Review Article

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Management of PCOS in Adolescent Girls

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Abstract

PCOS is heterogenous condition with complex pathophysiology. It is one of the commonest endocrine metabolic disorder affecting 6-10% of women in their reproductive age. PCOS in adolescent girl is a complex condition with psychological, reproductive and metabolic manifestations. Early detection of PCOS in adolescence can prevent many early and late complications. No "Magic bullet" exists, combination of therapies may be required. The basic treatment of PCOS consist of calorie restriction, exercise, insulin sensitizing agents combined oral contraceptive pill, antiandrogens according to clinical presentation. Management of PCOS in adolescent girls pose challenge to clinician.

Keywords: Polycystic Ovarian Syndrome; Hyperandrogenism; Menstrual Irregularities; Metformin; Metabolic Syndrome.

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An enigma wrapped in riddle and surrounded by mystery.

'! Sir Winston Churchill

Polycystic Ovarian syndrome, an ill-defined heterogeneous condition with a complex pathophysiology is one of the commonest endocrine metabolic disorder affecting 6-10% of women in their reproductive age [1].

Adolescent and Pcos

There is a hypothesis,which suggests that intrauterine androgen exposure may result in adult PCOS in humans [2]. Girls with premature pubarche are at increased risk for developing features of PCOS after puberty [3].

Introduction

The incidence of polycystic ovary (PCO) in adolescence is increasing, and the most important causative factor is abnormal lifestyle. PCOS arises from increase in male hormone attack on the females, and abnormal lifestyle is responsible for this. The fact is that PCO is basically a misnomer. There is no presence of cyst in the ovaries [4].

The etiology of PCOS is uncertain and pathophysiology is not clear, a definite standard treatment protocol cannot be formulated for all women with PCOS specially for adolescent girls where infertility is not the primary problem [5].

Management plan for adolescent PCOS has to be individualized. Basic defect in all women with PCOS is hyperandrogenicity and in majority hyperinsulinemia [5].

The therapeutic approach to Polycystic ovary syndrome depends on:

- Patient symptoms
- Etiological considerations
- Motivation and objectives.

Treatment decisions depend on whether the patient is seeking immediate fertility. if it is not an immediate goal, as in adolescent girls, then treatment goals fall into two broad categories-

1. Symptom management of hirsutism, acne, mentrual disturbances
2. Assessment and amelioration of health risk

The ideal agent for the treatment of PCOS:

- Reduce androgen secretion
- Improve metabolism and dyslipidemia
- Produce regular ovulatory cycles.

Because no "magic bullet" exists, combination of therapies may be warranted at any given time as patient's conditions or objectives change [6]. Medical history and physical examination is essential. Estimation of FSH and LH is important [7,8].

The initial endocrinologic hyperandrogenic evaluation includes

- Total Serum Testosterone
- Free Testosterone
- SHBG
- DHEAS and
- Early morning Serum 17- hydroxyprogesterone level.

Clinical findings guide other hormone estimations:

- Thyrotropin
- Prolactin
- Insulin-like growth factor-I
- Serum cortisol [7,9].

Lipid profile and oral GTT are recommended in PCOS girls with obesity or family risk factors [10].

Oral Contraceptive Pills

Cyclic administration of estrogenprogestin in the form of combined COC pills is the first-line medical treatment of most adolescents [9,11].The OC pill significantly improves hirsutism and acne and protects against unopposed estrogenic stimulation of the endometrium, but these drugs have potential adverse effects on insulin resistance, vascular reactivity and coagulability.

Hence long term use of OC pill for adolescent PCOS patients is not indicated especially when insulin-lowering agents are available now [5]. Progestin monotherapy is the major alternative to COCs for the control of menstrual irregularity for those opposed to or with contraindications for COCs [10].

Antiandrogens

Combination of ethinyl estradiol and cyproterone acetate is effective in treating hyperandrogenicity, regularization of cycles. The drug specially suits adolescent PCOS, where hirsutism, acne and menstrual Irregularities and menstrual problems are the primary distressing symptoms at the same time, pregnancy is not desired [5].

The recommended dose is one tablet daily from day 1 to day 20- which can be repeatedly cyclically for a period of 6 months. While the patient is on medication, menstrual cycles will remain normal. Irregularity may start as soon as the drug is stopped. However, along with the drug treatment, weight reduction must be emphasized. If at least 7% weight reduction is achieved during drug therapy, it is expected that menstrual cycles will resume after withdrawal of drugs. In case of failure, or where there is clinical or biochemical evidence of gross hyperandrogenicity or hyperinsulinemia, addition of Metformin with combination of Ethinylestradiol and cyproterone acetate for a further period of 3 months is recommended [12].

Regarding progesterone, Cyproterone Acetate (CPA), Drosperinone, Levonorgestrel (LNG) and Desogestrel, all are of similar importance. The selection depends on clinical presentation [4].

In hirsutism and hypertrichosis, Cyproterone Acetate is a better choice. Though it is hepatotoxic in pharmacological doses, a minimal dose of 2 mg of CPA and 30-35 µg dose of Ethinyl Estradiol (EE) per day acts at all levels as antiandrogens [13].

Insulin Sensitizing Agents

When simple weight reduction is not enough for achieving the desired clinical results, as in case of severe obesity and evidences of hyperandrogenicity, Insulin sensitizing agents will be helpful.

The mechanism of action of insulin sensitizing agents in the treatment of Polycystic Ovary Syndrome is through two ways:

1. Improves hyperinsulinemia
2. Regulates reproductive endocrine axis [14].

Dose, Duration and Schedule of Metformin Treatment

The dose is 500 mg to 1500 milligram daily in divided doses. Average period of treatment is between 6 to 9 months. In adolescence PCOS, the drug can be

used alone or with a combination of ethinyl estradiol and cyproterone acetate.[14]

Troglitazone is useful in treating women with PCOS, improving insulin sensitivity and androgen excess. It has hepatotoxicity. Newer agents of this group viz Rosiglitazone and pioglitazone may be useful [13]. Spironolactone, typically used as mineralocorticoid also possesses moderate antiandrogenic effects when administered in large dose(100-200 mg daily) [15].

Cosmetic Treatment

Androgens used in PCOS will prevent further hair growth. But the hairs which have already grown will not be removed by taking androgens only. These unwanted hairs can only be treated by epilation, waxing or by electrolysis.

Management of Oligomenorrhea and Amenorrhea

For an adolescent girl, the first line of treatment even for onset of a regular menstruation is weight reduction with or without use of low dose oral contraceptive pills [18]. Estrogen combined with low dose anti androgens cyproterone acetate may be used with added advantage of getting the benefit of anti androgen drug. If this simple treatment does not help, insulin sensitizing agent (Metformin) alone or in combination with either low dose OC pills or ethinyl estradiol-cyproterone acetate combination may be helpful.

Numerous studies [14,16] have shown that lowering of insulin level only may increase ovulatory status thereby restoring cyclic menses. For lean PCOS, oligomenorrhea and amenorrhea are treated in the same lines as for obese PCOS, except weight reduction is not essential. Lean PCOS may also have insulin resistance and therefore, if they do not respond to oral contraception alone, insulin-sensitizing agents may have to be added.

Fertility

In adolescents desiring conception Clomiphene Citrate with or without combination with other agents is the treatment of choice for ovulation induction. The other agents include:-

- HMG
- Pulsatile GnRH-Q
- Neurotransmitter modulators
- Surgical wedge resection/ ovarian drilling [17].

Choice of Preparation

Hormones Defects	Choice of Drugs
Only Sr. Insulin	Metformin
Only Testosterone	Cyproterone Acetate+Ethinyl Estradiol
Testosterone, Dihydroepiandrosterone	Metformin+Dexamethasone+ Cyproterone Acetate+Ethinyl Estradiol+Dexamethasone
Thyroid stimulating hormone, Testosterone	L-Thyxn+Metformin
Thyroid stimulating hormone, Testosterone	L-Thyroxine
Prolactin, Dihydroepiandrosterone	Bromocriptine/Cabergoline+ Dexamethsone[12,18]

About 10% of PCOS girls develop signs and symptoms of PCOS due to stress, obesity and abnormal lifestyle. Healthy diet combined with exercise should be adviced, especially in overweight adolescent girls.

Although PCOS is traditionally considered a disorder afflicting women of reproductive age, in fact it affects the entire life of the woman, starting from intrauterine development and going through menopause and beyond into later life. The clinical manifestations of the symptoms can be observed starting around menarche; however, there are signs that may alert us to its earlier onset [19].

The parents of these girls are very much hesitant to use OCPs, due to common fear and social taboo. In these cases, low dose estrogen along with progesterone is used to maintain regular cycles [4].

The basic treatments of PCOS consists of calorie restriction, exercise, sometimes use of insulin sensitizing agents (Metformin) and occasionally anti-androgen (cyproterone acetate).

Ethinylestradiol + Cyproterone acetate has been advocated but a dual therapy using Ethnylestradiol+ Cyproterone Acetate with metformin is more effective than monotherapy. This is also applicable for 'lean' adolescents with insulin resistant PCOS.

Response to treatment is assessed by

1. Improvement of menstrual cyclicity and features of hyperandrogenisity (hirsutism, acne etc)
2. Improvement of biochemical parameters
   - Reduction of free serum testosterone.
   - normalisation of fasting glucose/ fasting insulin ratio (N-4.5)

Discussion

For the care of adolescent girls with PCOS, following recommendations may be made-

- Careful monitoring of body weight and extra counseling to maintain normal weight
- Aggressive treatment of obesity
- Annual screening of all patients for hypertension
- Baseline screening of obese patients with PCOD for fasting lipid levels,with treatment where indicated
- Screening of patients at risk for glucose intolerance (Obese, family history of diabetes, acanthosis nigricans) [20].

Pathogenesis of PCOS is based on interaction between genetic and certain environmental factors. Recognition of early signs of PCOS during or even before adolescence is vital. It is essential to diagnose PCOS and rule out other causes of androgen excess in young women. Early treatment will prevent long-term complication of syndrome.

The pathogenesis of PCOS is based on interactions between genetic and certain environmental factors. The recognition of the early signs of PCOS during or even before adolescence is of great importance.

Further research is necessary to explore the mechanisms by which PCOS disturbs the endocrine harmony of the young female body in that crucial, transitional period of a woman's life [19].

Conclusion

Polycystic ovarian syndrome is a complex condition with psychological, reproductive and metabolic manifestations. Early detection of PCO in adolescence can prevent many early and late complications. Management of PCOS in adolescent girls pose challenges to gynecologist. Cyclic administration of estrogen-progestin reduce menstrual irregularities and also the androgen level.Combination of oestradiol and cyproterone acetate is effective in treating androgen excess. Metformin alone or in combination with OCP's is helpful in management of adolescent PCOS.

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