

Adolescent Polycystic Ovary Syndrome: A Management Dilemma

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ABSTRACT

Since the description by Stein and Leventhal the enigma of polycystic ovarian syndrome keeps on unfolding day by day. Recently due to changes in lifestyle the incidence of adolescent PCOS is on rise and form the basis of metabolic and endocrinological diseases in later life. Hence, it is of utmost importance to recognize the pathology at earliest and treat it before the features become resistant.

Keywords: Adolescence, Polycystic ovarian syndrome rising incidence.

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INTRODUCTION

In 1935, Stein and Leventhal first described the association of polycystic ovaries, amenorrhea, hirsutism and obesity.¹ However, the key features necessary for diagnosis of polycystic ovarian syndrome (PCOS) were not detailed until 1990 at a conference convened by the National Institutes of Health (NIH). These key features included hyperandrogenism, menstrual dysfunction and exclusion of other causes of hyperandrogenism. Probable criteria included insulin resistance, perimenarchal onset, elevated ratio of luteinizing hormone (LH) to follicle stimulating hormone (FSH) ratio and polycystic ovaries identified using ultrasonography.

Recently, there has been an increase in the incidence of adolescent PCOS, which is more commonly observed in urban compared to those in rural areas. Puberty is the transitional period between childhood to adulthood. Significant metabolic and endocrinologic changes occur at puberty which form the background for this physical and physiological transformation. These changes are usually reversible but they may sometimes persist and behave abnormally to contribute to the genesis of pathophysiological changes observed in women effected with PCOS.

Causes of Increase in Adolescent PCOS

Persistence of physiological hyperinsulinemia may be the cause for adolescent PCOS, but environmental factors play significant role.

The probable causes of persistent hyperinsulinemia and increased incidence of urban adolescent PCOS may be:

- Changing lifestyle of modern society, i.e. overeating, eating junk food.
- Competition for upliftment of social and financial status which increases stress on growing children.

- Too much academic load at school level with lack of outdoor exercise.
- Genetic factors.

Pubertal Endocrine Changes Related to Adolescent PCOS

In normal puberty, initially there may be abnormal feedback mechanism between the tropic and target gland hormones which is usually restored to normal within a period of 6 months to 2 years. In adolescent girls predisposed to PCOS, abnormality of regulatory mechanism continues. The abnormality basically involves gonadotropic axis with simultaneous involvement of somatotrophic and adrenocorticotrophic hormones leading to hyperandrogenecity which is a constant association of PCOS.

Clinical Diagnosis of PCOS in Adolescence

The three main diagnostic criteria of PCOS namely, irregular delayed menstrual cycles, anovulation and presence of cysts in ovaries are not applicable as diagnostic criteria for PCOS in adolescents.¹

Anovulation or irregular menses is very common finding in normal adolescents. The distinction between pubertal physiological anovulation and anovulation due to PCOS may create a diagnostic dilemma.

Similarly, Rotterdam criteria of presence of ≥ 12 follicles of 2 to 9 mm size arranged peripherally in ovary and size of ovary 1.5 to 3 times normal is not applicable for diagnosis of adolescent PCOS as multicystic ovaries occur in normal girls during pubertal development.²

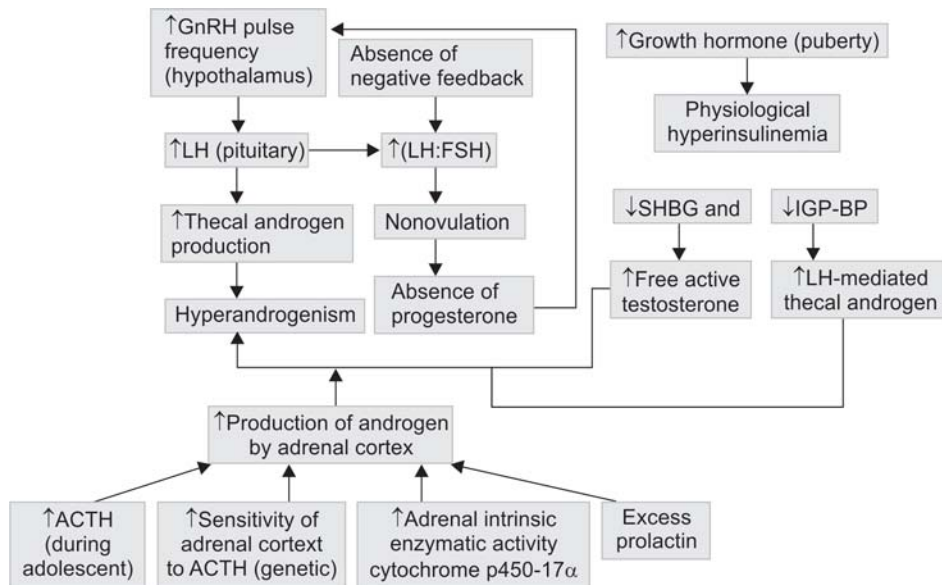
The clinical criteria by which PCOS in adolescent girls can be identified include:

- Obesity or increased BMI (>25)
- Features of hyperandrogenism (hirsutism, acne, acanthosis nigricans) and premature pubarche. Biochemical markers-fasting glucose: Fasting insulin ratio (less than 4.5), elevated free testosterone (>200 ng/dl), serum LH to FSH ratio on day 3 of menstrual cycle (>3) and elevated 17 hydroxy-progesterone are more confirmatory evidences of onset of PCOS in adolescence (Flow Chart 1).³

Patient should be investigated to rule out hyperprolactinemia, hypothyroidism and 21-hydroxylase deficiency (CAH) which can present with clinical features similar to those of PCOS.

Treatment Plan of Adolescent PCOS

The management plan for adolescent PCOS has to be individualized keeping in mind that the basic defect in all these individuals is hyperandrogenicity with majority of them having hyperinsulinemia also; infertility is not their primary problem.

Flow Chart 1: The hormonal interactions between HPO axis and ACTH axis in adolescence

Objectives of Treatment of Adolescent PCOS

- Treatment of oligomenorrhea/amenorrhea
- Management of hirsutism and acne
- Reducing the far reaching consequences of insulin resistance and glucose intolerance.

Protocol of Management

1. Weight reduction and lifestyle modification is most important and first-line of treatment for overweight patients with PCOS. They should be advised carbohydrate and fat restricted diet. Low glycemic index diet up to 85% will improve menstrual cycle irregularity. Even 7% weight reduction may lead to spontaneous resumption of menses by increasing SHBG levels and by lowering circulating free androgen and insulin levels. Therefore, moderate physical activity for 30 to 60 minutes per day should be goal of all patients with adolescent PCOS.
2. Oral contraceptive pills-estrogen component of oral contraceptive suppresses LH and thus reduces ovarian androgen production. It also enhances hepatic production of SHBG, thereby the level of free testosterone declines. Instead of estrogen-progesterone oral contraceptive pills, ethinyl estradiol can be used in combination with cyproterone acetate, drospirenone and desogestrel with the added advantage of getting the benefit of antiandrogen drugs.

Combination of ethinyl estradiol (0.35 µg) and cyproterone acetate (2 mg) is most scientific in treating hyperandrogenicity as well as maintaining the menstrual cycle. Cyproterone acetate competitively inhibits the binding of testosterone and 5 α-dihydrotestosterone to the androgen receptor. Various pharmaceutical preparations are available (Diane 35, Krimson 35) dose is 1 tablet daily from D1 to D21 which has to be repeated cyclically for a period of 6 months.

Combination of ethinyl estradiol (30 µg) with drospirenone (3 mg) available as Yasmin, Rasmin, Tarana, Dronis have also been used.

Ethinyl estradiol (30 µg) in combination with desogestrel (20 µg) can also be used.

3. *Insulin sensitizing drugs:* If this simple treatment with weight reduction and oral contraceptive pills fails or there is clinical or biochemical evidence of gross hyperinsulinemia or hyperandrogenicity, addition of insulin sensitizing drug like metformin for a further period of 3 months is recommended.^{4,5}

Mechanism of Action of Insulin Sensitizing Drugs

Metformin is given in dosage of 500 to 1,500 mg daily in divided doses for 6 to 9 months.

Hyponidd (β chiro-inositol) is also being used as an insulin sensitizing agent in insulin resistant PCOS (Flow Chart 2). Other drugs used are spironolactone and finasteride (dose, 1-5 mg/day).

4. *Cosmetic treatment:* Antiandrogens used in treatment of PCOS prevent further hair growth but cosmetic treatment in form of epilation, waxing, electrolysis and laser treatment is required to remove the hair which have already grown.

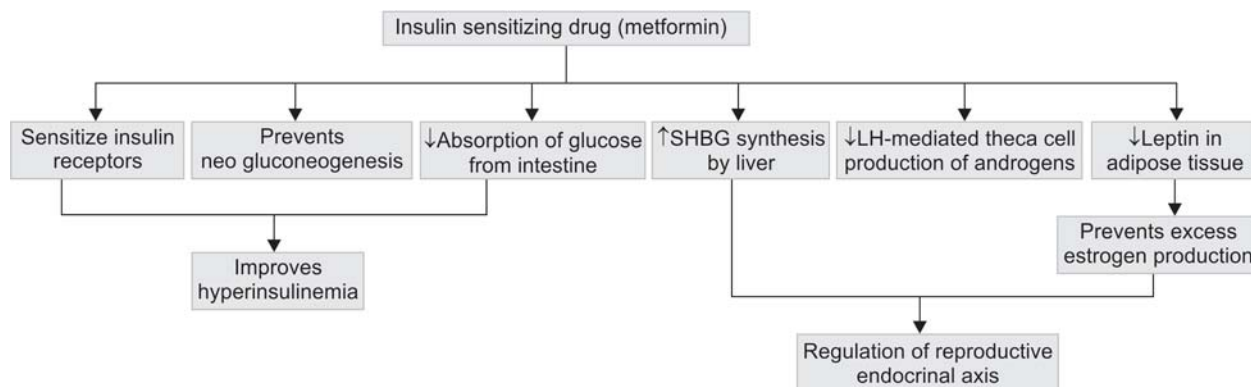
Oral antibiotics like erythromycin and isotretinoin ointment may be used for treatment of acne.

Management of a lean adolescent PCOS is the same as obese PCOS, except weight reduction is not essential. Lean PCOS may also have insulin resistance, and therefore, if they do not respond to oral contraceptives alone, insulin sensitizing agents may have to be added.

Response to treatment is assessed by resumption of menstrual cyclicity, reduction in features of hyperandrogenicity and improvement of biochemical parameters like reduction of free serum testosterone and normalization of fasting glucose: insulin ratio.

CONCLUSION

PCOS, if identified at young adolescent age, the biochemical features which form the basis of clinical consequences at adult

Flow Chart 2: Postulated role of insulin sensitizing agents in women with PCOS

age are more easily treatable and reversible. Relatively these biochemical features become more resistant and less amenable to treatment when women with PCOS are diagnosed in the reproductive age group.

Offering psychosocial support can be one of the most important aspects of managing this disease. This begins by building positive, supportive relationships with adolescent diagnosed PCOS. Such relationship will allow the adolescents to express their feelings and concerns regarding having a chronic disease whose signs and symptoms can greatly impact one's body image and self-esteem.

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