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POLYCYSTIC OVARIAN SYNDROME IN ADOLOSCENTS

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INTRODUCTION

Polycystic ovarian syndrome encompasses a spectrum of variably associated clinical features of hyperandrogenism and anovulation. Polycystic ovarian syndrome is most common cause of infertility affecting 5- 21% of women.[1] It has a lifelong implications with increased risk of metabolic syndrome, type 2 Diabetes Mellitus, cardiovascular disease and endometrial carcinoma. It frequently manifests during adolescent as high as 30% females.[2]

Over the past 25 years, internationally accepted diagnostic criteria have been developed for adults based on unexplained hyperandrogenism, anovulation and a polycystic ovary, which are all encompassed by Rotterdam consensus criteria.[3-4] These diverse criteria have been problematic when applied to adolescents. This is due to overlap between normal pubertal development and characteristic features of PCOS and this may confound an accurate diagnosis of PCOS among adolescent girls. The purpose of this article is to use these consensus criteria for the early diagnosis and treatment of PCOS in adolescents.

Diagnosis in Adoloscents

Menstrual irregularity can normally occur within two years of menarche. Moreover, no androgen ranges are specific to the adolescent group. Other disorders associated with irregular menses or hyperandrogenism also need to be excluded in this group. Manifestations of PCOS are cutaneous symptoms like hirsutism, treatment-resistant acne, male pattern alopecia, acanthosis nigricans and anovulatory symptoms like amenorrhea, oligomenorrhea.

International consensus diagnostic criteria for polycystic ovary syndrome in adolescents are- Otherwise unexplained combination of: 1. Abnormal uterine bleeding pattern a. Abnormal for age or gynecologic age b. Persistent symptoms for one to two years 2**.** Evidence of hyperandrogenism a. Persistent testosterone elevation above adult norms in a reliable reference laboratory b. Moderate-severe hirsutism is clinical evidence of hyperandrogenism c. Moderate-severe inflammatory acne vulgaris is an indication to test for hyperandrogenemia.[5]

Evidence of Menstrual Irregularity

Physiologic adolescent anovulation is a well-known phenomenon.[5] However, there is a widespread misconception that any degree of amenorrhea or menstrual irregularity is acceptable. Rather, normal adolescent menstrual cycle differs only slightly from that of reproductive-age adults: cycles shorter than 19 days or longer than 90 days are abnormal at any stage. Oligomennorhoea is considered when postmenarcheal year one: Average cycle length >90 days (fewer than four periods per year) or Postmenarcheal year two: Average cycle length >60 days (fewer than six periods per year) or Postmenarcheal years three to five: Average cycle length >45 days (fewer than eight periods per year).[6,7] In the absence of clinical evidence of any endocrine disorder, persistent abnormal menstrual bleeding for 1 year carries an approximately 25% risk of the ongoing cases will have PCOS.

Evidence of Clinical Hyperandrogenism

An adult level of hirsutism ordinarily is reached by two years after menarche.[8,9] It is documented using the Ferriman-Gallwey score [Moderate /Severe >15][10] Other specific history of shaving, depilation, or drugs causing hirsutism should be taken such as anabolic-androgenic steroids, valproic acid etc. Acne rather than hirsutism, may be the only pilosebaceous manifestation of hyperandrogenism.[11] Comedonal acne is common in adolescent girls, but inflammatory acne that is moderate or severe (ie,.10 facial lesions) is uncommon during the perimenarcheal years. Girls with acne that is persistent and poorly responsive to topical therapy should be assessed for hyperandrogenemia before instituting systemic medical treatments.[12,13]

Diagnosis

Clinical or laboratory demonstration of hyperandrogenemia, ultrasonography of the ovaries and adrenal glands and laboratory tests to rule out other common non-PCOS causes of hyperandrogenemia is required. Initial, Urine pregnancy test /B-hCG in sexually active adolescents with menstrual irregularities

should be done. FSH, LH tests: high LH slightly low FSH indicates PCOS. TSH and prolactin to rule out these disorders causing menstrual irregularities. Total and free testosterone is also measured. The serum free testosterone concentration is approximately 50 percent more sensitive than the total testosterone concentration. Normal serum total testosterone in adult women is 40 to 60 ng/dL. In PCOS; these range from 29 to 150 ng/dL while values >150ng/dl suggest virilizing ovarian or adrenal neoplasm.[14]

Ultrasound demonstration of polycystic ovaries
Adult PCOM criteria are especially problematic when applied to adolescents.An accurate antral follicle count cannot be defined by the abdominal ultrasonographic approach in virginal adolescents.[15] On the other, 10%–48% of adolescents who do not have PCOS may have polycystic-appearing ovaries. These challenges to ultrasound evaluation make this diagnostic criterion much less useful in the adolescents.

Evaluation of Non Pcos Hyperandrogenism
The approach to the differential diagnosis of PCOS begins with a thorough medical history and physical examination. Most disorders other than physiologic adolescent anovulation are uncommon to rare. History where one should suspect other differentials are rapidly progressive hirsutism, clitoromegaly, hirsutism or menstrual abnormality that fails to respond to medical therapy of PCO. All guidelines recommend screening for nonclassic congenital adrenal hyperplasia (NCCAH), which is the most likely disorder to mimic PCOS although it accounts for only ~5% of hyperandrogenic anovulation.[5,16] Other differentials include adrenal or virilising ovarian tumour, cushing's syndrome, acromegaly, hypothyroidism, hyperprolactinemia and drugs like anabolic-androgenic steroids, valproic acid.

The initial endocrinologic hyperandrogenism workup typically includes serum total testosterone, free testosterone, DHEAS, 17hydroxyprogesterone level in addition to all the initial battery of tests. Beyond that, the workup is individualized. 17-hydroxyprogesterone (17OHP) is a screening test for nonclassic congenital adrenal hyperplasia (NCCAH) secondary to 21-hydroxylase deficiency. Early morning sample is to be taken. NCCAH is suggestive when values are >200 ng/dL. Values >1000 ng/dL (30 nmol/L) are diagnostic of NCCAH.[17] If values are In between 170-1000 ng/dl,it calls for ACTH [cosyntropin] stimulation test. Another investigation is testing for DHEAS which is exclusively secreted by adrenals and elevated levels are a marker of adrenal hyperplasia or tumour. In Virilising Adrenal tumour, values >700 mcg/dL.

Treatment in Adoloscents
Lifestyle modification is first-line treatment for the overweight and obesity. Weight loss in obese adolescents with PCOS improves menstrual regularity and hyperandrogenemia.[18] Endocrine Society guidelines suggest COCs as first-line pharmacologic therapy of menstrual irregularity and hirsutism.

Combined Oral Contraceptive Pills
They suppress the hypothalamic-pituitary-ovarian axis and reduces excess androgen production by the ovary, which improves menstrual regularity and decreases anovulatory uterine bleeding, hirsutism, and acne. The progestin component also inhibits endometrial proliferation, preventing hyperplasia.[19,20] COC that contains at least 30 µg ethinyl estradiol should be used, unless the adolescent is at risk for COC side effects.

COCs should be continued until the patient is gynecologically mature (five years postmenarcheal) or has lost a substantial amount of excess weight. At this time, a trial off therapy is reasonable to document the persistence of the syndrome.

Type of Ocp Depending On Progesterone
Drospirenone-a progestational analogue of spironolactone. It has antiandrogenic and antimineralocorticoid properties. Its given in a dose of 20 mcg or 30 mcg for 21/28 days. Its natriuretic effect minimizes the fluid retention.[21]

Cyproterone Acetate –It's a antiandrogen and progestin used in the treatment of acne, excessive hair growth. It can be given in combination with ethinyl estradiol in a dose of 2mg.[22]

Progesterone
If the adolescent patient is unable or unwilling to take COCs, the main other therapeutic option is progestin. Menstrual irregularities in sexually mature adolescents often can be controlled with cyclic progestin alone. Cyclic treatment with oral progestins relies on their direct inhibitory effects on endometrial proliferation.Transient reduction in androgen levels is achieved, but this is variable and generally insufficient to expect improvement in hirsutism.[23] Intramuscular depot progestin therapy that provides high and sustained doses (eg Depo-Provera) can suppresses gonadotropins. Micronized progesterone or medroxyprogesterone acetate can be used for 7 to 10 days out of each month.

Other Androgen Reducing Therapies
Gonadotropin-releasing hormone (Gnrh) agonist can be used instead of COCs to suppress ovarian function in the rare patient who cannot tolerate COC.[24] A glucocorticoid therapeutic trial may be considered in the unusual situation of the non-obese patient whose PCOS seems solely due to functional adrenal hyperandrogenism (as occurs in 5 percent of PCOS).[25]

Addition of Antiandrogen
The decision to add an antiandrogen to a COC depends on the severity of the hirsutism and considerations of efficacy, side effects, and costs.

Spironolactone-competitive binder of androgen to androgen binding receptor. Guidelines recommend starting with a dose of 100 to 200 mg given in two divided doses daily.

Flutamide-non steroidal competitive inhibitor of androgen binding to the androgen receptor.
Finasteride-competitive 5αreductase inhibitor

Insulin Lowering Agents
They improve ovulation in approximately one-half of cases and modestly reduce androgen levels. They are not as effective as COCs in controlling menstrual cyclicity or hirsutism. Metformin is often used as an adjunct to the management of obesity and insulin-resistant metabolic abnormalities in patients with PCOS.[26]

CONCLUSION

To conclude.the evaluation for polycystic ovary syndrome begins with a focused clinical evaluation for the presence of hyperandrogenism such as hirsutism, acne that is resistant to topical or oral antibiotic therapy and menstrual abnormality. The clinical evaluation is followed by laboratory testing for common causes of abnormal menses, including testing for androgen exces. Several treatment options are available for adolescents with polycystic ovary syndrome. The choice of therapy depends on the individual adolescent's symptoms, her goal for treatment, and preferences. Use of combination oral contraceptives (COCs) as first-line treatment for adolescents who suffer the menstrual and cutaneous symptoms rather than other therapies is suggested.

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