A Mini-Review on Drug Treatment for Polycystic Ovary Syndrome

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Abstract

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in females of reproductive age. It is characterized by hyperandrogenism, polycystic ovaries, and chronic or acute anovulation along with insulin resistance, hyperinsulinemia, obesity, hypertension, and dyslipidemia as frequent metabolic traits (metabolic syndrome) that culminate in serious long-term consequences such as type 2 diabetes mellitus, endometrial hyperplasia, and coronary artery disease. It is one of the most common causes of anovulatory infertility. A complete understanding of the underlying pathophysiology of PCOS is still lacking. Because of the heterogeneity of this disorder, there are most likely multiple underlying pathophysiologic mechanisms. Pathogenesis of PCOS is explaining as alteration in gonadotropin-releasing hormone secretion results in increased luteinizing hormone (LH) secretion. An alteration in insulin secretion and insulin action results in hyperinsulinemia and insulin resistance. A defect in androgen synthesis that results in increased ovarian androgen production. Treatment of polycystic ovary syndrome is individualized based on the patient’s presentation and desire for pregnancy. For patients who are obese, weight loss is recommended. Drug treatment for PCOS patient is Clomiphene and letrozole are first-line medications for infertility. Metformin is the first-line treatment for metabolic manifestations, such as hyperglycemia. Hormonal contraceptives are first-line treatment for irregular menses and benzyl peroxide used for acne. Spironolactone, flutamide are first-line treatment for hirsutism.

Keywords: Polycystic Ovary Syndrome; Luteinizing Hormone; Hyperandrogenism; Anovulation

Abbreviations

PCOS: Polycystic Ovary Syndrome; LH: Luteinizing Hormone; FSH: Follicle Stimulating Hormone; PRL: Prolactin

Introduction

Polycystic Ovarian Syndrome, commonly known as PCOS, is an endocrine disorder seen in females of reproductive age. It is the most common endocrine disorder females involving cyst formation on ovaries which eventually affects the hormonal imbalance in their body. It has significant reproductive and non-reproductive consequences. PCOS mainly categorized by two types. They are Insulin-Resistant PCOS and Non-Insulin resistant PCOS. PCOS is also referred to as Type 1 PCOS which include weight gain, facial hair, Ovulatory interruptions, hair loss, and acne. Non-insulin resistance PCOS is referred to as Type 2 PCOS but don't represent with insulin resistance. The main cause of this type of disease is Vitamin-D deficiency, hormone-disrupting toxins, thyroid disease and hypertension disease. Major criteria involve anovulation; oligomenorrhoea, hyperandrogenaemia, severe hirsutism; insulin resistance and minor criteria involve ultrasound, elevated FSH, LH, obesity, hirsutism, and acne. PCOS means that the ovaries aren’t getting the right (hormonal) signals from pituitary gland. Without these signals, women won’t ovulate (make eggs) every month. The period may be irregular, or they may not have a period [1, 2].
**Epidemiology and pathophysiology**

PCOS is the most common endocrinopathy among reproductive aged females in the United States, affecting approximately 7% of female patients. PCOS is currently thought to emerge from a complex interaction between genetic and environmental traits [3]. The pathogenesis of PCOS has been linked to altered luteinizing hormone (LH) action, insulin resistance, and a possible predisposition to hyperandrogenism. One theory maintains that underlying insulin resistance exacerbates hyperandrogenism by suppressing synthesis of sex hormone-binding globulin and increasing adrenal and ovarian synthesis of androgens, thereby increasing androgen levels. These androgens then lead to irregular menses and physical manifestations of hyperandrogenism [4].

**Clinical presentation**

Patients may be asymptomatic or they may have multiple gynecologic, dermatologic, or metabolic manifestations problems. Females with PCOS most commonly present with signs of hyperandrogenism and oligomenorrhea, amenorrhea, or infertility, hirsutism, acne. Others sometimes prompted by an incidental finding of multiple ovarian cysts after ultrasonography [5,6].

**Diagnostic**

PCOS diagnosed from the patient’s past history and physical exam. Clinically PCOS patients focus on menstrual history, any weight fluctuations of the patient and their impact on PCOS symptoms, and findings (e.g. unwanted hair growth, acne and alopecia, Nigerian acanthosis, and skin tags). Patients asked about factors associated with more common PCOS comorbidity. Acc. The Endocrine Society recommends that clinicians use the 2003 Rotterdam criteria to diagnose PCOS patients, although recommendations vary across guidelines. According to the Rotterdam criteria, diagnosis requires at least two or more findings such as: hyperandrogenism, ovulatory dysfunction and polycystic ovaries [7]. PCOS diagnosis generally performed with careful history, PCOS diagnosis generally performed with careful history, physical examination, and basic laboratory testing, without the need for ultrasonography or other imaging. Hyperandrogenism can be diagnosed with excessive acne, androgenic alopecia or hirsutism (unwanted hair growth in a male pattern distribution) or chemically, by elevated serum levels of total, free testosterone or dehydroepiandrosterone sulphate [8]. Measurement of androgen concentrations is very useful when an androgen-secreting tumor is suspected. Ovulatory disturbance relates to oligomenorrhea (cycles longer than 35 days apart but less than six months apart) or amenorrhea (lack of menstruation for six to 12 months after a cyclic model has been developed). PCOS is described as an ovary comprising 12 or more follicles (or 25 or more follicles using new ultrasonography technology) Measuring 2 to 9 mm in diameter or an ovary with an ultrasonography quantity higher than 10 mL. Single ovary gathering both of these terms is adequate to diagnose polycystic ovaries. However, ovarian ultrasonography is useless or unless inspection is required out of the tumor or the person has fulfilled only one of the other PCOS Rotterdam requirements. PCOS complying with the above parameters can be discovered in 62% of patients with normal ovulation, with lowering incidence as patients aged increased [9,10]. Other laboratory tests also helpful to simulate PCOS but they are not necessary for detecting the PCOS. Including measurement of LH and follicle stimulating hormone (FSH) levels prolactin (PRL) to determine a serum ratio of LH/FSH. FSH level is more useful to detect ovarian failure. Patient account are preferences because selection of treatment may otherwise try to interfere with results that are also essential to importance Metabolic complications should be addressed in every patient via a blood pressure evaluation, a lipid panel, and a two-hour oral glucose tolerance test. Patients who are overweight should be evaluated for signs and symptoms of obstructive sleep apnea [11].

**Treatment**

Treatment should be individualized based on the patient’s desire for pregnancy Devices and medications used to treat PCOS manifestations and their associated adverse effects, a team approach involving main care and doctors may be useful in solving multiple syndrome manifestations. Goals for treatment (e.g. treating infertility; regulating menses for endometrial protection; controlling hyper androgenic features, including hirsutism and acne).
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Anovulation and infertility
Modification of lifestyle and weight loss reduces insulin resistance and can improve ovulation significantly. Modification of lifestyle is therefore 1st-line treatment for obese females. A calorie-restricted diet is advised for all obese PCOS patients. Weight loss on fertility and metabolic profile have been shown to have a metabolic impact. The Endocrine Society suggests the induction of ovulation by clomiphene or letrozole (Femara). Recent research suggest that letrozole is combined with increasing levels of live birth and ovulation similar to clomiphene in patients with PCOS patients. The effects of metformin on fertility is controversial although infertility was once thought to improve [12-14].

Menstrual irregularity
Patient not pregnancy, then Endocrine Society recommended the hormonal contraception (i.e. oral contraceptive, dermal patch, or vaginal rings) as the initial medication for treatment of irregular menses and hyperandrogenism manifesting (acne or hirsutism). Small studies have been shown the metformin help to regular menses in up to 50% to 70% of females with PCOS, but oral contraceptives and metformin have been shown the regulating menses and lowering androgen levels in the PCOS female patients. Prevention of severe anovulation (endometrial hyperplasia) can be performed whether through progesterone derivatives, progestin-containing oral contraceptives, or by levonorgestrel release (Mirena). Patient comfort and preference should also be taken into account when treating irregular [15,16].

Hirsutism
First-line treatment for mild hirsutism is oral contraceptives. Spironolactone used 100 mg daily, and flutamide, 250 mg twice daily, are safe for PCOS patient used, but the evidence for their effectiveness is minimal. Other therapy include efornithine (Vaniqa), electrolysis, or light-based therapies such as lasers and intense pulsed light. Any of these can be used as monotherapy in mild cases or as adjunctive therapy in more severe cases [17,18].

Acne
Acne is the more common problems with PCOS patients. Hormonal contraceptives are first-line medications for treating acne associated with PCOS and can be used with combination of oral contraceptives or topical acne therapy (e.g. retinoid, antibiotics, benzoyl peroxide) or as monotherapy. Antiandrogens, spironolactone being the most common, can be added as second-line medications [17,19].

Conclusion
It can be concluded that PCOS, an ill-defined symptom complex need its due attention. More than half of the females were overweight. The clinical features like menstrual disturbances, infertility, hirsutism, acne, and acanthosis nigricans were present in most of PCOS women irrespective of weight. Therapeutic timely intervention can halt this on-going process.

Bibliography

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