal functions were assessed at baseline and those having the normal value were included in the study. The same parameters were assessed at 90th day and at the end of the treatment, i.e., 180th day. Though some changes were observed in the values, but those were in the normal range. The details about the parameters and their values at different points are given in Table 7. Further, no subject reported any adverse event during the treatment period.

Effect of the Trial Drugs on QOL of Study Subjects

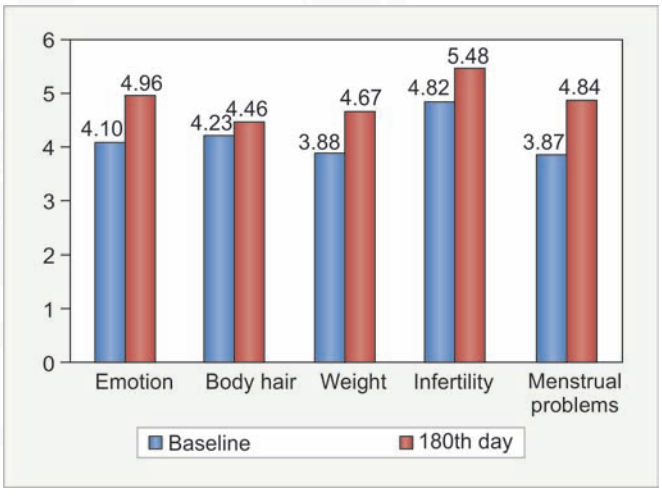
The QOL of the study subjects was assessed at baseline and 180th day. It is observed that after 180 days of treatment, the QOL increased significantly with a p-value of 0.001 (Graph 4).

DISCUSSION

Polycystic ovarian syndrome is considered as the most frequently encountered health disorders by the women in their reproductive age in present days. It is associated with important reproductive morbidities like infertility, increased pregnancy loss, and complications of pregnancy along with the other clinical features, i.e., menstrual irregularities, hyperandrogenism, and other metabolic syndromes. Besides these, in long term it leads to diabetes mellitus, cardiovascular diseases, carcinoma, and also social stigma (due to infertility).



Graph 3: Effect of the drugs on ovarian cyst



Graph 4: Effect of the drugs on quality of life of the study participants

Table 6: Effect of the drugs on hormonal profiles (n = 60)

	Baseline	*90th day*							
Variables	*Mean ± SD*	*Mean ± SD*	*95% CI*		*p-value*	*180th day*	*95% CI*		*p-value*
FSH (IU/L)	5.72 ± 2.02	6.3 ± 4.6	−1.8	0.6	0.36	5.07 ± 2.5	−0.1	1.4	0.1
LH (IU/L)	7.4 ± 4.3	12.9 ± 10.7	−8.3	−2.8	<0.001	10.1 ± 8.4	−5.0	−0.4	0.02
Prolactin (µg/mL)	0.01 ± 0.02	0.02 ± 0.03	−0.01	0.08	0.76	0.14 ± 0.99	−0.38	0.13	0.3
Testosterone (ng/mL)	0.7 ± 0.36	0.69 ± 0.35	−0.12	0.13	0.9	0.69 ± 0.3	−0.12	0.11	0.9
DHEAS* (ng/mL)	2449.97 ± 1291.96	2700.2 ± 1567.2	−487	−13.5	0.04	2639.6 ± 1570.96	−450.4	71.2	0.15
OHP (ng/mL)	1.06 ± 0.67	1.84 ± 1.15	−1.06	−0.49	0	1.62 ± 1.2	−0.84	−0.3	0
Estradiol (pg/mL)	49.7 ± 26.35	73.0 ± 87.6	−45.9	−0.71	0.04	80.7 ± 113.7	−59.5	−2.65	0.03

CI: Confidence interval of the difference

Table 7: Effect of the drugs on safety laboratory parameters (n = 60)

	Baseline	*90th day*	*180th day*
Parameters	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
Kidney function test			
Serum uric acid (mg/dL)	4.4 ± 0.9	–	4.5 ± 0.96
Serum creatinine (mg/dL)	0.8 ± 0.1	–	0.81 ± 0.1
Serum urea (mg/dL)	21.23 ± 6.0	–	21.18 ± 6.05
Liver function test			
SGOT (AST)	20.8 ± 6.3	22.02 ± 7.4	22.9 ± 8.3
SGPT (ALT)	22.6 ± 11.3	22.98 ± 14.02	24.13 ± 14.35
Alkaline phosphatase (IU/L)	139.95 ± 77.7	144.6 ± 82.5	136.3 ± 78.35
Serum albumin (gm/dL)	4.5 ± 0.3	4.4 ± 0.34	4.4 ± 0.34
Total bilirubin (mg/dL)	0.6 ± 0.2	0.6 ± 0.2	0.57 ± 0.2
Conjugated bilirubin (mg/dL)	0.2 ± 0.08	0.2 ± 0.05	0.2 ± 0.05
Gamma glutamyltranspeptidase (IU/L)	17.54 ± 7.24	18.9 ± 8.9	18.95 ± 8.4

SGPT: Siamane glutamate pyruvate transaminase; SGOT: Serum glutamic oxaloacetic transaminase; AST: Aspartate transaminase; ALT: Alanine transaminase

The aim of this study was to assess the efficacy of the trial drugs *Rajahpravartini Vati*, *Kanchanar Guggulu*, and *Varunadi Kashaya* on various cardinal signs and symptoms of PCOS, i.e., oligomenorrhea/amenorrhea, ovarian cysts, hyperandrogenism (both biochemically and clinically), and other associated signs, i.e., acne. Due to derangement of Dhatwagni, PCOS occurred mainly, which causes metabolic disorders like obesity, dyslipidemia, etc. and also leads to hormonal disorders. According to Ayurveda, the food digested by the Pachakagni further digested by the Dhatwagni mainly at liver for proper assimilation in the body. *Rajahpravartini Vati* was selected for this study keeping in view that it contains *Kumari satwa*, which is a good liver stimulant drug and also act as Rajah pravartaka (menstruation). *Kanchanar Guggulu* and *Varunadi Kashaya* were selected for their effects on cysts.

From the result, it is observed that the most of the study participants were between the age group of 18 and 30 years, i.e., 54 (90%), 43 (71.7%) were unmarried and 33 (60%) were students. As most of the women were between 18 and 30 years of age, so the percentage of unmarried girl and student is more. The mean score of BMI was 27.2 ± 5.5. In a study, it is established that PCOS is more prevalent in obese women.[18] Most of the women were having *Vata-pittaja* and *Pitta-kaphaj prariti*. But it is difficult to establish the causal association of prakriti with PCOS as no such study has been reported so far.

The most common feature observed in PCOS is hyperandrogenism. More than 80% PCOS women have complaint of hirsutism.[19] This study also corroborated the same as almost all the women have the complaint of hyperandrogenism either clinically or biochemically. At baseline, the level of DHEAS was elevated. Though the level of DHEAS was not significantly altered, but clinically significant changes have been observed in hirsutism. The severity of hair growth (hirsutism) was assessed by Ferriman–Gallwey score and drugs have shown statistically significant effect on both the point, i.e., 90th and 180th day, of treatment. Five (8.3%) women got complete relief at the end of 90th day of treatment and 22 (36.7%) women got relief from hirsutism at the end of the treatment, i.e., 180th day, which suggested the long-term effect of the trial drugs.

The drugs have shown encouraging results on menstrual cycle as the interval between two cycles reduced considerably after the treatment (Table 4), which may be due to *Rajahpravartini Vati* which was one of the trial drugs and a drug of choice for amenorrhea/oligomenorrhea. Infertility is a common feature in PCOS and most common cause is anovulation. But a limitation of this study is the ovulation study had not been conducted and it was also neglected while deciding the inclusion criteria. Majority of the participants were unmarried.

The trial drugs also have not shown any significant effect both on size and number of ovarian cyst. Only some significant changes occurred in the number of cysts in both the ovaries (Graph 3). This study is the first study with Ayurvedic formulations which assessed the QOL of the women affected with PCOS.

As far as the clinical safety is concerned, the result on safety laboratory parameters shows that all the drugs are safe for use even for a long period. Further, no adverse event was reported by the study participants during the treatment period and no one have also withdrawn from the study. All the trial drugs are classical Ayurvedic formulations and in use since long period. These findings corroborate the safety of classical Ayurvedic formulations.

CONCLUSION

From the result, it is concluded that the trial drugs have a significant effect on hirsutism, oligomenorrhea, and overall improvement in the QOL of women with PCOS. This study was an exploratory study to generate a

preliminary data for treatment modality in a recent emerging gynecological condition called PCOS. However, because of open label and noncomparative nature of the present study, the findings may further be corroborated through a randomized controlled study.

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हिन्दी सारांश

"पोली सिस्टिक ओवेरियन सिंड्रोम"(PCOS) के प्रबंधन में *रजःप्रवर्तिनी वटी, कांचनार गुग्गुलु* एवं *वरुणादी कषाय* की प्रभावकारिता का नैदानिक मूल्यांकन – एक बहुकेंद्रीय प्रत्याशित अध्ययन

[1]सुष्मिता पी ओता, [2]रिंकू तोमर, [3]शारदा ओता, [4]एस इन्दिरा कुमारी, [5]राजेश सण्ड, [6]नीरा व्यास
[7]राकेश राणा, [8]रिचा सिंघल, [9]भारती, [10]नारायणम श्रीकांत

भूमिकाः ऑलिगो–एनोव्यूलेशन, नैदानिक या जैव रासायनिक हाइपर एंड्रोजेनिज्म, और पॉलीसिस्टिक अंडाशय ये तीनों लक्षण "पॉलीसिस्टिक ओवेरियन सिंड्रोम" (पी.सी.ओ.एस) को लक्षित करते है। यह एक चयापचय संबंधी विकार है और प्रजनन की उम्र के लगभग 4–9% महिलाएँ इससे प्रभावित होती हैं।

उद्देश्यः PCOS के प्रबंधन में *रजःप्रवर्तिनी वटी, कांचनार गुग्गुलु* एवं *वरुणादी कषाय* (आयुर्वेदिक औषधियों) की प्रभावकारिता के साथ ग्रसित महिलाओं के जीवन की गुणवत्ता में सुधार का चिकित्सीय मूल्यांकन।

सामग्री एवं विधिः यह चिकित्सीाय अध्ययन बहु–केंद्रीय स्तर पर किया गया था। कुल 60 महिलाओं को अध्ययन में शामिल किया गया था जिनकी वय 18–40 वर्ष के अन्तराल की थी एवं इन महिलाओं में PCOS की पुष्टि रोटर्डम मानदंड 2003 के अनुसार की गई थी। इस में *रजःप्रवर्तिनी वटी* (250मि.ग्रा.), *कांचनार गुग्गुलु* (500 मि.ग्रा.) और *वरुणादी कषाय* (20 मी.ली.) को दिन में दो बार खाना खाने के बाद हल्के गुनगुने पानी के साथ 180 दिनों तक दिया गया था। PCOS से प्रभावित महिलाओं के मासिक चक्र की अवधि, मुँहासे के स्कोर, हीरुटिस्म, जैव रासायनिक मापदंडों, हार्मोन संबंधी मापदंडों में लाई जाने वाली प्रकृतिस्थता और जीवन की गुणवत्ता में सुधार यह इस अध्ययन के परिणाम थे।

परिणामः अध्ययन के अंत में उपचार के प्रभाव स्वरूप रोग के लक्षणों में महत्वपूर्ण सांख्यिकीय प्रभाव (पी<0.001) पाया गया था एवं ग्रसित महिलाओं की जीवन की गुणवत्ता में भी सुधार था। परिणाम स्वरूप औषधियों का दोनों अंडाशयों में पायी गयी पुटिकाओं की संख्या को कम करने पर भी महत्वपूर्ण प्रभाव था। इसके अतिरिक्त अध्ययन के दौरान रोगियों में लिवर और किडनी के प्रयोगशाला मापदण्डों में कोई महत्वपूर्ण अन्तर नहीं पाया गया था एवं कोई भी प्रतिकूल घटना रिपोर्ट नहीं हुई।

निष्कर्षः इस अध्ययन से स्पष्ट होता है कि PCOS में *रजःप्रवर्तिनी वटी, कांचनार गुग्गुलु* एवं *वरुणादी कषाय* जैसी आयुर्वेदिक औषधियों का उपयोग प्रभावकारी व सुरक्षित है।

सूचांकः अतः *रजःप्रवर्तिनी वटी, कांचनार गुग्गुलु* एवं *वरुणादी कषाय* के प्रयोग से PCOS के कारण होने वाली अन्य समस्याएँ (रोग) कम हो सकती है।

मुख्य शब्दः "पोली सिस्टिक ओवेरियन सिंड्रोम" (PCOS), *रजःप्रवर्तिनी वटी, कांचनार गुग्गुलु* एवं *वरुणादी कषाय* तथा मासिक धर्म चक्र।

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