

Concept of Polycystic Ovarian Syndrome: Perspectives of Ayurveda and Modern Science

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ABSTRACT

Polycystic ovarian syndrome is a hormonal disorder affecting 12-18% women of reproductive age. Women with PCOS have irregular menstrual cycle, excess of androgens, insulin resistance, serum lipids alteration, anovulation, acne, hirsutism and infertility. According to Ayurveda this type of clinical features are found in *Pushpadhni jataharini* (disease similar to Polycystic ovarian syndrome mostly having hyperandrogenism and anovulatory cycle) and *Nashtartva* (no proper growth of follicles and chronic anovulation). It involves the imbalance of *dosha*, *dhatu* and *upadhatu*. Evidence based medical management of PCOS is done by controlling irregular menses, treatment of hirsutism and acne, management of infertility and insulin resistance. The chemical based drugs induce ovulatory cycle in women, instead of allowing it to restore to its original healthy rhythm. The successful treatment of infertility is usually possible in the majority of patients with PCOS by using natural, non-invasive and non-chemical remedies. The present review provides information about some herbal plants, extracts of plants, active constituents from plants and some formulations clinically tested in animal models inducing PCOS and humans suffering from PCOS.

Keywords: Polycystic ovarian syndrome, anovulation, hyperinsulinemia, Ayurveda, *dosha*.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) may clinically be manifested in young women of reproductive age as oligo-ovulation, biochemical or clinical hyperandrogenism, hirsutism, male pattern baldness, acne, acanthosis nigricans and polycystic ovaries. But PCOS has a long prodrome with detectable abnormalities that present as the metabolic syndrome like hyperinsulinemia, obesity, dyslipidemia related to decrease high density lipoprotein cholesterol and hypertriglyceridemia, hypertension, atherosclerosis, increased risk of development of type II diabetes and cardiovascular disease throughout the life of affected women¹.

PCOS is a heterogeneous disorder that affects at least 7% of adult women. According to the National Institute of Health Office of Disease Prevention, PCOS affects approximately 5 million women of child bearing age. Research suggests that 5-10% of females at 18 to 44 years of age are affected by PCOS making it the most common endocrine abnormality among women of reproductive age².

As no specific sole cause of PCOS has been determined, the most accepted evidence is a multifactorial model where interactions between environmental cues and factors intrinsic to individual act in consonance towards a common result, which is development of hyperandrogenemia, a biochemical hallmark of this

pathology. This alteration is the main culprit behind most clinical manifestations of PCOS. There are no single criteria sufficient for clinical diagnosis because of multiple aetiologies and presentations. Though globally it has an alarming incidence, its diagnosis is difficult as it manifests as a spectrum of symptoms rather than a specific one³.

Pathophysiology

Modern perspective of PCOS

PCOS has a heterogeneous etiology involving a variety of combination of reproductive, metabolic and genetic determinants. No single etiology has so far been found to have particular predictive power in explaining the occurrence of PCOS. Furthermore no single etiological gene or inheritance pattern has been found for occurrence of PCOS. Clearly improvements in our understanding of the developmental process causing PCOS are necessary to clarify the relative importance of the multifactorial components in PCOS development and to focus clinical initiative in prevention, diagnosis and treatment.

PCOS is imbalance of female sex hormones. The ovaries are the part of female reproductive system along with uterus, fallopian tubes and vagina. The ovaries contain the lifetime supply of eggs. These eggs are immature and stored in tiny fluid filled follicles.

Pituitary gland located at the base of brain produces hormones which direct the function of ovaries. Each

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month the pituitary gland secretes Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) in blood stream. After these hormones reach the ovaries several hundred immature eggs start maturing expanding the size of follicles which simultaneously secretes estrogen, the main female sex hormone. Once the level of estrogen reaches to certain level, the pituitary gland senses the surge of luteinizing hormone to the ovaries causing the most mature follicle to release the egg called ovulation. The free egg travels the fallopian tube where it awaits fertilization, eventually the remaining follicles and eggs dissolves. If the egg is not fertilized the lining of uterus sheds during the menstruation.

In PCOS the pituitary gland releases abnormally high amount of Luteinizing hormone in blood stream disrupting the normal menstruation cycle. As a result the follicle does not mature and ovulation does not occur which can lead to anovulation. The immature follicle which does not dissolve remains as fluid filled sacs or cysts. These cysts lead to a hormonal imbalance because of an increased amount of testosterone. This can result in acne, an increase in facial and body hair and irregular periods.

In addition there is high level of insulin hormone produced by pancreas. Insulin combines with luteinizing hormone and lead to excess production of male hormone testosterone in ovaries. Abnormally high amount of testosterone in the ovaries prevent ovulation which can lead to infertility. Along with it, PCOS raises the risk of Type II diabetes because of excess of insulin or insulin resistance, heart disease, high blood pressure, cholesterol abnormality and endometrial cancer⁴.

Irregular periods

When you have PCOS, the hormone activity becomes irregular as ovulation is not occurring in an expected way. The body gives mixed signals and the menstrual cycle is disrupted. Periods can vary widely from woman to woman. It can change from irregular, infrequent periods (oligomenorrhoea) or heavy to absent periods (amenorrhoea)⁵.

Insulin resistance

Insulin resistance accompanied by compensating hyperinsulinemia (elevated fasting blood insulin level) is important biochemical feature of PCOS. Hyperinsulinemia increases ovarian androgen production (particularly testosterone and androstenedione) and decreases the sex hormone binding globulin (SHBG) concentration⁶.

Research at the University of Oxford and The Imperial College London revealed that a gene implicated in the development of obesity is also linked to susceptibility to PCOS. A study revealed that elevated levels of androgen than normal subjects were found in mothers and sisters of patient suffering from PCOS. It is also manifested that PCOS is genetically transferred ovarian syndrome and it is heterogeneous disorder which involves the interaction of the other genes with the environment⁷.

Histomorphology of ovaries

Polycystic ovaries are six fold larger than normal ovarian size. There is large number of immature follicles

(subcortical cysts) which causes the change in the shape of ovary. The ovary becomes whitish in color and there is multiple cystic follicles covered by a dense fibrous capsule. There is luteinization of the theca cells (hyperthecosis) and thickening of tunica albugenia (connective tissue covering the ovaries)⁸.

Changes in hormonal level

The ovarian and adrenal glands of women with PCOS are usually the sites of production of elevated androgens. It is also proposed that women with PCOS have a hyper production of CYP17 enzyme, which is found to be responsible for forming androgens in the ovaries and adrenals⁹. Ovaries makes several androgens of which testosterone is the most prominent others include androstenedione and dehydroepiandrosterone (DHEAS). The most typical feature of polycystic ovary is the stroma and theca cells make excessive of testosterone¹⁰.

Signs and Symptoms

The major signs and symptoms related to PCOS includes menstrual disturbances ranging from amenorrhoea to oligomenorrhagia to episodic menometrorrhagia with anemia, hyperandrogenism, increased muscle mass, androgenic alopecia, deepening of voice, clitoromegaly, hirsutism, acne, insulin resistance, acanthosis nigricans, dyslipidemia, infertility and miscarriage¹¹.

Diagnosis

Women may have cysts in the ovaries for a number of reasons and so it is the characteristics constellation of symptoms, rather than the presence of cysts themselves that is important in establishing the diagnosis of PCOS.

The Rotterdam criteria of assessment: presence of two out of the following three criteria:

Oligomenorrhoea and/or anovulation

Hyperandrogenism (clinical and/or biochemical)

Polycystic ovaries with exclusion of other etiologies.

The other methods of diagnosis are gynecological ultrasonography, laparoscopic examination which reveals a thickened, smooth, pearl white outer surface of the ovary, serum (blood) elevated levels of androgens (male hormones), including androstenedione, testosterone and dehydroepiandrosterone sulphate, the ratio of Luteinising hormone and Follicle stimulating hormone being greater than 1:1 as on the day 3 of menstrual cycle, reduced levels of sex hormone binding globulin (SHBG), fasting biochemical and lipid profile, prolactin to rule out hyperprolactinemia, TSH to rule out hyperthyroidism¹².

Ayurvedic perspective of PCOS

Ayurveda describes PCOS to have an equal involvement of the *Dosha*, *Dhatu* and *Upadhatu*. It does not correlate the condition to a single disease or syndrome but the symptoms bears a resemblance to the terminologies defined as *Anartava*- Amenorrhoea, *Yonivyapad*- anatomical and physiological disorder of the reproductive system like *Arjaska*- oligomenorrhoea due to vitiation of *vata dosha*, *Lohitakshaya*- oligomenorrhoea due to vitiation of *vata-pitta dosha*, *Vandhya*-Infertility, *Pushpaghni*- *Revati*- Idiosyncratic anovulatory menstruation, *Abeejata*- anovulation, *Rajodushti* and *Ashtartava Dushti*- Menstrual flow disorder due to vitiation of *Dosha*, *Shandhi Yonivyapad*- Vitiation of *vata*

Table 1: Herbal Drugs screened for PCOS.

Name of Drug	Part/ extract used	Dosage	Animal Model	Parameters used
<i>Thuja occidentalis</i> ²⁰	Oil	500 mg/kg	Letrozole induced PCOS model	Serum gonadotropins, steroids, blood lipid, leptin and glucose. Histopathology of ovaries
<i>Tephrosia purpurea</i> ²¹	Seed powder	0.2 gm/kg	Letrozole induced PCOS model	Ovary weight, Hormonal assay Testosterone, Luteinizing Hormone, Follicle stimulating hormone, Estrogen Examination of Estrous cycle
<i>Camellia sinensis</i> ²²	Green tea	50, 100, 200 mg/kg	Estradiol valerate induced PCOS model	Hormonal assay, histological study of ovary
<i>Labisia pumila</i> ²³	Entire herb	50 mg/kg	Dihydrotestosterone induced PCOS model	Uterine weight, insulin sensitivity, estrogenic effects and lipid profile
<i>Nardostachys jatamansi</i> ²⁴	-	-	Estradiol valerate induced PCOS in rat	Antiandrogenic activity, estrous cyclicity, steroidal hormone levels
<i>Tribulus terrestris</i> ²⁴	-	-	Estradiol valerate induced PCOS in rat	Antiandrogenic activity, estrous cyclicity, steroidal hormone levels
<i>Symplocos racemosa</i> ²⁵	Aqueous extract of stem bark	250-1000 mg/kg	Letrozole induced PCOS rat model	Ovarian and uterine weight, hormonal assay, histology of ovaries
<i>Aloe barbadensis</i> ²⁶	Gel from leaves	10 mg/day	Letrozole induced PCOS rat model	Insulin sensitivity by OGTT, steroidogenic enzyme assay. Histological examination of ovaries
<i>Commiphora mukul</i> ²⁷	Gum-guggulu	40 mg/100 gm body weight	Letrozole induced PCOS rat model	Estrous cycle is monitored by daily examination of vaginal smear, body weight, histomorphometry of ovary, western blot analysis of IL-6 in ovarian tissue. Determination of C- protein, testosterone, superoxide dismutase, catalase, LPO, etc.
<i>Commiphora wightii</i> ²⁸	Ethanollic extract	100 mg in sesame oil	Dehydroepiandrosterone (DHEA) induced PCOS in rats	Measurement of body weight, ovary weight, liver weight, Serum analysis T3, T4, TSH, FSH, LH, Testosterone, estradiol, progesterone, histology of ovaries
<i>Saraca asoca</i> ²⁹	Bark extract	500 mg /kg body weight	Estrogenicity in adult female ovariectomised mice	Induction of estrous cycle, detrimination of size and weight of uterus
<i>Mentha piperita</i> ³⁰	Herbal tea	40 gm/l	Letrozole induced PCOS rat model	Hormonal analysis, histomorphology of ovary and uterus, immunohistochemical investigations in ovary.
<i>Pergularia daemia</i> ³¹	Fresh juice	-	Testosterone propionate induced PCOS model	Study of vaginal smears.
<i>Corylus avellana</i> ³²	Seed oil	2 ml/day	Letrozole induced PCOS rat model	Determination of serum gonadotropins, serum lipids, leptin, glucose levels, histology of ovary.
<i>Mimosa pudica</i> Linn. ³³	Aqueous extract	250,500 and 1000 mg/kg	Letrozole induced PCOS rat model	Determination of testosterone, estrogen, progesterone, cholesterol levels, weight of ovary and uterus was determined, histology of ovary was done.

due to genetic factors causes menstrual irregularities which may or may not be associated with anovulation¹³. *Vishama ahara* and *vihara* (improper diet and activities) which causes reduced digestion and metabolism leading

to immaturity of digestive extract and formation of immature rasa which vitiates menstrual blood and leads to increase in *meda dhatu* and *kapha* which causes

obstruction of body channels and *vata prakopa* causing obesity and amenorrhoea.

Vata and *Kapha doshas* as well as *vishama aahar* and *vihara* leads to reduced digestive fire and causes production of *Ama* (undigested food). This *ama* production causes improper enzymatic reactions leading to incomplete metabolism and hormonal imbalance. This hormonal imbalance causes hyperinsulinemia and hyperandrogenism ultimately leading to anovulation and amenorrhea/oligomenorrhoea and ovarian abnormalities like polycystic ovaries¹⁴.

Ayurveda does not speak in the terms of "hormones". It has its own unique language and terms. Hormones are considered as fire elements in the tissue. The action of hormones expresses the nature of pitta, the energy responsible for transformation. All stages of the female reproductive process are a result of the interplay of hormones. The fact behind the alteration of each stage is due to pitta replicated in the effect of the hormones on the various stages of the ovarian and menstrual cycles. If pitta predominates it manifests as hair loss, acne, painful menses, clots and heart problems.

Kapha's heavy cool qualities nourish the development of the tissues that form and support the reproductive system including the nurturing energy supporting growth of the follicle during the ovarian cycle. *Kapha* predominance

manifests as increased weight, subfertility, hirsutism, diabetic tendencies and coldness.

Vata is reliable for affecting the movement of the follicle during the ovarian cycle, the breakdown of the ovary wall for releasing the matured ovum, the movement of the fimbriae - directs the ovum into the fallopian tubes and the movements of the ovum near the uterus. The predominance of *vata* is manifested as painful menses, scanty or less menstrual blood and severe menstrual irregularity¹⁵.

Management of PCOS

Allopathic management of PCOS

The medical management of PCOS can be divided in to four components: three of them are acute issues which include control of irregular menses, treatment of hirsutism and management of infertility. One that is more chronic is the management of insulin resistance syndrome¹⁶.

To regulate menstrual cycle, combination of birth control pills containing both estrogens and progestin are used. The birth control pills decrease androgen production and give body a break from the effects of continuous estrogen, lowering the risk of endometrial cancer and correcting abnormal bleeding.

To treat the hirsutism Co-cyprinol and Eflornithine can be used. Eflornithine is a topical cream that has been

Table 2: Formulations screened for PCOS.

Name of formulation	Dosage	Animal Model/ Clinical Trail	Parameters used
Stanya Soadhana Gana ³⁴	10 gm bd in empty stomach with luke warm water	30 year old women with PCOD	-
Gynocare ³⁵	1 capsule per day	Women with PCOS	Changes in menstrual cycle, changes in ovarian volume with USG, ovulation etc.
Ugyanetone forte capsules ³⁶		Open labeled non comparative study for female patients aged between 12-55 and fulfilling ESHRE/ ASRM Rotterdam criteria for PCOD, 2003	Chronically irregular menstruation (CIM), Ovarian size, Obesity, Acne, Hairloss and Hirsutism. Hb %, TLC, DLC, ESR, USG.
Evecare syrup ³⁷	2-3 tablespoon twice daily	Double blind placebo controlled study in women aged above 18 years suffering from infertility due to PCOS presenting with symptoms such as hirsutism, acne and obesity	BMI, duration of infertility, acne, hirsutism, obesity, oligomenorrhea
Kanchnar guggulu ³⁸	750 mg bd	28 years aged women with PCOS	Pelvic pain, irregular menstruation cycle, USG of uterus and ovaries.
Ovaryl tablet ³⁹	Tablet twice a day	Open observational trail in women with PCOS	Regularity or irregularity of menstrual cycle, hirsutism, ovulation, no. of cysts, size of ovary, serum insulin level, BMI
Shilajatu rasayana-herbomineral formulation ⁴⁰	25.31 mg rasayana/ 200 gm body weight	Letrozole induced POCOS model	Determination of ovarian cycle, ovarian histomorphology, hormonal assay for plasma testosterone, progesterone and estrogen.
Mehani ⁴¹	50 mg/100 gm body weight	Testosterone propionate induced PCOS model	Determination of androgens.

Table 3: Active constituents screened for PCOS.

Name of Active constituent	Dosage	Animal Model/ Clinical trail	Parameters used
α Thujone ⁴²	-	Letrozole induced PCOS model	Serum gonadotropins, steroids, blood lipid, leptin and glucose. Histopathology of ovaries
Berberine ^{43,44,45}	1.5 gm/day	Women with PCOS undergoing IVF treatment Multicenter randomized double blind trail	Clinical, metabolic and endocrine effects of berberine Ovulation, effect on corpus luteum, implantation and obstetrics complications.
	500 mg three times a day	100 subjects with PCOS and insulin resistance	Antropometric measurements, serum concentration of TT, SHBG, insulin, glucose, TC, TG, HDTC, LDLC.
Curcumin ⁴⁶	100-200 mg/kg	Letrozole induced PCOS in female wistar rats	Hormonal assay, measurement of fasting blood glucose, glycosylated hemoglobin level, assessment of lipid profilr, antioxidant assay for superoxide dismutase, catalase, reduced glutathione, ovarian histomorphology.

approved by the US Food and Drug Administration for removal of unwanted facial hair in females. Eflornithine inhibits the enzyme ornithine decarboxylase in the skin, which inhibits cell division and synthetic functions, thus reducing the rate of hair growth. It should be used twice daily, at least 8 hours apart, on the affected areas of the face and chin¹⁷.

The management of infertility can be done using non-pharmacological and pharmacological approach. The first line non-pharmacological management of PCOS can be done by life style management which targets weight loss and prevention of weight gain and includes both reduced dietary energy intake and exercise. While the first line pharmacological treatment is clomiphene citrate which improves fertility. It is partially selective estrogen receptor modulator. Its antiestrogenic activity at the hypothalamus induces a change in gonadotropin releasing hormone (GnRH) pulse frequency leading to increased release of follicle stimulating hormone (FSH) from the pituitary gland.

The second line pharmacological management includes Metformin combined with clomiphene citrate to improve fertility outcome rather than persisting clomiphene citrate alone in women with PCOS who are resistant to clomiphene citrate.

Metformin if BMI < 30 Kg/m² can be used alone to improve ovulation rate and pregnancy rate in women with PCOS who are anovulatory and are infertile with no other infertility factors.

Gonadotropins can be used as second line pharmacological therapy in women with PCOS who have clomiphene citrate resistance or failure, and are anovulatory and infertile.

Aromatase inhibitors- Letrozole under caution can be offered as a pharmacological treatment for ovulation induction indicated for infertile anovulatory woman with

PCOS¹⁸. Laproscopic ovarian surgery and Bariatric surgery are also the options available.

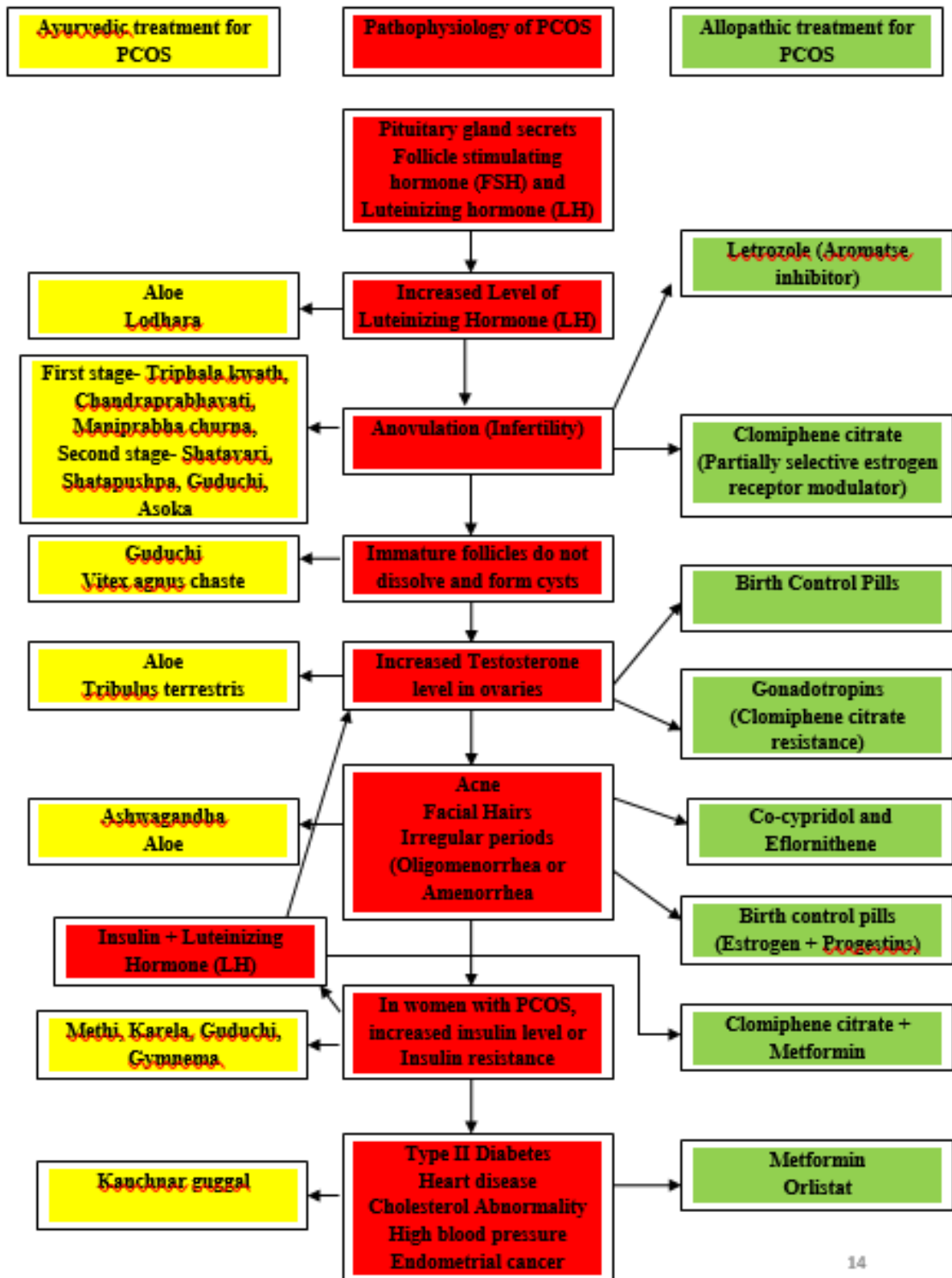
PCOS has a complex aetiopathogenesis involving mostly a combination of reproductive, metabolic and genetic elements. No single prognostic element has been able to strongly explain the pathophysiology and occurrence of PCOS. Furthermore, no single etiological gene or inheritance pattern has been found for occurrence of PCOS. Obvious enhancement in our understanding of the various progressions causing PCOS are required to simplify the relative importance of the multifactorial components in PCOS development and to focus clinical initiative in prevention, diagnosis and treatment.

Chemical based medications prescribed by allopathic medicines can be harmful to our body and have side effects including vaginal bleeding, blurred vision, nausea, ovarian hyper stimulation (ovarian enlargement), vomiting, flushing, breast tenderness, increased likelihood to multiple births, strokes, seizures, shortness of breath, etc.¹⁹.

These drugs chemically induce a women ovulatory cycle, instead of allowing it to be restored to its original healthy rhythm. The successful treatment of infertility is usually possible in the majority of patients with PCOS by using natural, non-invasive and non-chemical remedies. The herbal therapies are found to restore the normal rhythm of the menstrual cycle by balancing the hormones and also they are found to restore the imbalance of *doshas* occurring due to anovulation. Moreover there are herbs having phytoestrogens are available which can also be helpful in the treatment of disease. The plants maintaining the level of insulin and lipid lowering herbs can also be incorporated in the therapy for PCOS. The following tables provide the information about the drugs which were screened in animals as well as those who were clinically tested in the human volunteers. It also

Table 4: Clinical trials of Herbs performed for PCOS

Name of Drug	Part/ extract used	Dosage	Clinical trail	Parameters used
<i>Asparagus racemosus</i> (Shatavari) ⁴⁷	Powder of root	5 gm twice a day	25-40 aged subfertility women	Ultrasonography for changes in ovary, LH/FSH ratio
<i>Anethum graveolens</i> (Shatapushpa) ^{48,49,50}	Seed powder in the form of churna with Cow ghee Powder	5 gm thrice daily with 2.5 ml of cow ghee 5 gm twice a day	15-35 years women with oligomenorhoea 25-40 aged subfertility women	Hemoglobin %, weight of patient, amount of blood flow, subjective parameters like interval of menstruation, duration and pain throughout menstruation period Ultrasonography for changes in ovary, LH/FSH ratio
	Shatapushpa taila	60 ml for 7 days after cessation of menses	Patients fulfilling Rotterdam criteria for PCOD, 2003.	Hb %, TC, DC, ESR, Serum LH, FSH, USG for PCOD
<i>Tinospora cordifolia</i> (Guduchi) ⁵¹	Powder	5 gm twice a day	25-40 aged subfertility women	Ultrasonography for changes in ovary, LH/FSH ratio
<i>Mentha spicata</i> (Spearment) ⁵²	Herbal tea	Cup of tea twice a day	Female hirsute patients with PCOS	Levels of androgens
<i>Mentha spicata</i> (Spearment) ⁵³	Herbal tea	-	Randomized control trail	Hormonal assay, hirsutism
<i>Glycyrrhiza glabra</i> (Liquorice) ⁵⁴	-	3.5 gm/day	Clinical study in 32 women with PCOS	Blood pressure, BMI, Serum electrolytes, Plasma renin, Plasma aldosterone and cortisol, serum testosterone, urinary tetrahydrocortisol/cortisone ratio.
<i>Trigonella foenum graecum</i> (Fenugreek) ^{55,56}	Seed extract enriched with 40% furostanolic saponins (Furocyst)	2 capsules per day	Multicentric, open labeled, single arm, non randomized study in female (18-45 years) suffering from PCOS.	Effect on leutenising hormone (LH), Follicle stimulating hormone (FSH), change in ovary volume, effect on cyst, menstrual cycle and pregnancy, effect on hemoglobin level and total leucocyte count, plasma glucose, serum triglyceride, serum HDL cholesterol levels etc.
	Seed extarct	2 x 500 mg daily	Clinical study in women with POCS aged 20-35 years whose chief complaints were menstrual disturbances and infertility and/or clinical signs o hyperandrogenism	Clinical assessment including menstrual cycle frequency, height, weight, BMI and hirsutism. Concentration of prolactin, LH, FSH, TSH, free testosterone, DHEA-S (dehydroepiandrosterone sulfate, 17- α OHP(Hydroxy progesterone) , fasting glucose and insulin, SGPT, SGOT, etc.
<i>Cinnamomum cassia</i> ⁵⁷	Bark extract	1 gm per day	14 women with PCOS (mean BMI 28.8 \pm 1.3 kg/m ² , mean age 31.1 \pm 2.0 year) according to the 2003 Rotterdam consensus	Blood samples were assayed for glucose, insulin, FSH, LH, prolactin, TSH, testosterone, estradiol, and SHBG by chemoilluminescence.
<i>Cimicifuga racemosa</i> ⁵⁸	Extract	40 mg/ day	Women with PCOS	Blood tests included follicle-stimulating hormone (FSH), luteinizing hormone (LH) and progesterone. Transvaginal ultrasound was performed to document follicular size and growth as well as endometrial thickness. If a follicle achieved a size of 18 mm or greater, human chorionic gonadotropin (HCG) was given and then intercourse was recommended.



provides information about some herbal formulations which give combined effect in the treatment of PCOS.

CONCLUSION

Polycystic ovary syndrome is a complex disorder with multiple etiologies for which multiple treatment

approaches are required depending on the reason a patient seeks treatment. To treat PCOS one needs controlled and balanced diet and exercise for weight reduction along with medication and lifestyle management. Modern and traditional management together can have better results. Thus adopting a holistic treatment, good life style with

appropriate diet, *yoga*, *pranayamas* and stress free living can prove to be effective in the management of PCOS.

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