



Polycystic Ovary Syndrome (PCOS) - Hormonal Change In Reproductive Women

Sudhanshu Mishra* and Aishwarya Singh Rajput

Abstract

Polycystic Ovary Syndrome (PCOS) has become one of the major concern of not only gynecologists but also internists worldwide. It affects 6%-20% of reproductive-aged women. It is characterized by high androgen level and hyperinsulinemia. These disrupt folliculogenesis, causing menstrual abnormalities and infertility. There are many ways to reduce the effects of PCOS and feel better like weight loss, healthy diet and exercise. Its treatment involves metformin, clomiphene, letrozole, and finasteride. Some herbal drugs are also available, which may have relatively few adverse drug events. In this review, we summarize medication of PCOS, with special reference to herbal treatments.

Keywords

PCOS; Hirtism; Hormonal changes; Hyperinsulinemia; Metformin; Letrozole; *Paeonialactiflora*, *Origanummajorana*

Abbreviations

PCOS: Polycystic Ovary Syndrome; AMH: anti-Mullarin Hormone; LH: Luteinizing Hormone; FSH: Follicular Stimulating Hormone; PCOD: Polycystic Ovary Disease; GI: Gastrointestinal

Introduction

Polycystic Ovary Syndrome (PCOS) is a disorder that can be seen in nearly 6%-20% of reproductive females and is comprise of heterogeneous factors contributing to its physiology. It can be initially characterized by acne, hirsutism, and irregular menstrual cycle. As the factors and symptoms involved are distinct so the treatment of PCOS is also done by drugs and agents that belong to different categories like hormonal agents for hormonal symptoms and insulin-sensitizing agents for metabolic symptoms [1].

Management of PCOS involves, learning about the disorder, its regulation, adapting healthy lifestyle choices and proper diet. The intervention of drugs is required for the people with confirmed PCOS diagnosis. There are number of drugs that are available in the market for the treatment [2].

Along with various allopathic medicines, the emerging concept of sustainable ayurvedic era is also knocking the door with the cure of PCOS. In this review, we will try to understand the basics of altered physiology of PCOS and its treatment with natural remedies (Figure 1). The major reason behind us leaning forward and choosing

Ayurveda is the side effects caused by allopathic medicines which are chronic in many cases [3-8].

Diagnosis of PCOS

Suppose there is a patient who has been examined for PCOS and get a positive report for PCOS scan with no history of any symptoms that are associated with the disorder. So the question that will arise is that, will you label her as a patient of PCOS? The answer is you can't label someone as PCOS patient just by the scan, to label someone as PCOS there is a specific criteria to it [9].

Rotterdam Criteria

According to this criterion, you should have seen any two of these three symptoms in a person who has been suspected to have PCOS [10].

- Oligomenorrhea or Anovulation/Anovulatory Cycle.
- Hyperandrogenism: Symptoms may include Acne, Hirsutism and Elevated serum testosterone level.
- Polycystic ovaries (>12 peripheral follicle or increased ovarian volume >10 cm³).
- Exclusion of other etiologies.

Other criteria include

1. NIH 1990
 - Menstrual Irregularities
 - Hyperandrogenism
 - Exclusion of other etiologies
2. AES 2006
 - Menstrual Irregularities +/- USG Polycystic ovaries
 - Hyperandrogenism

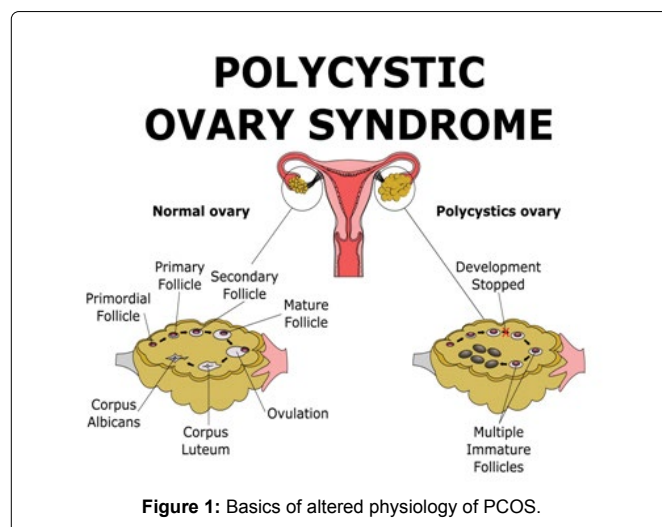


Figure 1: Basics of altered physiology of PCOS.

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Etiology of PCOS

Insulin resistance/Hyperinsulinemia

Insulin resistance is defined as a reduced glucose uptake response to a given amount of insulin. Approximately 70% of females are found to be having hyperinsulinemia which directly or indirectly contributes to [11]:

Hyperandrogenism: Hyperandrogenism is another major cause of PCOS. Hyperandrogenism contributes to acne, hirsutism, the emergence of masculine features [12].

Neuroendocrine Alterations: Neuroendocrine Alterations causes change in GnRH and Gn secretion along with several endocrine and metabolic modifiers like anti-mullarin hormone (AMH).

Genetic and Epigenetic Factors: Both genetic and epigenetic factors are responsible for excess hormonal imbalance that leads to the rest of the causes to occur as all of them are interconnected, yet the pinpoint explanation is relatively unclear and is vast enough to be compiled in this review article (Figure 2) [13].

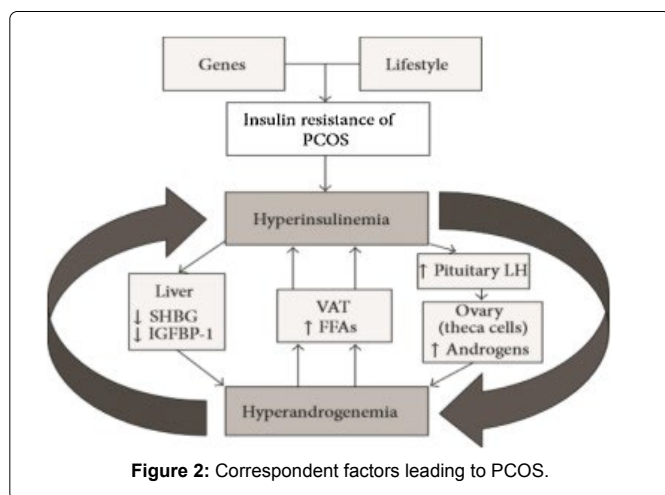


Figure 2: Correspondent factors leading to PCOS.

Pathophysiology of PCOS

There are number of metabolic and ovarian dysfunctions that are associated with PCOS, leading to its multiple symptoms [14]. The understanding of the basics of the pathophysiology of PCOS begins with the understanding of the following cases [15]:

Defective Aromatization in Ovary (Decrease Estradiol E2)

This defect particularly causes an increase in the concentration of less potent estrogen. The estrogen in ovarian cells comes from the androgen. According to the two cell two gonadotrophin theory, there are two cells one is granulosa cell and the another is theca cell, the theca cells are stimulated by Luteinizing Hormone (LH) and secret androgen which upon entering the granulosa cell gets converted into estrogen by the enzyme called aromatase and by a gonadotrophin Follicular Stimulating Hormone (FSH). When this conversion occurs in the ovary it releases estradiol which is a potent estrogen, but whenever this conversion occurs in the peripheral fat cells are releases estrone (E1) [16].

Theca Cell Hypertrophy (Increase Androgen)

Increase LH cause increase theca cells hypertrophy that is increase production of androgen, so due to hypertrophy androgen concentration increases.

Normal Peripheral Aromatization (Increase Estrone E1)

The excessive androgen gets converted into estrone in the peripheral adipose tissues. Along with these, the conversion and development of gonadotropin independent primary follicle to gonadotropin dependent antral and preovulatory follicle altered by many of the other factors (Figure 3), that are Anti-Mullerian Hormone and Insulin [17].

The overall effect is anovulation, here is how

The high LH/FSH ratio is the main reason here (Figure 4), explains as whenever the estrogen concentration is high it sends the positive feedback to LH, so it becomes a continuous circle. Along with that, it sends the negative feedback to FSH, due to which the follicles

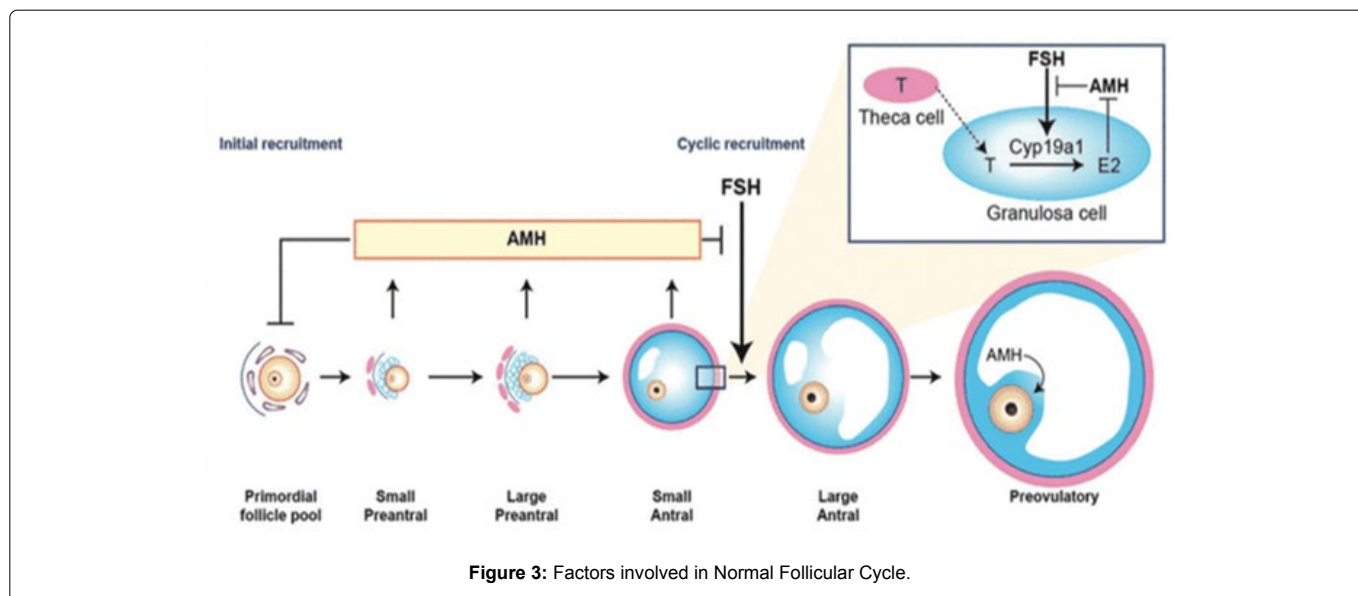


Figure 3: Factors involved in Normal Follicular Cycle.

become atretic, all the follicles make their way to Artesia (No development of primary follicle to Secondary or Antral follicle) that will lead to anovulation [18]. And as mentioned earlier there is an increase in insulin resistance, so the insulin level will increase along with Insulin Growth Factor 1 (IGF1), and this increased insulin stimulates LH to perform theca cells hypertrophy. Also, we can say that PCOS is a misnomer there are only follicles (which gets arrested) but no cysts. So basically it is a poly follicular disease and upon scan the peripheral arrangement of undeveloped follicles is visible just like a chain of pearls (Figures 5 and 6) [19-21].

Treatment of PCOS

In regard to treatment, it is advised to continue with effective diet/lifestyle changes which can lead to weight loss, anovulation improvement and indirectly reduce systolic arterial pressure. Several studies have shown that 30 minutes of moderate-intensity exercise will help people with PCOS lose weight, at least three days a week. Weight reduction with exercise also increases ovulation and hormone levels (Table 1) [22,23].

Natural Remedies Use To Treat PCOD

Paeonialactiflora: The biological name of white peony is *Paeonialactiflora* family Paeoniaceae. The plant extract used by both Chinese and Western herbalists for gynecological disorders, and is used by Western herbalists for PCOS, hyperprolactinemia, endometriosis, ovarian dysfunction, and excess androgen [24]. The plant also helps in fertilization by regulating the hormone progesterone, reduces the elevated androgen, and also modulate estrogen and prolactin. Due to the presence of paeoniflorin which is a pinanemonoterpene glycoside, which helps to regulate the enzyme aromatase. Aromatase enzyme

help in the regulation of estrogen and prolactin secretion, also important for conception [25].

Gymnemasylvestre: The plants *Gymnemasylvestre* (Asclepiadaceae) commonly known as „Gudmar” is a large woody,

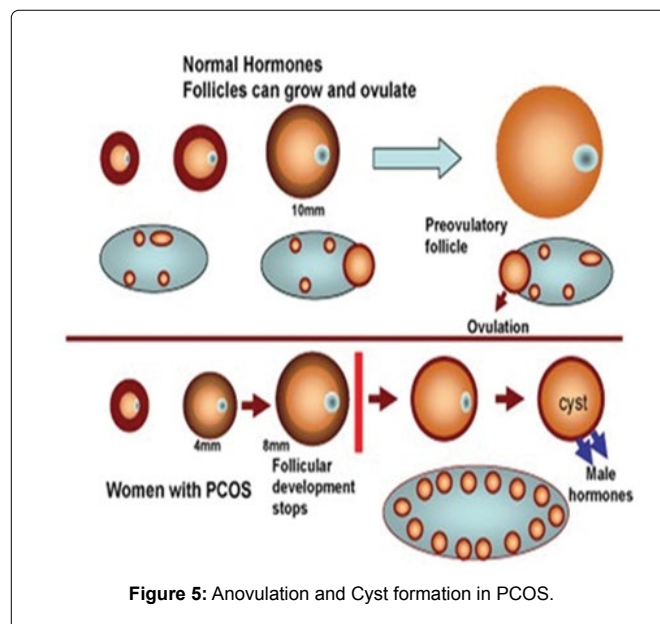


Figure 5: Anovulation and Cyst formation in PCOS.

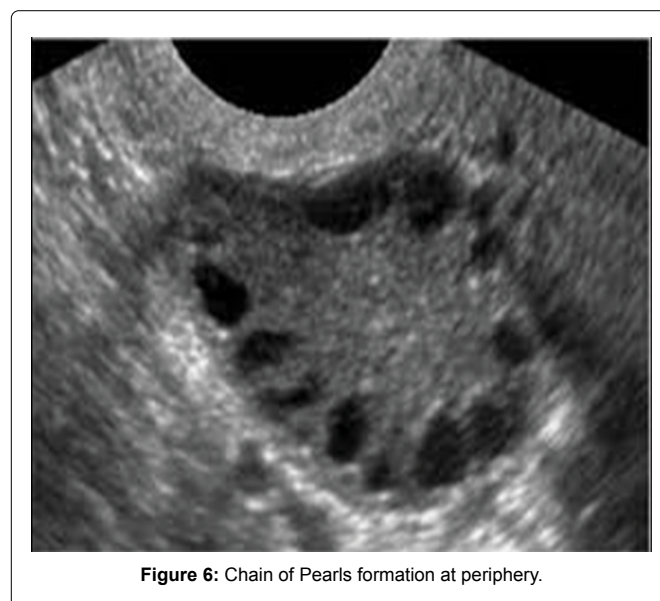


Figure 6: Chain of Pearls formation at periphery.

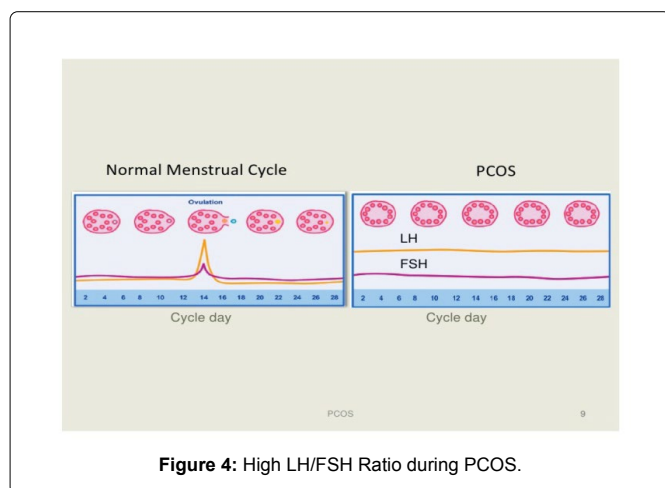


Figure 4: High LH/FSH Ratio during PCOS.

Table 1: Treatment of PCOS.

S. No.	Medication	Description	Adverse Effect
1	Metformin	Insulin-sensitizing and hypoglycemic agent.	The gastrointestinal issue, bloating, diarrhea, lactic acidosis
2	Clomiphene	Selective estrogen receptor modulator and ovulation induction agent	Abnormal vaginal/uterine bleeding, ovarian hyper-stimulation syndrome, breast tenderness or discomfort
3	Finasteride	Increased 5 α -reductase activity associated with idiopathic hirsutism and androgenic alopecia	Hirsutism, reduced libido, depression, gastrointestinal disorder
4	Letrozole	Inhibits estrogen production by repressing the enzyme aromatase	Unusual menstrual bleeding, breast pain, hot flashes, osteoporosis
5	Rosiglitazone	Decreases ovarian androgen production and improves insulin resistance and glucose tolerance	Hepatic failure, fluid retention, congestive heart failure
6	Eflornithine	Inhibit hair growth by blocking ornithine decarboxylase enzyme.	Dry & tingling skin, stinging, skin itching.

heavily branched, pubescent climber. Adolescent segments up to 600 m tall in the dry forest. The chemical constituents of *Gymnema* include gymnemic acid, gurmarin, calcium oxalate, glucose, stigmasterol, tartaric acid, betaine, and choline. *Gymnema* used for PCOS treatment, regardless of the regulation of insulin. Intervention and associated advantages of elimination of elevated PCOS related triglycerides. Besides this the plant is also used as anti-diabetic, hypolipidemic, anticancer, wound healing astringent, larvicidal etc [26].

Pergulariadaemia: *Pergulariadaemia* (Asclepiadaceae), widely recognized in Sanskrit as „Uttaravaruni,” is a perennial herb that grows widely along the roadsides. The analysis demonstrated the existence of flavonoids, tannins, alkaloids, glycosides, terpenoids, sugars, and steroids. Many researcher find the five bioactive elements, namely 2-hydroxy-methyl ester, 2-methoxy-4-vinylphenol, phthalic acid di-(1-hexen-5-yl) ester, l-(+)-ascorbic acid 2,6-dihexadecanoate and methyl (Z)-5,11,14,17-eicosatetraenoate. *Pergulariadaemia* has a strong effect on the normalization of menstrual disturbances and normalization of the estrous cycle. The maintenance of the estrous cycle thus decreases the production of follicular cysts and regains natural FSH and LH levels when *Pergulariadaemia* is supplemented [24].

Urticadioica: The stinging nettle, *Urticadioica* (UD) is the most important member of the Urticaceae family and has long been considered as a medicinal herb [27,28]. Nettle is an annual herbaceous, flowering herb. The plant contains various active chemical constituents like sterols, tannins, flavonoids and volatile oils. In the treatment of PCOD nettle help by increasing insulin production from beta cells, reduction of glycosylated albumin and fructosamine, activation of intestinal alpha-glucosidase and decrease of glucose absorption. Also this is also help to reducing hepatocrosis by reducing the inflammation and improve metabolic symptoms during PCOS [29].

Origanummajorana: *Origanummajorana* is also known as sweet marjoram belonging to the family of mint perennial plant Lamiaceae, cultivated as a culinary herb. With a combination of plant extracts, various tea formulations are used historically for maintaining hormonal equilibrium and controlling menstrual cycles. The Majorana tea extract decreased dehydroepiandrosterone (DHEA) substantially and increased insulin sensitivity and lowered the adrenal androgens amount. Other than PCOS the plant extract also help in the treatment of gastrointestinal and respiratory disease [30].

Conclusion

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders among females that may lead to infertility, menstrual disorders, obesity, acne, and hirsutism. Various conventional drugs are used to treat the PCOS but in some cases, it also may show side effects after prolonged use like GI disorder, breast pain, abnormal vaginal bleeding etc. To overcome these problems, herbal drugs are also used for the treatment of PCOS. Herbal medications play a positive role in PCOS diagnosis and have a gradual impact with less or no side effects. Herbal remedies improve the immunity of the body and can be assumed to control the menstrual cycle without altering hormone levels. The next aim of our study to evaluate the mechanism of action of various herbal phytoconstituents with the formulation of a nano drug delivery system.

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