A SHORT REVIEW ON POLYCYSTIC OVARY SYNDROME

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Polycystic ovary syndrome (PCOS) is said to be the most common endocrine disorder in women of reproductive age with a heterogeneous presentation, which includes hyperandrogenism and ovulatory dysfunction. PCOS usually has a peripubertal onset; the present review discusses the causes, complications, risk factors, diagnosis, and treatment.

Keywords: Polycystic ovary syndrome, Hyperandrogenism, Treatment.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder. As one of the leading causes of anovulatory infertility, it is believed that 5-10% of the reproductive-aged female population is living with PCOS. First recognized by Stein and Leventhal, in 1935, PCOS is characterized by the presence of polycystic ovaries, menstrual irregularities, and clinical/biochemical hyperandrogenism. The development of PCOS has been linked to hereditary and environmental factors including genetics, insulin resistance, obesity, and birth weight. The presence of PCOS is associated with an increased prevalence of adverse health conditions such as the metabolic syndrome, cardiovascular disease, and Type II diabetes mellitus. Insulin resistance is believed to play a key role in the development of PCOS and the development of related conditions. In the past few years, research has been done to better understand the mechanisms behind the development PCOS and the impact it has on the female body, particularly in relationship to insulin resistance.

DEFINITION

PCOS is a common endocrine system disorder among women of reproductive age. Women with PCOS may have enlarged ovaries that contain small collections of fluid called follicles located in ovaries and have abnormalities in the metabolism of androgens and estrogen (Fig. 1).

TYPES OF PCOS

Type 1 PCOS: (a) Insulin-resistant PCOS
(b) Non-insulin-resistant types of PCOS
Type 2 PCOS: Pill-induced PCOS or post-pill PCOS
Type 3 PCOS: Inflammatory PCOS
Type 4 PCOS: Hidden-cause PCOS

Fig. 1: Polycystic ovary syndrome
Type 4 PCOS

Hidden-cause PCOS

There is one simple thing that is blocking ovulation. Once that single thing is addressed, this type of PCOS resolves very quickly, usually within 3-4 months. Common hidden-causes of PCOS include:

- Soy, because it is anti-estrogen and can block ovulation in some women
- Thyroid disease because your ovaries need T3 thyroid hormone
- Vegetarian diet because it causes zinc deficiency, and ovaries need zinc
- Iodine deficiency because ovaries need iodine
- Artificial sweeteners because they impair insulin and leptin signaling
- Too little starch in diet because the hormonal system needs gentle carbs.

EPIDEMIOLOGY

The exact prevalence of PCOS is not known as the syndrome is not defined precisely. Globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26%. The estimated prevalence in women of reproductive age is 5-10%. Under the new criteria (Rotterdam, 2003), the prevalence among the general female population will raise up to 10%.

ETHIOLOGY/CAUSES

The exact cause of PCOS is unknown, but it is related to abnormal hormone levels.

Resistance to insulin

Insulin is a hormone produced by the pancreas to control the amount of sugar in the blood. It helps move glucose from the blood into cells, where it is broken down to produce energy. Insulin resistance means the body’s tissues are resistant to the effects of insulin. The body, therefore, has to produce extra insulin to compensate. High levels of insulin cause the ovaries to produce too much testosterone hormone, which interferes with the development of the follicles (the sacs in the ovaries where eggs develop) and prevents normal ovulation. Insulin resistance can also lead to weight gain, which can make PCOS symptoms worse because having excess fat causes the body to produce even more insulin.

Hormone imbalance

Many women with PCOS are found to have an imbalance in certain hormones including:

- Raised levels of testosterone: A hormone often thought of as a male hormone, although all women normally produce small amounts of it
- Raised levels of LH: A hormone that stimulates ovulation but may have an abnormal effect on the ovaries if levels are too high
- Low levels of sex hormone-binding globulin: A hormone that helps reduce the effect of testosterone
- Raised levels of prolactin (only in some women with PCOS): A hormone that stimulates the breast glands to produce milk in pregnancy.

The exact reason why these hormonal changes occur is not known. It’s been suggested that the problem may start in the ovary itself, in other glands that produce these hormones, or part of the brain that controls their production. The changes may also be caused by the resistance to insulin.

Genetics

The methylenetetrahydrofolate reductase (MTHFR) mutation test is used to detect two relatively common mutations in the MTHFR gene that are associated with elevated levels of homocysteine in the blood and also cause hypothyroidism.

RISK FACTORS

- Diabetes
- 4-7 times higher risk of heart attacks
- High blood pressure or hypertension
- High cholesterol
- High lipids
- Sleep apnea
- Risk of endometrial cancer
- Infertility
- Higher rate of miscarriages
- Higher risk of gestational diabetes
- Obesity which can also lead to low self-esteem and depression
- Liver disease.

PATHOPHYSIOLOGY (FIGS. 2 AND 3)

- Defective sex steroid synthesis and metabolism ovary and adrenal gland contribute to steroid production through a similar pathway
- Increased LH, adrenocorticotropic hormone, and insulin increase production of androgens.

Hyperandrogenism results

- Insulin resistance
  - Found in both lean and obese women
  - Post-binding defect in insulin-receptor signaling
  - Insulin sensitivity is selective and tissue dependent
  - Androgen production and/or beta cell defects may exacerbate insulin resistance
  - Strong predictor of sleep apnea for PCOS patients.

- Hyperinsulinemia results
  - Compensatory increase in insulin secretion secondary to peripheral insulin resistance.

SIGNS AND SYMPTOMS

The major features of PCOS include menstrual dysfunction, anovulation, and signs of hyperandrogenism 70% (hirsutism, acne, and male pattern alopecia), anovulation (70-75%) (usually chronic-presents as oligomenorrhea and/or amenorrhea), infertility, and recurrent miscarriages common).

Other signs and symptoms of PCOS may include the following:

- Obesity (50%)
- Abdominal obesity
- Waist to hip ratio >0.8
- Diabetes due to insulin resistance (75%)
- Obstructive sleep apnea
- Oligomenorrhea/amenorrhea
- Infertility/first-trimester miscarriage
- Acanthosis nigricans.

COMPLICATIONS

- Type 2 diabetes
- High blood pressure
- Cholesterol and lipid abnormalities such as elevated triglycerides or low high-density lipoprotein cholesterol, the “good” cholesterol
- Metabolic syndrome – a cluster of signs and symptoms that indicate a significantly increased risk of cardiovascular disease
- Nonalcoholic steatohepatitis – a severe liver inflammation caused by fat accumulation in the liver
- Infertility
- Sleep apnea
- Depression and anxiety
- Abnormal uterine bleeding
- Cancer of the uterine lining (endometrial cancer), caused by exposure to continuous high levels of estrogen
- Gestational diabetes or pregnancy-induced high blood pressure.

DIAGNOSIS

On examination, findings in women with PCOS may include the following:
Virilizing signs
Acanthosis nigricans
Hypertension
Enlarged ovaries: May or may not be present; evaluate for an ovarian mass.

Testing
Baseline screening laboratory studies for women suspected of having PCOS include the following:
- Thyroid function tests (e.g., thyroid-stimulating hormone, free thyroxine)
- Serum prolactin level
- Total and free testosterone levels
- Free androgen index
- Serum human chorionic gonadotropin level
- Cosyntropin stimulation test
- Serum 17-hydroxyprogesterone level
- Urinary free cortisol and creatinine levels
- Low-dose dexamethasone suppression test
- Serum insulin-like growth factor-1 level
- Other tests used in the evaluation of PCOS include the following:
  - Androstenedione level
  - Follicle stimulating hormone and LH levels
  - Gonadotropin-releasing hormone stimulation testing
  - Glucose level
  - Insulin level
  - Lipid panel.

Imaging tests
The following imaging studies may be used in the evaluation of PCOS (Fig. 4):
- Ovarian ultrasonography, preferably using transvaginal approach
- Pelvic computed tomography scan or magnetic resonance imaging to visualize the adrenals and ovaries.

TREATMENT
Pharmacological treatment

Surgery
Surgical management of PCOS is aimed mainly at restoring ovulation. Various laparoscopic methods include the following (Fig. 5):
- Electrocautery
- Laser drilling
- Multiple biopsy

Fig. 2: Pathophysiology of polycystic ovary disease
### Selected treatment options for polycystic ovary syndrome

<table>
<thead>
<tr>
<th>Drug class (example)</th>
<th>Purpose of therapy</th>
<th>Mechanism of action</th>
<th>Effective dose</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined oral contraceptive</td>
<td>Menstrual cyclicity; Hirsutism, acne</td>
<td>Suppresses LH (and FSH) and this ovarian androgen production; increase sex hormone-binding globulin, which decreases free testosterone</td>
<td>One tablet orally daily for 21 (or 24) days, then 7 days (or 4 days) pill-free interval</td>
<td>Breast tenderness, breakthrough bleeding, mood swings, libido changes</td>
</tr>
<tr>
<td>(estrogen and progesterone)</td>
<td></td>
<td>Suppression of LH and FSH levels, increase sex hormone-binding globulin, which decreases free testosterone</td>
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</tr>
<tr>
<td>Progestins (medroxyprogesterone)</td>
<td>Menstrual cyclicity</td>
<td>Creates withdrawal bleeding by transforming proliferative endometrium</td>
<td>5-10 mg orally daily for 10-14 days every 1-2 months</td>
<td>Breakthrough bleeding, spotting, mood swings</td>
</tr>
<tr>
<td>Bigunide (metformin)</td>
<td>Menstrual cyclicity, ovulation induction, hirsutism, acne, insulin lowering</td>
<td>Decreases hepatic glucose production, secondarily reducing insulin levels; may have direct effects on steroidogenesis</td>
<td>1500 mg orally daily in divided doses (up to 2550 mg/d)</td>
<td>Gastrointestinal problems, diarrhea, abdominal pain</td>
</tr>
<tr>
<td>Thiazolidinediones (pioglitazone)</td>
<td>Menstrual cyclicity, ovulation induction, hirsutism, acne, insulin lowering</td>
<td>Improves insulin sensitivity at target-tissue level (muscle, adipocyte); may have direct effects on steroidogenesis</td>
<td>Pioglitazone: 15-30 mg orally; maximum 45 mg orally</td>
<td>Edema, headache, fatigue, abdominal pain</td>
</tr>
<tr>
<td>Antiandrogen (spironolactone)</td>
<td>Hirsutism, acne</td>
<td>Inhibits androgen from binding to androgen receptor</td>
<td>50-100 mg orally twice daily</td>
<td>Hyperkalemia, polymenorrhea, headache, fatigue</td>
</tr>
<tr>
<td>Antiestrogen (clomiphene citrate)</td>
<td>Ovulation induction</td>
<td>Increase GnRH secretion, which induces rise in FSH and LH</td>
<td>50 mg orally for 5 days; may increase or 100 mg</td>
<td>Vasomotor symptoms, gastrointestinal problems</td>
</tr>
</tbody>
</table>

FSH: Follicle stimulating hormone, GnRH: Gonadotropin-releasing hormone, LH: Luteinizing hormone

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**Fig. 3**: Relationship of gonadotropin secretion, androgen production, and insulin in polycystic ovary disease
Non-pharmacological treatment

- Weight reduction
  - Decreasing body weight 5-10% significantly reduces hyperandrogenism, insulin resistance, and anovulation
  - Incidence of eating disorders higher in PCOS.
- Psychotherapy
- Hair removal
- Chemical bleaching and waxing
- Laser removal.

CONCLUSION

Although PCOS is one of the most common endocrine disorders in women of reproductive age, there is currently no cure for PCOS. For this reason, early diagnosis of the disease based on established criteria is important. With an early diagnosis, it is possible to manage the manifestations of PCOS. With proper management, obesity and insulin resistance can be controlled for as well as the associated diseases.

REFERENCES