ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 9| Issue: 4| April 2023|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2023: 8.224 || ISI Value: 1.188

AYURVEDIC APPROACH TOWARDS PCOS AND ITS MANAGEMENT THROUGH PANCHAKARMA

[1]Dr. Neeraja Priya. P, [2]Dr. Pradeep L Grampurohit (M.D Ayu), [3]Dr. Vasudev R (M.D Ayu), [4]Dr. Velagapudi Sai Anuhya,

[1]Final year PG Scholar, Department of Panchakarma, Kaher's Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi.
[2]Professor and HOD, Department of Panchakarma, Kaher's Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi.
[3]Assistant Professor, Department of Panchakarma, Yenapoya Ayurveda Medical College, Mangalore, Karnataka.
[4]Final year PG Scholar, Department of Panchakarma, Kaher's Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi.

ABSTRACT

Polycystic ovarian syndrome (PCOS) is an endocrine disorder, which constitutes the most prevalent cause of infertility in women, with increasing incidence day by day affecting one in seven women. It affects the ovaries due to imbalance of reproductive hormones causing ovarian cysts, causing problems like infertility, insulin resistance, and type 2 diabetes. Objective of the study is to understand PCOS through Ayurvedic Samhithas and it's clinical management. This paper gives an idea for Ayurvedic approach towards PCOS and its suitable Panchakarma treatment according to different presentation and duration. This paper deals with line of treatment that includes medohara, grantihara chikitsa, since it involves cyst formation and also vatanulomana for proper apana vayu regulation and in correcting menstrual irregularity. And in chronic conditions more than some years urdhwa, adhoghata shodhana, yoni prakshalana, garbhasaya shodhana followed by shamana chiktsa yields a good result.

KEYWORDS: ***PCOS, medahara chiktsa, granthihara chikitsa, vatanulomana, apana vayu, shodhana, shamana.***

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is an endocrine disorder, which constitutes the most prevalent cause of infertility in women, with increasing incidence day by day affecting one in seven women. "Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" according to (the WHO-ICMART glossary) and (Trends in Prevalence). [1,2] The Incidence of infertility is 8-12 % of couples during their reproductive lives. There are nearly 20 million infertile couples in India. [3] PCOS is one such metabolic disorder and a more severe form of PCOD can lead to anovulation where ovaries stop releasing eggs and ultimately affects fertility in women. It affects the ovaries due to an imbalance of reproductive hormones causing ovarian cysts, causing problems like infertility, insulin resistance, type 2 diabetes, heart disease, high blood pressure, and endometrial cancer in later stages.

CAUSES OF PCOS

The possible causes according to modern science are excess insulin production, excess androgen production, low-grade inflammation, and heredity**.** Excess insulin levels in the body might increase androgen production (a male hormone which is very less in females) that causes difficulty with ovulation. The ovaries produce abnormally excess androgen hormones that can lead to acne and hirsutism. As per a recent study, females with PCOS are having low-grade inflammation that causes increased levels of androgen production which can lead to blood vessels or heart problems. Also, certain women with PCOS show certain genetic correlations.

Nidana according to Ayurveda are *atimatra* (eating in excess), *akala* (untimely intake of food), *ahita bhojana* (incompatible foods) leading to *annavaha srotodushti*; *Guru* (heavy for digestion), *sheeta* (cold items), *atisnighdha ahara* (excessive unctuous food) followed by *samasana* (continuous sitting) causing *rasavaha sroto dushti; Chintyayaam cha ati chinthanat* (excessive thinking and worry), *Rithou anaharam* (not following seasonly foods), *virookshanam* (excessive food items that are drying consistency), *Vegavinigraham* (controlling natural urges), *mitya vihara* (unhealthy practises) such as *divaswapna* (day sleep), *ratri jagarana* (awakening at night) and *yonidosha* (disorders of uterus and menstruation).

PATHOPHYSIOLOGY

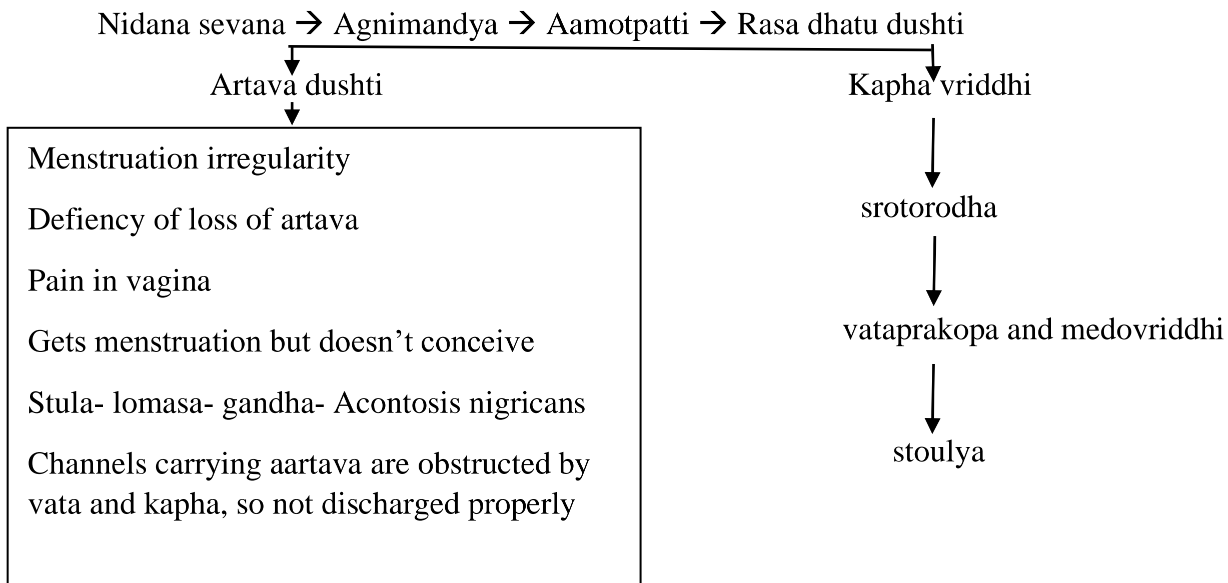
High levels of LH and low levels of FSH causes low chance of healthy follicles in the ovary and low 'Estrogen' from day 0 to day 5. Due to no estrogen secretion in the blood, there is no dominant follicle and thus no mature egg from day 6 to day 14. Follicle does not break due to low hormones, immature eggs can't travel to the fallopian tubes, uterus, and cervix that supposed to happen normally on day 15. There is no presence of egg in the uterine membrane so cervical lining becomes dry

and unhealthy from day 16 to day 28 during the luteal phase. The uterine lining is normal but no periods occur. There remains a pathology of abnormality of the HPO Axis, Hyper-insulinaemia arising from receptor dysfunction, Hyperandrogenemia (Adrenal/Ovarian), and Genetic factors.

Due to insulin resistance and its elevated level, the ovaries disturb that rises androgen level which leads to anovulation [4] Anovulation Disorders are divided into 3 groups by the World Health Organization. Group I Disorders: Hypothalamic failure leading to Hypogonadotropic hypogonadism which is responsible for 10% of anovulation cases. Examples: Pan hypopituitarism, autoimmune destruction, adenoma, or infections. Postpartum hemorrhage or head trauma can also cause hypothalamic failure that is irreversible or transient. Group II Disorders: HPO axis dysfunction which is responsible for 85% of anovulatory cases. The most common cause of female infertility is ovulatory dysfunction, in which a variety of hormonal factors interfere with the complex sequence of hormonal events required to trigger ovulation. Problems can occur at any point in this pathway (hypothalamus, pituitary, ovary) and can lead to failure to ovulate. The most common cause of chronic ovulatory dysfunction is Polycystic Ovarian Syndrome, or PCOS, which interferes with ovulation at multiple points. Examples: PCOS Immature Hypothalamic-pituitary-ovarian Axis. It is understood, hyperandrogenism is the result of the balance derangement between Androgen hormone levels and LH/FSH levels. The exact mechanism for how this is caused is not entirely understood, but research supports the thought that the peripheral conversion of estrogen into androgens by adipose tissue is one mechanism for elevating serum androgen levels and depleting estrogen. Hyperinsulinemia secondary to insulin resistance (IR) is thought to play a role in PCOS. During puberty, it is common for a degree of Insulin resistance to be seen resulting from Insulin-growth factor-1 (IGF-1). This process is considered largely normal if IR is confined to glucose metabolism. In women with PCOS, IR affects multi-systems including the liver resulting in decreased sex-hormone-binding globulin (SHBG) synthesis. Reduced SHBG levels contribute to the elevation of free androgens, further deranging the hormone balance.

Anovulation that presents with irregular menstruation in adolescent females as a result of an immature hypothalamic-pituitary-ovarian axis can be a common, expected finding. An anovulatory pattern of menstruation can be seen during the first year after the onset of menarche and persist till 18 years of age. The HPO axis is believed to have reached maturation. Persistent irregularities should be further evaluated for “non-functional” causes of inoculation.

Samprapti: [5]



In a survey of sleep patterns during the Steps to Swasthya program for PCOS, nearly 40% of them prefer to study for 4-5 hours at night as their home environment is quieter and more conducive for studying during those hours. The others may simply engage themselves in watching TV, playing video games or are busy chatting with friends during the wee hours of the night. [6] Chronic loss of sleep causes overeating, obesity, type 2 diabetes, and metabolic perturbations. [7]

TO DIAGNOSE PCOD OR PCOS

A pelvic examination must be performed to look for masses, anomalies, or any growth in the reproductive organs. Choose blood tests that will aid in understanding hormone levels, such as glucose tolerance tests and fasting lipid profiles (to evaluate levels of total cholesterol, HDL, triglycerides, and low-density lipoprotein, or LDL). To examine the uterine lining, the size of the ovaries, and ovarian cysts, imaging techniques such as ultrasound imaging can be used.

Apart from these following additional tests, may be performed to look for complications: routine blood pressure, glucose tolerance, cholesterol, and triglyceride levels checks; screening for depression and anxiety, obstructive sleep apnea (OSA) screening, Follicular analysis to check for ovulation, follicle size, and number on days 15 and 17. Finally, rule out prolactinemia and hyperlipidemia.

Apart from the above, additional tests to check for complications may include- Periodical monitoring of blood pressure, glucose tolerance, cholesterol, and triglyceride levels, Screening for anxiety and depression, Screening for obstructive sleep apnea (OSA), Follicular study on the 15th day, and 17th day to check for ovulation, follicular number, and size. At last rule out –hyperlipidemia and prolactinemia.

Elevated levels of Testosterone and androstenedione- by LH stimulation, Estrone, DHEA- S- Dehydroepiaandrosterone- androgen pathology, LH and FSH ratio =3:1, Hyperinsulinemia- frequent in obese PCOD, (fasting insulin to glucose ratio<4.5, abnormal glucose tolerance test) leads to increased ovarian production of androgens are noticed in PCOD and PCOS conditions.[8] Low levels of FH, Sex binding globulin- by hyperandrogenism and obesity, estradiol is also noticed.

AYURVEDIC UNDERSTANDING

Ayurveda attributes the disruption in healthy ovulation to Kapha and VataDosha imbalances. Akasha Mahabhuta, or Space, is represented in the female body by the hollow space of the reproductive cavity. During the ovarian cycle, Vata is responsible for follicular movement, the rupture of the ovarian wall releasing the matured ovum and the movement of fimbriae that guide the ovum through the fallopian tubes and into the uterus. Kapha provides nourishment for the uterus, aids follicular growth, and the development of (a fertilized) egg into a foetus. What we understand as hormones, represent the 'fire' elements of human tissue, and therefore, Pitta Dosha, which stands for transformation in the way that Vata stands for mobility, and Kapha for consolidation and 'structure.'Sheeta and picchila qualities of an imbalanced Kapha affect Dhatavagni and Jataragni, which in turn affects the metabolic rates of the tissues, or dhatus. The dhatus affected in PCOD are rasa dhatu, medha dhatu, and artava upa dhatu.

In ayurveda it can be understood in terms of Pusphaghni jataharani (unovulatory menstruation), Vandya, Anartava (primary amenorrhea), Artava kshaya, Nastartava, Alpartava (hypomenorrhea), Arajaska (diseased endometrium), Ksheenartava (oligomenorrhea), Granthi bhoota artava (clotted mensus), Asrighdara (menorrhagia), Vata pitta rajodushti (infection of the genital tract, amenorrhea), Raktaja rajodushti (infection of the genital tract, abnormal hemorrhage), Vataja rajodushti (chronic salpingo porosis, dysmenorrhea).

In the Revati Kalpaadhyaya of Kalpasthana in the Kashyapa Samhita, Acharya Kashyapa describes Pushpagni Jataharini, where Jataharini is a set of illnesses that affects women at various phases of life when they are of reproductive age, as well as their fetuses, newborns, and children.Some Jataharinis are described as having amenorrhea or irregular menstruation, having more similarities with features of PCOD/PCOS. Pushpagni Jataharini, according to Kashyapa, is a Sadhya Jataharini, a condition in which women experience unovulatory menstruation (Vritha Pushpam), Yathakalam Prapashyati (i.e., menstruation occurs at regular intervals), fatty cheeks covered in hair, Sthula Ganda (a sign of obesity), and Lomasha Ganda (hair present on the face/hyperandrogenism).[9]
PCOD/PCOS at times can also be related to a condition called Anartava where the doshas obstruct the arthava vaha strotas, thus artava is destroyed and is not released on a monthly basis. The passage of artava is obstructed by aggravated vata and kapha, which prevents the flow of menstrual blood.

Dosa wise presentations:
Patients with a kapha dominance may have weight gain, hirsutism, or diabetic tendencies. Patients with a Pitta dominance have hair loss, acne, uncomfortable menstruation, clots, and cardiac issues. Patients with a vata dominance have painful menstrual cycles, sparse or little menstrual blood, and severe menstrual irregularities. Due to kapha avarana to vata, spotting can be noticed.

CHIKITSA

The primary treatments for PCOS/PCOD, avoidance of causative factor (nidana parivarjana) followed by panchakarma procedures such as Vamana, Virechana, Nasya, and Vasti, which are included in the shodhana chikitsa. These purification therapies aid in the body's purification and detoxification. The accumulation of impurities and toxins in the body results in srothorodha (channel blockage), which causes menstruation irregularities and PCOS. Detoxifying the body is crucial, thus these treatment modalities play a vital role.

Shodhana chikitsa:
Shodhana includes sarvadehika shodhana, such as procedures like the vamana, virechana, vasti, etc., and sthanika shodhana comprises treatment that only affects a certain place, such as yoni prakshalana, yoni pichu, and uttara vasti.

1. Vasti (therapeutic enema):

It is well recognized to clear obstructions in the way and improve genital tract responsiveness, helpful for anovulatory cycles, uterine antagonism, and nidation problems. To increase physiological vigor and uterine antony, balya, a medicated ghee, and oil, can be utilized which is called as Matra vasti. Matra Basti after absorption reaches into the systemic circulation and the concept of CNS resembles Enteric Nervous System (ENS) the endogenous opioids in the ENS especially endorphins (βendorphin) are influenced which will affect GnRH release regularizing HPO axis regulating the ovarian cycle and ovulation. Endogenous opioids are a group of peptides, which play an important role in the ovarian cycle through the inhibitory effect on GnRH secretion. The Basti stimulates the ENS generates a stimulatory signal for CNS causes stimulation of the hypothalamus for GnRH and pituitary for FSH and LH with the help of neurotransmitters. Basti given through the rectum will stimulate parasympathetic nervine supply which helps for release of ovum from the follicle in the ovary. [10] Thus for apana vayu correction and regulating periods, maintaining endometrial thickness, increasing the

receptivity of genital tract, removing the obstruction in passage vasti plays a major role in PCOS and infertility.

2. Vamana (therapeutic emesis):

Vamanacan be administered in avarana (obstruction conditions), bahudosha avastha, kapha medo vriddhi, in obese pcod symptoms, since it causes negative feedback of adipose tissue and help in stimulation of estrogen production in bahudoshavasta.

3. Virechana (therapeutic purgation):

When ovarian follicles are immature and small, they are numerous in number, to expel the excess follicles and regulate stimulation and regulate stimulation in bahudoshavasta by negative feedback mechanism on adipose tissue and helps in boosting the body metabolism. Thus particularly affecting liver metabolism aids in weight loss. This controlled metabolism will help to maintain the regulation of the HOP Axis and control the conversion of estrogen to androgens. Additionally, it improves the quality of rutu, kshetra, ambu, and beeja by increasing Jataragni and Dhatwagni, Shroto shodhana, and anulomana, and regulating the production of Rasaadi Dhatus.

However, since a certain amount of pitta is necessary for the development and menstrual cycle, caution should be exercised to avoid pitta kshaya.

4. Nasya (medication through nasal route):

The use of Narayana Taila Nasya may stimulate olfactory nerves and limbic system, which stimulates hypothalamus leads to GnRH secreation in the pulsetile manner, leading to ovulation. Shatavari, tilataila also having phytoestrogenic or oestrogenic properties like narayana taila which regulates the activity of gonadotropin secretion. Pratimarsha nasya with adraka swarasa is also recommended. Nasya karma plays a major role to generate follicles, stimulate ovulation, rupture of the ovary, after removing avarana (obstruction). Nasya can be used from ovulation after the tenth day for effective outcomes, while it is not preferred prior to removal.

Sthanika shodhana:

Uttara vasti is widely practised for fertility issues, blockage in fallopian tubes, garbhashaya shuddhi, to regularize the imbalanced doshas. It helps in formation of garbha, vandyatva conditions, yoni roga, remove sanga of artava vaha srotas, rupture of ovary.

Mahanarayana taila Uttara vasti is the most commonly used in conditions of infertility. Hingutriguna taila can also be a choice as to remove tubal adhessions. Best time for administering uttara vasti is follicular phase before ovulation. But care should be taken in cervical erosion.

Other sthanika shodhana procedures like yoni prakshalanam can be beneficial in gynecological disorders, treat inflammation, erosions, infertility and provide strength to vaginal muscles. Triphala Kashaya is widely used for prakshalana. To alleviate the pathology, Udwartana chikitsa or any variants of medohara chikitsa may be employed.

The pathophysiology that leads to PCOS differs slightly in obese and lean persons, thus the treatment options also vary depending on the symptoms and type of PCOS.

Line of management in obese PCOD:

Deepana, pacana, and ushna veerya dravyas are advised to be used first. Since there is a kaphaavarana vata and medovriddhi, kaphaghna vatahara chikitsa, Stoulya chikitsa or medhohara, lekhaniya chikitsa, as well as pramehaghna chikitsa, are adopted more frequently in practice. It is possible to correct menstrual abnormalities by implementing vatanulomana, Shodhana, Shamana, and Shothahara, which also helps in reducing BMI. Finally, Rasayana, vrishya, and Daiva vyapasraya chikitsa can be adopted.

Line of management in lean PCOD:

In lean PCOD higher mental functions are more affected due to HPO axis affected

Deepana pacana is preferred at initial stages. It is also advisable to look for the factors like

1. Menstrual irregularity due to anovulation by ruling out by presence of fluid in POD bag. The stimulation for anovulation by means of shodhana or shamana should be adopted.
2. Endometrial thickness needs to be checked since a thin endometrium than 8mm can cause infertility. Since endometrial thickness below a range of 6 to 8mm showed negative predictive value for IVF outcomes.[11,12] Endometrial thickness can be enhanced by Vasti and shatavari grita, shatavari churna.
3. Follicular number, size and rupture should be examined. Check for the root cause, and if there is an undeveloped follicle, tikshana nasya can assist in the formation of follicles and trigger the HPO axis. Virechana therapy assists in regulating stimulation and removing follicles in a more effective manner if the number of follicles is high and they are smaller in size. Trivanga bhasma and shatavari prayoga are examples of Shamana yogas that can be administered to boost follicular size and encourage rupturing of the follicle. It is recommended to use Uttara Vasti and Nasya methods to stimulate follicular rupture by correcting the HPO axis. To enhance the functioning of the uterus, shamana chikitsa will be combined with sneha vasti. To increase metabolism, one can use the shamana-tikta pacana method. The treatment that relieves vata and pitta, and eliminates granthi.

Modern Technology and Ayurvedic Management

Modern management includes use of

1. Insulin sensitizers like metformin (Glucophage) to restore menstrual cycle and induce ovulation in PCOS by decreasing glucose production in liver.[13] It reduces insulin resistance, androgens, LH, atherogenic lipids. Metformin and Troglitazone are used as it is an antidiabetic agent found recently to have promising effects on testosterone levels.[14] In Ayurveda PCOS an arthava vyapad having medavriddhi due to kapha vriddhi and srotorodha is treated in lines of Prameha chikitsa and stoulyahara chiktsa that we correlate to obese PCOD.
2. Steroid hormones and anti-androgens (OCPs) for restoration of menstruation- does androgen suppression by stimulating sex-binding globulin that reduces bioavailable androgen. Permanent removal of hair by electrolysis or laser ablation after the suppression of hyperandrogenism is advised in modern science. Ayurveda focuses on regulating the menstrual cycle in accordance with normal physiology; it stimulates the efficient functioning of

three phases of the menstrual cycle beginning with the follicular phase, ovulation phase, and luteal phase. As mentioned earlier luteal phase is controlled by vata the proper functioning of vata is to be taken care for normal menstrual flow. So vatanulomana drugs are given that channelizes the vata towards the proper direction. Followed by other panchakarma treatments that promote estrogen production, cause negative feedback of adipose tissue, and regulate body metabolism.

3. Assisted fertility with clomiphene citrate or gonadotropins for ovarian stimulation. It is not advisable to give CC more than 12 cycles and sensitivity to these drugs should be taken care of. In Ayurveda to stimulate the proper functioning of the HPO axis and thereby induce ovulation, tikshna nasya places a major role. It triggers the blood supply to the brain and activates the hypothalamus by nerve endocrine neurovascular stimulation and through the lymphatic system.
4. Laparoscopic ovarian drilling/ follicular aspiration is a surgical method adopted when conservative methods fail to produce ovulation. It is a procedure where several punctures are made in polycystic ovaries. It is associated with risks of periovarian adhesions and the possibility of ovarian failure. Whereas in Ayurveda, virechana karma acts on the body's liver metabolism and helps to maintain HPO axis regulation that controls the conversion of estrogen to androgens, by negative feedback mechanism on adipose tissue that helps in boosting the body metabolism and to expel the excess immature follicles.
5. Intrauterine insemination is an initial step in unexplained infertility and male factor infertility. It is a procedure consisting of the placement of a trans-cervical catheter with 0.3-0.5 ml of washed, processed, and concentrated sperm into the intrauterine cavity. It is usually done after controlled ovarian hyperstimulation with gonadotropins or clomiphene, timed out about 34-36 hours following hCG injection. A minimum of 3 and a maximum of 6 IUI cycles are attempted.[15] The demand for herbal medicines has increased due to high economic costs and a high number of unfavorable effects associated with the use of allopathic medicines. Since ancient times, herbal plants remain a major source of medicinal preparations. [16] In Ayurveda shodhana procedures vamana, virechana, matravasti and uttara vasti can be adopted for total detoxification, removing aggrevated doshas and boosting body metabolism and cleansing and strengthening uterine channels and regulating the normal physiological functions of the body.

DISCUSSION

PCOS can be correlated to an artava vyapad according to dosha predominance and presentaions, it is a rasa pradoshaja vikara, caused mostly by Kapha and medaja vriddhi, where adharma (Faulty Life style), may be the main reason.

General line of treatment involves

1. Nidana parivarjana- involves identifying and avoiding the causative factor by examination, detail history taking and investigations.

2.Langhana and ama nirharana – before starting panchakarma done as a poorvakarma, since there is a avarodha pathology doing exercise(vyayama) and following diet and lifestyle is essential along with the treatment.does correction of agni-jataraghni and dhatwaghni.

3.vatanulomana and deepana- for proper channelising of vata in its direction.

4.Manasaupasadana- since HPO axis imbalance and higher mental functions are also affected it is essential.

5.Koshtashodhana and sroto shodhana- Vamana, Virechana, Uttara vasti, Nasya for proper Shuddhi and stimulation of menstruation.

6.Rasayana- vrishya- vaeejikarana drugs

Excess androgen levels in PCOS can cause symptoms including hirsutism, acne, or alopecia, which might vary from patient to patient. Addressing insulin resistance, addressing obesity, lowering cholesterol, and addressing hormonal imbalance is to be followed. And following seasonal Panchakarma for preventive purposes.

Where shodhana plays an important role in removing the avarana pathology and retaining normal physiology, also helps in metabolic correction leading to a healthy menstrual cycle. Shodhana followed by shamana and rasayana vajeekarana along with proper ahara (diet), vihara (lifestyle corrections and exercise) gives excellent results in PCOS/PCOD.

REFERENCES

1. *Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. Fertil. Steril. 2009; 92:1520–1524. doi: 10.1016/j.fertnstert.2009.09.009.*
2. *Direkvand-Moghadam A, Sayehmiri K, Delpisheh A, Direkvand-Moghadam A, "The global trend of infertility: an original review and meta-analysis", Int J Epidemiol Res. 2014; 1 (1): 35-43.*
3. *Puspha M Bhargav Chairman of the Drafting Committee for the Assisted Reproductive Technologies (Regulation) Bill, 2013*
4. *E.K.H. Diamanti-Kandarakis, R.S. Legro, "The role of genes and environment in the etiology of PCOS (Review)", Endocrine, Volume 30, Issue 1, August (2006), Pages 19-26.*
5. *Rajpoot Purnima, Pradhan Pradeep', Singh Balendra, Das Nalini, "Ayurvedic approaches to Polycystic Ovary Syndrome (PCOS): A Review", Int. J. Res. Ayurveda Pharm. 7(4), Jul-Aug 2016, DOI: 10.7897/2277-4343.074123.*
6. *Spiegel K, Leproult R, Van Cauter E, "Impact of sleep debt on metabolic and endocrine function, Lancet",1999 Oct 23;354(9188):1435-9, doi: 10.1016/S0140-6736(99)01376-8. PMID: 10543671.*
7. *Spiegel K, Knutson K, Leproult R, Tasali E, Van Cauter E, "Sleep loss: a novel risk factor for insulin resistance and Type 2 diabetes", J Appl Physiol (1985), 2005 Nov;99(5):2008-19, doi: 10.1152/japplphysiol.00660.2005. PMID: 16227462.*
8. *Dr. Hemalatha Kapoorchand, "A comprehensive treatise on striroga (gynacology)", Chaukhambha Visvabharati, Edition: 2018, pg 467, ISBN: 9789381301975.*

9. *Kashyapa, Kashyapa Samhita or Vriddhajivakiya Tantra, Edited By Prof. (Km.) P.V.Tewari, Kalpasthana, Chapter-6, Verse 33.2-34.1, Version-2, Varanasi, Chaukhambha Visvabharati; 2002, p- 357-358.*
10. *Donga KR, Donga SB, Dei LP, "Role of Nasya and Matra Basti with Narayana Taila on anovulatory factor", Ayu. 2013 Jan;34(1):81-5, doi: 10.4103/0974-8520.115453. PMID: 24049410; PMCID: PMC3764886.*
11. *Zhang T, Li Z, Ren X, Huang B, Zhu G, Yang W, Jin L. "Endometrial thickness as a predictor of the reproductive outcomes in fresh and frozen embryo transfer cycles: A retrospective cohort study of 1512 IVF cycles with morphologically good-quality blastocyst", Medicine (Baltimore), 2018 Jan;97(4):e9689, doi: 10.1097/MD.0000000000009689. PMID: 29369190; PMCID: PMC5794374.*
12. *Zhao J, Zhang Q, Wang Y, Li Y, "Endometrial pattern, thickness and growth in predicting pregnancy outcome following 3319 IVF cycle" Reprod Biomed Online, 2014 Sep;29(3):291-8, doi: 10.1016/j.rbmo.2014.05.011. Epub 2014 Jun 13. PMID: 25070912*
13. *Dr. Hemalatha Kapoorchand, "A comprehensive treatise on striroga (gynacology)", Neoplasms in gynecology, Chaukhambha Visvabharati, Edition: 2018, pg 468-469, ISBN: 9789381301975.*
14. *Dunaif A, Scott D, Finegood D, Quintana B, Whitcomb R, "The insulin-sensitizing agent troglitazone improves metabolic and reproductive abnormalities in the polycystic ovary syndrome", J Clin Endocrinol Metab, 1996 Sep;81(9):3299-306, doi: 10.1210/jcem.81.9.8784087, PMID: 8784087.*
15. *Dr. Hemalatha Kapoorchand, "A comprehensive treatise on striroga (gynacology)", female infertility, Chaukhambha Visvabharati, Edition: 2018, pg 377, ISBN: 9789381301975.*
16. *Arentz S, Abbott JA, Smith CA, Bensoussan A, "Herbal medicine for the management of polycystic ovary syndrome (PCOS) and associated oligo/amenorrhoea and hyperandrogenism; a review of the laboratory evidence for effects with corroborative clinical findings", BMC Complement Altern Med, 2014 Dec 18;14:511, doi: 10.1186/1472-6882-14-511. PMID: 25524718; PMCID: PMC4528347.*