IJPSR (2018), Volume 9, Issue 6 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 27 August, 2017; received in revised form, 13 March, 2018; accepted, 18 March, 2018; published 01 June, 2018

# A RANDOMIZED CLINICAL TRIAL TO EVALUATE THE EFFICACY OF SATAPUSHPASHATAVARI POWDERED DRUG WITH SATAPUSHPA-SHATAVARI GRITA FOR THE MANAGEMENT OF POLYCYSTIC OVARY SYNDROME (PCOS)

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**Keywords:**

Polycystic Ovarian Syndrome, Satapushpa, Satavari, US scan

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**ABSTRACT:** Sri Lankan Ayurveda clinical practice Satapushpa Shatavari powder (SSP) with or without Satapushpa Shatavari Grita (SSG) enema is used for manage menstrual disturbances due to polycystic ovary syndrome (PCOS). Objective of Present study was to evaluate the efficacy of Satapushpa Shatavari Churna with Satapushpa Shatavari Grita Matra Vasti for the management of PCOS by an open label comparative clinical trial. Successful screening 60 PCOS participants were randomly divided into three groups (n = 20) *viz* Group A (Oral Administration of SSP 05g t. d. s. with 10 ml of cows ghee for 2 weeks), Group B (Rectal Administration of SSG as enema, 60 ml / day for 2 weeks with 1 week gap) and Group C (oral and rectal administration of SSP and SSG drugs respectively). After one month administration period participants in group A, B and C were assessed on PCOS appearance of the ovary, volume of the ovary, endometrial thickness by US scan. Further volume of menstrual flow, intermenstrual period and hirsutisum was assessed by standard scoring system. The study revealed that all treated groups were reduced their ovarian volumes when compare with pretreated stages. Endometrial thickness of each groups were improved and group C was shown significant improvement. Hirsutisum ratings score was significantly improved in group C. Quantities of the menstruation of all drug treated groups were significantly improved. The findings of the present study indicate that SSP therapy leads to comparable reduction of ovarian volume in a manner, which correlates with the degree of reduction of PCOS and related signs.

**INTRODUCTION:** Polycystic ovary syndrome (PCOS) is a complex endocrine disorder with an estimated prevalence of 4 - 21% in reproductive aged women depending on the diagnostic criteria and population examined [1, 2]. PCOS clinical manifestations include oligomenorrhea or amenorrhea, clinical or biochemical signs of hyperandrogenism and present of polycystic ovaries on ultrasound examination [3, 4].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.9(6).2494-99

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(6).2494-99

Annually around 30% of women were suffering from PCOS who were seeking treatment at Ayurveda gynecology clinic, Ayurveda teaching hospital, Borella in Sri Lanka. Modern medical system offers hormonal therapy and surgical procedures to the above disorder which may have more side effects.

In Ayurveda clinical practice Satapushpa Shatavari powder (SSP) with or without Satapushpa - Shatavari Grita (SSG) Matra Vasti (therapeutic enema) is commonly used treatment for manage menstrual disturbances due to polycystic ovary syndrome (PCOS) [5]. But its efficacy was not clinically evaluated by a standard clinical research. Therefore present study was carried out as a randomized open labeled comparative clinical trial

to evaluate the efficacy of oral administered SSP with SSG administered as therapeutic enema for the management of polycystic ovary syndrome (PCOS). Satapushpa (*Anethum graveolens*) and Shatavari (*Asparagus racemosus*) are indicated for conditions of oligomenorrhoea, hypomenorrhoea, an ovulation in Ayurveda and traditional medicine in Sri Lanka. It has being further noted that this drug can be used in oral and / or enema and/or nasal instillation [5, 6]. Therefore the main objective of this research was to evaluate the clinical efficacy of oral root administration and per rectal administration of Satapushpa - Shatavari formula on PCOS patients.

## MATERIALS AND METHODS:

**Drugs Used:** Plant materials and drugs were authenticated from Bandaranayke International Memorial Ayurvedic Research Institute, Navinna and Institute of Indigenous Medicine, Sri Lanka (Plant authentication voucher specimen no IIM/DG /HS/005/006).

**Preparation of Satapushpa - Satavari Powder (For Oral Administration):** Equal parts of Satapuspa seeds and Satavari roots were pulverized and made fine powder (passes through a no. 80 sieve).

**Preparation of Satapushpa - Satavari Grita (For Oral and Rectal Administration):** Satapushpa - satavari Grita will be prepared by the combination of cow's ghee with Satapushpa - Satavari as per standard method given in Ayurveda authentic text Sharngadhara Samhita [5] and Ayurveda Formula of India.

**Ethical Approval:** Ethical approval for the study was obtained from the Ethics Review Committee of the Institute of Indigenous Medicine, University of Colombo, Sri Lanka (ERC no: 14/33) (http://iim.cmb.ac.lk/erciim/) Written consent was obtained after explaining the study procedure to each volunteer prior to commencement of the study (n = 70).

**Clinical Study:** A randomized single blind study was conducted in the Ayurveda gynecology clinic of National Ayurveda Teaching Hospital Borella and Bandaranaike Memorial Ayurvedic Research Institute in Sri Lanka.

Aged 18 years to 42 years of total 60 patients **Table 1** were included in this clinical study on the criteria laid in the diagnosis of PCOS. History of the condition, previous history and present general condition, signs and symptoms, necessary investigations were recorded and during the subsequent visits progress of the signs and symptoms were recorded ones in two week. Cases were selected according to inclusion and exclusion criteria.

**TABLE 1: GROUP DESIGN FOR CLINICAL STUDY (N = 60)**

| Group A | Group B | Group C |
|---|---|---|
| Satapushpa-Shatavari Powder (SSP), 5g t.d.s. per oral with 10 ml of cows ghee | Satapushpa-Shatavari Grita (SSG), 60 ml / day as enema, for 2 weeks with one week gap in between | SSP, 5 g t.d.s. per oral with 10 ml of cows ghee and SSG as enema, 60 ml / day for 2 weeks with one week gap (combination of Group A and B) |

**Inclusion Criteria:**

- Premenopausal between 18 - 42 years of age.
- Diagnosed with PCOS as defined by Rotterdam criteria for diagnosis of PCOS [6].
- Able to provide signed informed consent.
- Able to comply with study requirements.

**Exclusion Criteria:**

- Known diabetics or those with clinically significant and known pulmonary, cardiac, renal, hepatic, neurologic, psychiatric, infectious, neoplastic and malignant disease.
- Current use of hormonal contraceptives.
- Seeking pregnancy; use of fertility drugs within 6 months of study.
- Ingestion of any investigational drug within two months prior to study onset.

**Following Criteria of Assessments were used Pre and Post Treatment:**

- Ultra sound scan - PCOS appearance of the ovary, volume of the ovary, endometrial thickness.
- Body weight.
- Hirsutisum rating score [7, 8].

The modified Ferriman and Gallwey FG scoring system.

**Method:** If terminal hair growth was not present in the examined area a score of zero was given. Minimal amounts of visible terminal hair growth represent a score of 1, a score of 2 was given if hair growth was more than minimal but not yet that of a man, and a score of 3 was that of a not very hairy man while a score of 4 was that typically observed in men.

- Volume of menstrual flow and inter menstrual period was assessed by scoring pattern designed.

Study participants (n = 60) were grouped randomly in to test groups A (SSP oral), B (SSP oral and SSG enema) and C (SSG enema) (every other patient from a list was included in to one group by the researchers). Each patient was in the test group for 01 month and follow-up for 03 months **Table 2**. One patient from the test group A, two patients from group C and three patients of group C discontinued participation on their own reasons. Thus the analyses included 54 patients (Flow diagram of study design, **Fig. 1**). At the end of one month study period the groups were assessed for PCOS appearance of the ovary, volume of the ovary, endometrial thickness by US scan. All the patients were advised to report every 14 days for follow up for two months period.

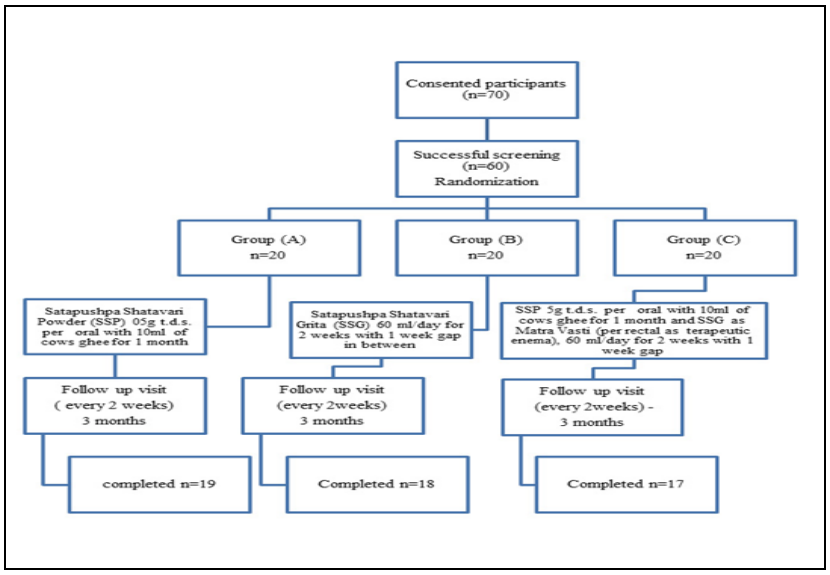


**FIG. 1: FLOW DIAGRAM OF STUDY DESIGN**

**Statistical Analysis:** The findings at pre and post treatment were compared using paired 't' test. The analysis was performed using Statistical Package for Social Sciences (SPSS, version 16.0). A p value of <0.05 was considered statistically significant.

**RESULTS:** Demographic data of the research participants were presented in **Table 2**. Total 60 patients (n = 60) recruited for the study and 54 patients were completed (n = 19 in group A, n = 18 in group B and n = 17 in group C). Six patients where discontinued the study. No serious drug-related adverse events were observed.

Reducing the volume of the ovary measured by ultrasound scan (US) in all three groups **Fig. 2** and all treated groups were reduced their ovarian volumes when compare to pretreatment stages. The study revealed that endometrial thickness of each groups were improved **Fig. 3** and group C was shown significant improvement ($p < 0.05$) of endometrial thickness when comparing other two groups. Hirsutisum ratings score was significantly ($p < 0.05$) improved in drug treated group C **Fig. 4** when compare to drug treated groups A and B. Quantity of the menstruation **Fig. 5** of drug treated groups A ($p < 0.05$), Band C ($p < 0.01$) were significantly improved. Duration of the menstruation **Fig. 6** of all drug treated groups was improved.

**TABLE 2: DEMOGRAPHIC DATA OF THE STUDY POPULATION**

| | |
|---|---|
| Number | 60 |
| Age | 18 - 42 |
| Location | Colombo district |
| Marital state | 79% married |
| BMI | High BMI in 65% |
| Inter-menstrual period | >35 days |

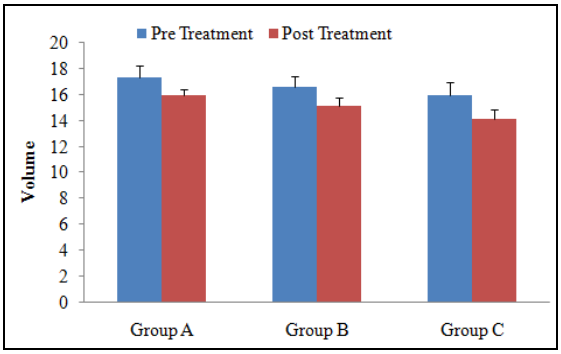


**FIG. 2: COMPARATIVE EFFECT OF THERAPY ON VOLUME OF THE OVARY**
Results are expressed as mean ± SEM; * = p<0.05

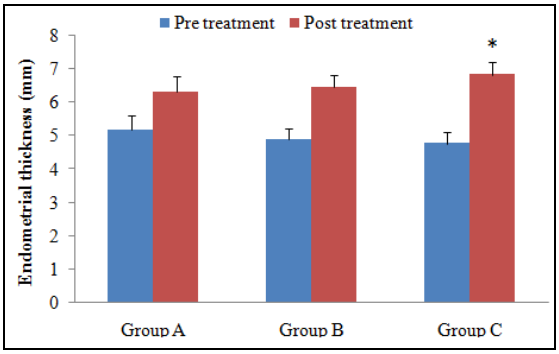


**FIG. 3: COMPARATIVE EFFECT OF THERAPY ON ENDOMETRIAL THICK-NESS (mm) FORM USS**
Results are expressed as mean ± SEM; * = p<0.05

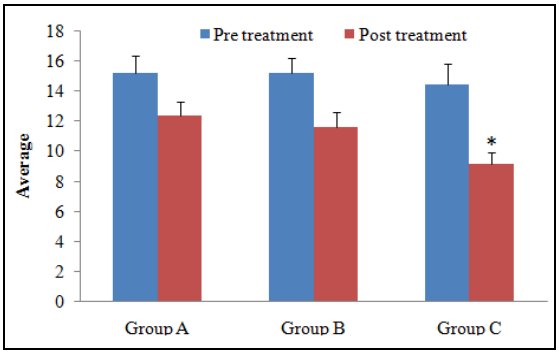


**FIG. 4: COMPARATIVE EFFECT OF THERAPY ON HIRSUTISM VALUES OF THE BODY**
Results are expressed as mean ± SEM; * = p<0.05

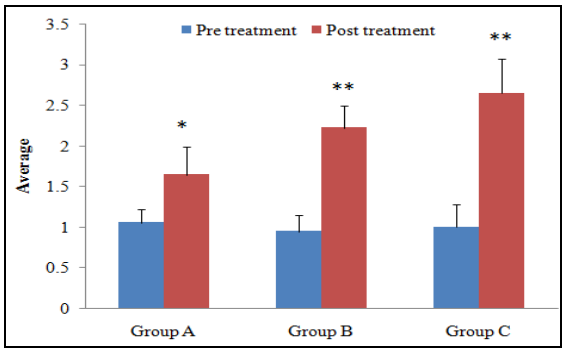


**FIG. 5: COMPARATIVE EFFECT OF THERAPY ON QUANTITY OF MENSTRUAL BLOOD (NO. OF PADS PER CYCLE)**
Results are expressed as mean ± SEM; * = p<0.05;**= p<0.05

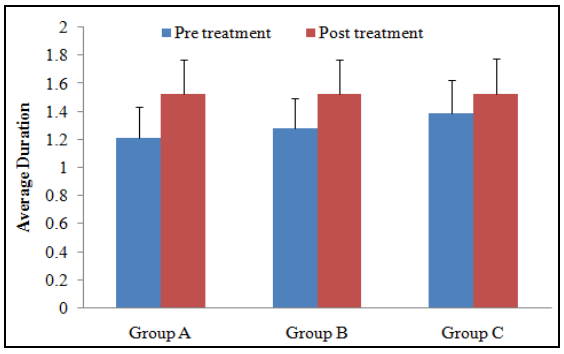


**FIG. 6: DURATION OF MENSTRUATION**
Results are expressed as mean ± SEM; * = p<0.05

Group A: Satapushpa - Shatavari Powder (SSP), 5 g t. d. s. per oral with 10 ml of cow's ghee;
Group B: Satapushpa - Shatavari Grita (SSG), 60 ml /day as enema, for 2 weeks with one week gap in between;
Group C: SSP, 5 g t. d. s. per oral with 10 ml of cow's ghee and SSG as enema, 60 ml /day for 2 weeks with one week gap (combination of Group A and B).

**DISCUSSION:** There is currently no single medical PCOS therapy that fully reverses underlying pathogenesis. There is much variation in the treatments prescribed following a PCOS diagnosis, the widespread prescribing of oral contraceptives and metformin generally reflects the prognostic concerns raised in PCOS consensuses. Medical management places strong emphasis on a multidisciplinary approach as pharmaceutical treatments appear to be only moderately effective in treating individual symptoms [9, 10]. Conventional pharmaceutical management is limited by the prevalence of contraindications in women with PCOS [11], non-effectiveness in some circumstances [10], side effects [12] and by preferences of women with PCOS for alternatives to pharmaceutical management [13]. Herbal medicines are complex interventions with the potential for synergistic and antagonistic interactions between compounds [14].

Effects within the body may also exhibit complexity by simultaneous interactions with various body systems, both biochemically and by altering organ function [4]. This three arm clinical trial was designed to investigate the efficacy of commonly used herbal formula for PCOS with different route of interventions in gynecological clinical setting in Sri Lankan Traditional Medicine and Ayurveda.

Pelvic ultrasound scans have assumed an increasing importance in the diagnosis and management of ovulatory disorders. Assessment of ovarian morphology by the use of ultrasound has become a substitute for histologic examination in diagnosing PCOS [15]. Although, increased stromal volume is a feature of PCO, it has been shown that the measurement of the ovarian volume is a good surrogate for the quantification of stromal volume in clinical practice [16]. Our results were found on reducing the volume of the ovary measured by ultrasound scan (US) in all three groups **Fig. 2**. The study revealed that endometrial thickness of each groups were improved and group C was shown significant improvement ($p < 0.05$) of endometrial thickness when comparing other two groups **Fig. 3**.

Hirsutism is a symptom of medical disorders associated with the hormones called androgens. Polycystic ovary syndrome (PCOS) is in which the ovaries produce excessive amounts of androgens. Therefore hirsutisum rating is a marker for excessive amounts of androgens level in PCOS. We used the most common visual method of scoring the extent of body and facial terminal hair growth based on a modification of the method originally described by Ferriman and Gallwey in 1961 [17]. These study results of hirsutisum scores were significantly low drug treated group C **Fig. 4**.

Furthermore, our finding that the prevalence of obesity and high androgen levels (hirsutism rating) within the patients with larger ovarian volume is seems to confirm the possibility of an interaction between ovarian morphology and anthropometric characteristics [17]. Quantity of the menstruation **Fig. 5** of drug treated groups A ($p < 0.05$), B and C ($p < 0.01$) were significantly improved. Duration of the menstruation **Fig. 6** of all drug treated groups was improved. When we compared among three groups most effective group was the group C.

These research findings confirmed that clinical usage of Satapuspa seeds (*Anethum graveolens*) and Satavari roots (*Asparagus racemosus*) much effective in PCOS and combination with therapeutic enema was significant than single route usage.

**CONCLUSION:** The findings of the present study indicate that SSP therapy leads to comparable reduction of ovarian volume in a manner, which correlates with the degree of reduction of PCOS and related signs. In future larger scale studies will be planned to confirm our findings.

**ACKNOWLEDGEMENT:** We would like to thanks Director of Ayurveda Teaching Hospital Borella and Bandaranayke Memorial Ayurveda Research Institute of Nawinna Sri Lanka for their kind cooperation.

**CONFLICT OF INTEREST:** We declare that we have no conflict of interest.

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**How to cite this article:**
Kumarapeli M, Karunagoda K and Perera PK: A randomized clinical trial to evaluate the efficacy of satapushpa-shatavari powdered drug with satapushpa-shatavari grita for the management of polycystic ovary syndrome (PCOS). Int J Pharm Sci Res 2018; 9(6): 2494-99. doi: 10.13040/IJPSR.0975-8232.9(6).2494-99.