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REVIEW ARTICLE

Review on Polycystic Ovary Syndrome

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ABSTRACT

This research deals with PCOD (polycystic ovary syndrome) is a complex and heterogeneous disorder. It is the most common endocrine disorder of reproductive women. Worldwide 8-20% suffering by polycystic ovary syndrome and main cause of PCOD is infertility. Person who sufferings from PCOD are often obesity and will have Hirsutism, excessive facial, body hairs and this may cause excessive thickening of endometrium and heavy, irregular bleeding, infrequent menstrual cycles. The increased androgen producing blocks subsequent ovulation and cause the existing follicle to undergo degeneration or atresia. Over many years, endometrial cancer may result due to the continuous stimulation of the endometrium by estrogen unopposed by progesterone which is only produced if ovulation occurs. The typical medical history is that of irregular menstrual cycles, which are unpredictable and can be diagnosis by vaginal ultra sound method, pelvic exam, physical exam, and also can be by testing blood. This diagnosis can be confirmed by vaginal ultrasound which shows both the ovaries are enlarged, the bright central stroma is increased and there are multiple cysts in the ovaries. Acne will be form while ovary production COD also associated with glucose and insulin dysfunction, resulting in obesity, risk of diabetes, hypertension, high blood pressure, and this research describes the causes, symptoms, diagnosis, treatment, control, and prevention of PCOD in detail.

Keywords: PCOD, atresia, heterogeneous disorder

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1. Introduction

PCOS is also known as the Stein-Leventhal syndrome. It is one of the most common endocrine pathologies among women of reproductive age. It is estimated that if it affects 3-5% of all women of polycystic ovarian syndrome can be easily diagnosed in some patients the typical medical history is that of irregular menstrual cycles, which are unpredictable and can be very heavy. Patients suffering from PCOS are often obese and may have hirsutism, (excessive facial and body hair). As a result of high androgen levels. Remember not all patients with PCOS will have all or any of these symptoms. PCOS was first described in 1935 by Stein and Leventhal. According to the Rotterdam criteria at least two of the following are sufficient for diagnosis of PCOS: oligo and/or an ovulation, clinical or biochemical signs of hyperandrogenism, exclusion of other androgen. PCOS patients have been reported to have an increased risk of metabolic syndrome, type 2 diabetes mellitus (DM), coronary heart disease (CHD), infertility, hypertension, miscarriage, preeclampsia, gestational diabetes and endometrial cancer. Dysmenorrhea is defined as less than eight periods in one year. Amenorrhea is defined as no period for more than three months. Polycystic ovary measuring 2-9mm in diameter. Clinical manifestation for hyperandrogenism is hirsutism, acne, and alopecia. Biochemical hyperandrogenism is evaluated by measuring serum androgen levels.

2. Sign and symptoms of PCOS

Many of the symptoms of PCOS are caused by high levels of androgens circulating in your body causing hyperandrogenism. Androgens are also called male hormones and the main one is testosterone. All women produce small amounts of androgens in tissues including the ovaries and the adrenal glands. High levels of androgens can prevent ovulation and affect the menstrual cycle. PCOS symptoms present in many different ways and some women will have only some or mild symptoms whereas others will have severe symptoms.

Periods: Although some women with PCOS have regular periods, high levels of androgens and also the hormone insulin can disrupt the monthly cycle of ovulation (when eggs are released) and menstruation. If you have PCOS, your periods may be irregular or stop all together. The average menstrual cycle is 28 days with one ovulation but anywhere between 21 and 35 days is considered as normal. An irregular period cycle is defined as either.

- Eight or less menstrual cycles per year,
- Menstrual cycles longer than 35 years.

As menstrual cycles lengthen, ovulation may stop entirely or only occur occasionally. Some women with PCOS also experience heavier or lighter bleeding during their menstrual cycle.

Excess hair (Hirsutism):

Hirsutism is an excess of hair on the face and body due to high levels of androgens stimulating the hair follicles. This excess hair is thicker and darker. The hair typically grows in areas where it is more usual for men to grow hair such as the sideburn region, chin, and upper lip, around nipples,

lower abdomen, chest and thighs. Up to 60 percent of women with PCOS have hirsutism. Women with PCOS from ethnic groups prone to darker body hair in areas of Sri Lanka, Indian, and Mediterranean populations often find they are more severely affected by hirsutism.

Hair loss (alopecia):

For some women with PCOS, the high level of androgens causes hair loss or thinning of scalp hair in a male-like pattern (receding frontal hair line and thinning on the top of the scalp).

Acne: If you have PCOS, the higher level of androgens can increase the size of the oil production glands on the skin, which can lead to increased acne. Acne is common in adolescence, but young women with PCOS tend to also have more severe acne.

Infertility:

High levels of androgens and high insulin levels can affect the menstrual cycle and prevent ovulation. Ovulation can stop completely or it can occur irregularly. This can make it more difficult for women with PCOS to conceive naturally and some women can also have a greater risk of miscarriage. However, this does not mean that all women with PCOS are infertile. As being overweight can increase fertility problems. It is important to exercise regularly to maintain a healthy weight and/or prevent weight gain.

Psychological effects:

Depression and anxiety are common symptoms of PCOS. Approximately 29 percent of women with PCOS have depression compared to around seven percent of women in the general population and even more women with PCOS will have anxiety-57 percent compared to 18 percent of women in population. With hirsutism, severe acne, weight changes and fertility problem may affect your body image, self-esteem, sexuality and femininity. This may add to depression and anxiety level. Problem with fertility can impact on your mood, particularly if fertility has been a concern for a long time.

Sleep apnoea: Women with PCOS, particularly when they are overweight or insulin resistant, can be at an increased risk of developing sleep-disordered breathing or sleep apnoea. Sleep apnoea occurs when the upper airway is obstructed during sleep. Excessive fatty tissue in the neck can partially block the airway leading to sleep loss, fatigue, tiredness and reduced quality of life.

Weight:

Being above a healthy weight worsens insulin resistance and the symptoms of PCOS. Some women with PCOS report that when they are a healthy weight, they don't have symptoms such as menstrual irregularity or excessive hair growth. These symptoms only appear once they gain weight. A healthy lifestyle of nutritious food and physical activity can assist in treating PCOS and in preventing it.

Family history:

Immediate female relatives (i.e. daughter or sisters) of women with PCOS have up to a 50 per cent chance of having PCOS. Type 2 diabetes is also common in families of those with PCOS. There is no clear genetic contributor to PCOS currently identified and the link is likely to be complex and involve multiple genes.

Insulin resistance and lifestyle:

One of the roles of insulin is to keep the levels of glucose in the blood from rising after eating. If you are insulin resistant, your body doesn't use the available insulin effectively to help keep the glucose levels stable.



Etiopathogenesis:

A defect of the ovarian cells (most likely theca cells) is the underlying cause of PCOS, resulting in excessive androgen synthesis and the clinical and biochemical symptoms of the disease.^{1,2} In the literature, reference is made to the participation of genetic factors, including ethnicity; there is a higher frequency of PCOS in Spanish, native American and Mexican women.⁴¹ In their original description of the syndrome, Stein and Leventhal emphasized that a high ratio of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) is one of the basic disorders. It has also been suggested that the underlying causes of PCOS include increased frequency of gonadotropin-releasing hormone (GnRH) pulses that stimulate the theca cells to produce androgen; decreased levels of FSH (and thus a defect in the late luteal and early follicular phases); insulin resistance via a post-receptor defect in the fat tissue and skeletal muscles (abnormal phosphorylation of tyrosine kinase); pancreatic beta-cell dysfunction; and obesity.^{1,3} It is often impossible to determine definitively what is a cause and what is an effect in the development of PCOS. In addition, it is generally recognized that obesity increases menstrual disorders and hyperandrogenism, while weight reduction reduces the clinical signs. Reduced insulin sensitivity is an important issue in both obese and underweight women with PCOS; it is estimated that 50–70% of women with the condition show insulin resistance of varying intensities.

Pathogenesis of PCOS:

Polycystic ovaries develop when the ovaries are stimulated to produce excessive amounts of male hormones (androgens), particularly testosterone, by either the release of excessive luteinizing hormone by the anterior pituitary gland, high levels of insulin in the blood (hyperinsulinaemia) in women whose ovaries are sensitive to this stimulus or reduced levels of sex-hormone binding globulin (SHBG) resulting in increased free androgens. The syndrome acquired its name due to the common sign on ultrasound examination of multiple ovarian cysts which represent immature follicles. The follicles have developed from primordial follicles but the development has stopped

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at an early stage due to the disturbed ovarian function. The follicles may be oriented along the ovarian periphery appearing as a 'string of pearls' on ultrasound examination. Patients with PCOS have higher gonadotropin releasing hormone (GnRH), which in turn results in an increase in LH/FSH ratio in females with PCOS. The majority of patients with PCOS have insulin resistance and/or obesity. Their elevated insulin levels contribute to or cause the abnormalities seen in the hypothalamic-pituitary-ovarian axis that lead to PCOS. Hyperinsulinemia increases GnRH pulse frequency, LH over FSH dominance, increased ovarian androgen production, decreased follicular maturation and decreased SHBG binding. All these factors contribute to the development of PCOS.

PCOS is characterized by a complex positive feedback of insulin resistance and hyperandrogenism. In most cases, it cannot be determined which of those two should be regarded to be the causative agent. Experimental treatment with either anti-androgens or insulin sensitizing agents improves both hyper-androgenism and insulin resistance. Adipose tissue possesses aromatase, an enzyme that converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese patients causes them to have both excess androgens (which are responsible for Hirsutism and virilization) and estrogens (which inhibit FSH via negative feedback). PCOS may be associated with chronic inflammation of the ovary which may induce conformational, endocrinal and metabolic changes which may predispose to PCOS. Several studies correlate the inflammatory mediators and oxidative stress with anovulation and other PCOS symptoms.

It was previously suggested that the excessive androgen production in PCOS could be caused by a decreased serum level of insulin-like growth factor binding protein-1 (IGFBP-1), in turn increasing the level of free IGF-1 which stimulates ovarian androgen production, but recent data concludes this mechanism to be unlikely. PCOS has also been associated with a specific fragile X mental retardation 1 (FMR1) sub-genotype. Many studies suggested that women who have heterozygous-normal/low FMR1 have polycystic-like symptoms of excessive follicle-activity and hyperactive ovarian function. Clinical manifestations of PCOS: The most common symptoms of PCOS include menstrual disorders such as oligomenorrhea or amenorrhea, infertility, high levels of masculinizing hormones manifested by acne and Hirsutism and metabolic syndrome which appears as a tendency towards central obesity and other symptoms associated with insulin resistance. Serum insulin, insulin resistance and homocysteine levels are higher in females with PCOS than in the normal females.

3. Management of PCOS

It is important that all the symptoms of PCOS are addressed and managed long term, to avoid associated health problems. PCOS is a long-term condition and long-term management is needed. Depending on the symptoms you experience, management of PCOS can include.

- I. Lifestyle modifications: Increasing your physical activity levels and eating a healthy diet can both help to manage PCOS.
- II. **Weight reduction:** Research has shown that even five to 10 % weight loss can provide significant health benefits.
- III. Medical treatment:

a. The oral contraceptive pill

b. Hormonal medication:

To block hormones such as testosterone (for example, spironolactone).

c. Infertility medications: If infertility is a problem, clomiphene citrate (sold as Clomid) or metformin may be taken orally to bring about ovulation (egg production). For infertility, clomiphene is first-line treatment. For metabolic/glycemic abnormalities and for improving menstrual irregularities, metformin is beneficial. Metformin is of limited or no benefit for managing Hirsutism, acne, or infertility. Overall, thiazolidinedione's have an unfavorable risk benefit ratio.

d. Psychological counseling.

e. Novel Therapy:

Pineol & inositol are currently in trials for the management option. The various reason for taking inositol based powder and other medications. Reduced Insulin Resistance, Reduced Testosterone, Less Unwanted Hair Growth, clearer skin, Increased Chances of Ovulation, Higher egg quality, Lower Chance of Gestational Diabetes, Healthier Liver, Reduced Appetite and Food Cravings, More Stable Mood, Help for Symptoms of Menopause, Less inflammation and panic, Improved nerve function, lipolysis and cost effective.

Diagnosis of PCOS:

Not all women with PCOS have polycystic ovaries, nor do all women with ovarian cysts have PCOS. Although pelvic ultrasound is a major diagnostic tool, it is not the only one. Many definitions are used for diagnosis of PCOS such as National Institutes of Health (NIH) criteria, Rotterdam criteria and Androgen Excess PCOS Society criteria.

NIH criteria:

In 1990, a workshop sponsored by the NIH suggested that a patient has PCOS if she has oligoovulation, signs of androgen excess (clinical or biochemical) and other entities are excluded that would cause polycystic ovaries.

Rotterdam criteria:

In 2003, a consensus workshop held in Rotterdam indicated PCOS to be present if any 2 out of 3 criteria are met including oligoovulation and/or anovulation, excess androgen activity and polycystic ovaries (By gynecologic ultrasound). The Rotterdam definition is wider, including many more patients, most notably patients without androgen excess. Critics say that findings obtained from the study of patients with androgen excess cannot necessarily be extrapolated to patients without androgen excess.

Androgen excess PCOS Society criteria:

In 2006, the Androgen Excess PCOS Society suggested a tightening of the diagnostic criteria to all of the following including excess androgen activity, oligoovulation /anovulation, polycystic ovaries and other entities are excluded that would cause excess androgen activity.

Causes of PCOS:

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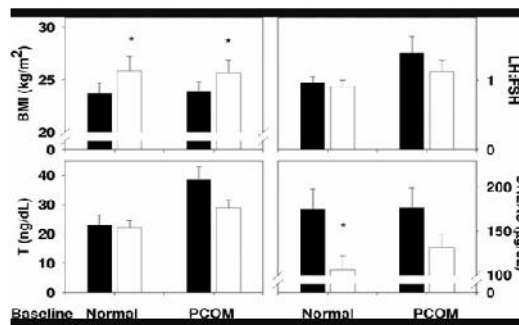
The cause of PCOS is not yet known but it often runs in families. If any of your relatives (mother, aunts, and sisters) are affected with PCOS, your risk of developing PCOS may be increased. The symptoms are related to abnormal hormone levels. Testosterone is a hormone that is produced in small amounts by the ovaries in all women. Women with PCOS have slightly higher than normal levels of testosterone and this is associated with many of the symptoms of the condition. Insulin is a hormone that controls the level of glucose (a type of sugar) in the blood. If you have PCOS, your body may not respond to insulin (this is known as insulin resistance), so the level of glucose is higher. To try to prevent the glucose levels becoming higher, your body produces even more insulin. High levels of insulin can lead to weight gain, irregular periods, fertility problems and higher levels of testosterone.

How many people are affected BY PCOS:

PCOS affects between 8% and 20% of reproductive age women worldwide. Because there is no universal definition of PCOS, the exact number of women in the United States with PCOS is unknown, but is thought to be approximately 5 million. Most women are diagnosed during their twenties or thirties, but PCOS may affect girls as young as 11 who haven't even had their first period.

Andrology and gynecology:

Gynecology and obstetrics; women's health care; fertility and sterility; gynecological endocrinology; human reproduction; international journal of gynecology and obstetrics; obstetrical and gynecological survey; European journal of obstetrical and gynecology and reproductive biology. BMI, LH to FSH ratio, testosterone, and DHEAS in women with normal ovarian morphology (normal) and PCOM at baseline (black bars) and follow-up visits (white bars). subjects were 29.7±6.7 years old (mean±SD) at baseline and 37.9±8.9 years old at follow-up visits. note that testosterone levels were available in only 19 subjects at baseline, and DHEAS in only 27 subjects at baseline. of note, testosterone levels were significantly different between women with normal ovarian morphology and PCOM at baseline (P<0.05). to convert to SI units, multiply testosterone by 0.035 and DHEAS by 0.02714. *, <0.05.



Treatment of Pcos:

Drug-Metformin

Effects: Restores regular bleeding and ovulation – reduces insulin resistance – improves arterial tension values – improves lipid profile – shows antioxidant activity – increases sex hormone binding globulin (SHBG) level – may

help reduce body weight– hypersensitivity – renal insufficiency – acute or chronic diseases that may cause tissue hypoxia, such as ardiac or respire tory insufficiency – lactation – hepatic damage – gastrointestinal – lactic acidosis

– dyspepsia, dia – metallic after

Oral Contraceptives

Restore regular periods – reduce symptoms of hyperon dragonish– reduce risk of endometrial Hyperplasma– past or current thromboembolic complications, cerebra- or cardiovascular disorders – obesity (BMI over 30 kg/m2) - pregnancy or suspected pregnancy – valvular heart disease – active hepatic disease – mammary or uterine cancer – reproductive tract bleeding of unknown etiology – estrogen-dependent tumors – arterial hypertension – nausea, vomiting – headache – dermal lesions (acne, Hirsutism) – body weight gain – turgid breasts – leg cramps – vaginal staining or bleeding.

Clomiphene – infertility treatment (ovulation induction)

Allergy to clomiphene – pregnancy – hepatic disease – primary hypopituitarism – disturbed thyroid or adrenal function – uterine bleeding of unknown etiology – hormone-dependent tumors – headache, vertigo – tiredness – disturbed vision – nausea, vomiting – vasomotor

Symptoms:

Facial flush, mastalgia, abdominal pain, – paramecia

Eflornithine – controls facial Hirsutism – hypersensitivity to Eflornithine or any adjuvant

Acne, chronic folliculitis barbae, alopecia, skin burning sensation, xerodermia, itching, erythema, skin formication,

GnRH analogs – inhibit androgens – hypersensitivity to any component of the product or other GnRH analogues:

Pregnancy or lactation, metabolic disorders of the skeletal system, menopausal symptoms, loss of bone mass, vaginal dryness, insomnia, mood swings, depression, and reduced libido.

Ketoconazole inhibits androgens – acute or chronic hepatic disease:

Pregnancy or lactation, nausea, alopecia, dry skin, uterine bleeding, headache.

Steroids – inhibit androgens: contraindicated in patients affected by symptoms or diseases which may be a side effect of their use, e.g. diabetes, hypertension, infections, adrenal suppression, infections, neuro-psychiatric abnormalities, carbohydrate metabolism disorders, diabetes, electrolyte imbalance, osteoporosis, changes in lipid and protein metabolism, Cushing's syndrome, gastric ulcer, muscle weakness, growth disorders in children, glaucoma, menstrual disorders

Spirolactone – inhibits androgens – hyperkalemia

Ttouch-sensitive nipples, mastalgia, menstrual disorders, Hirsutism, agranulocytosis headaches, sleepiness, ataxia, hypersensitivity, hypernatremia, hyperkalemia, primary adrenal insufficiency, severe renal and hepatic failure, acute renal failure.

Flutamide – inhibits androgens – hypersensitivity to any component of the product

Gynecomastia, mastalgia, galactorrhea, diarrhea, nausea, vomiting, increased appetite insomnia, fatigue, abnormal liver function

Finasteride – reduces alopecia – hypersensitivity to any component of the product: Pregnancy, planned pregnancy or breast feeding, decreased libido rash enlarged and tender treats hypersensitivity reactions.

Isotretinoin – severe acne (due to reduced AMH (levels), Hypersensitivity to isotretinoin, peanuts, soybeans or other ingredients, pregnancy or lactation, liver failure, hypervitaminosis A, increased blood lipid levels, use of tetracycline antibiotics, dry skin and eyes with conjunctivitis, dry mucous membranes, chelates contact lens intolerance, anemia, accelerated ESR,

Transaminase activity: Itching, skin inflammation, rash, skin, hypersensitivity, muscle and joint pain, abnormal lipid profile

Statins – pleiotropic effects

(anti-inflammatory, antioxidant, ant proliferative and lowers the level of lipids) inhibition of cell proliferation in the theca layer of the ovaries and reduction of steroid hormone synthesis active liver disease (ALT, AST exceeding 3 times the upper limit of normal values) pregnancy or lactation hypersensitivity muscle damage (myopathy) increase in liver enzymes in the serum, headache, blurred vision, insomnia, ailments of the digestive tract, rash, joint pain.

Fibroblast growth factors (FGFs)

Rregulation of carbohydrate and lipid metabolism, cardio protection, reduction of insulin resistance, Vitamin D3, improves insulin sensitivity, poisoning with or allergy to vitamin D, myocardial injury, gastrointestinal symptoms: nausea, vomiting, diarrhea, hypercalciuria, polyuria, renal damage, pain in the muscles or joints.

How is IVF used for treating patients with PCOS:

If 3 cycle of IUI have failed, then IVF is the best treatment option for patient with PCOD. However many IVF clinics have little experience in super ovulating the women, and they often mess up their super ovulation. Because these women grow so many eggs in response to the HMG injections used for super ovulation, and because doctors are very wrier about the risk of ovarian hyper stimulation syndrome, they often end up triggering egg collection with HCG when the eggs are immature. They congruently get lots of eggs, but since most of these are immature, fertilization rates and pregnancy rates are very poor .in our clinic, because we have extensive experience in dealing with women with PCOD, we do much better job at getting these women to grow many mature eggs.

Controlling PCOD through Yoga:



Is there a cure:

There is no cure for PCOS. Medical treatments aim to manage and reduce the symptoms or consequences of having PCOS. Medication alone has not been shown to be any better than healthy lifestyle changes (weight loss and exercise). Many women with PCOS successfully manage their symptoms and long-term health risks without medical intervention. They do this by eating a healthy diet, exercising regularly and maintaining healthy lifestyle.

4. Conclusion

PCOS is one of the most important endocrine disorders that affects females in the reproductive age and may lead to serious complications. Further studies are needed to determine the exact etiology of PCOS, methods of prevention and proper management.

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