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INFERTILITY MANAGEMENT

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INFERTILITY MANAGEMENT SERIES

POLYCYSTIC OVARIAN SYNDROME

Diagnosis and Management

Foreword
Rustom Phiroze Soonawala

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Contents

1. **Prevalence and Symptomatology of Polycystic Ovary Syndrome** **1**
   Aviva Pinto Rodrigues
   - Definition *1*
   - Adolescent Polycystic Ovary Syndrome *2*
   - Hyperandrogenemia or Hyperandrogenism *3*
   - Polycystic Ovary Morphology *4*
2. **Genetics and Pathophysiology** **11**
   Juan Giles Jiménez, Paula Celada, Carmen Vidal
   - Genetics *11*
   - Pathophysiology *15*
   - Fetal Programming *18*
   - Environmental Factors *18*
3. **Adolescent Polycystic Ovary Syndrome and Hyperandrogenism** **23**
   Saroja Koppala
   - Definition of Polycystic Ovary Syndrome *23*
   - Diagnosis of Polycystic Ovary Syndrome in Adolescence *24*
   - Pathophysiology *25*
   - Laboratory Evaluation *25*
   - Follow-up *26*
   - Treatment *26*
4. **Lifestyle Management and Role of Insulin-Sensitizing Drugs** **32**
   Esther Santamaría López, Cinzia Caligara, Manuel Fernández-Sánchez
   - Lifestyle *34*
   - Insulin-Sensitizing Drugs *36*
5. **Ovulation Induction in Polycystic Ovary Women** **40**
   Ujwala Rao, Anil Gudi
   - Pathophysiology *40*
   - Polycystic Ovary Syndrome and Anovulation *41*
   - Ovulation Induction in the Polycystic Ovary Syndrome Patients *42*
6. **Surgical Management of Polycystic Ovarian Syndrome** **48**
   Sujal Munshi, Jayesh Patel
   - Surgical Management *49*
   - Laparoscopic Ovarian Drilling *49*

7. Ovarian Hyperstimulation Syndrome: Identification and Management **63**
Sulbha Arora, Ritu Hinduja
- Diagnosis *63*
- Risk Factors *63*
- Clinical Presentation *64*
- Patient Assessment *64*
- Classification of Ovarian Hyperstimulation Syndrome *66*
- Management *67*
- Management of Complications and Intensive Care *74*
- Counseling *74*

8. Assisted Reproduction Techniques in Polycystic Ovary Syndrome **79**
Israel Ortega Sánchez, Juan A García-Velasco
- Ovarian Stimulation in Polycystic Ovary Syndrome *80*
- Adjuvant Therapies *84*
- In Vitro Maturation of Oocytes *85*

9. Long-Term Effects and Metabolic Syndrome in PCOS **90**
Juan José Espinós-Gómez

Index *111*

Chapter 3

Adolescent Polycystic Ovary Syndrome and Hyperandrogenism

Saroja Koppala

INTRODUCTION

Polycystic ovaries are common endocrinological problem that we encounter in our day to day life. In adult women it affects 6–8% of women.[1] Diagnosis of polycystic ovaries in adolescents can be difficult. The exact diagnosis of polycystic ovaries in adolescence is important because early diagnosis can prevent long-term complications,[2,3] and wrong diagnoses can cause lot of distress to the adolescent girl and her family. These girls present with myriad of symptoms and so they can present either to gynecologist, endocrinologist, dermatologist or general physicians. Hyperandrogenism (HA) is also one of the common presentation and they can present with hirsutism, menstrual disturbances, acne, alopecia, hoarseness of voice, infertility.[1] Many conditions can present with HA and few of them could be life-threatening.

DEFINITION OF POLYCYSTIC OVARY SYNDROME

Polycystic ovaries have been described in the literature for many years. But it was Stein-Leventhal who identified an entity consisting of oligomenorrhea, infertility, hirsutism and bilateral enlarged polycystic ovaries.[4] National Institutes of Health's (NIH) criteria for polycystic ovaries was oligo-anovulation and biochemical or clinical HA.[5] In 2004, the Rotterdam consensus criteria for polycystic ovary syndrome (PCOS) was (two out of three of oligo-anovulation, clinical and/or biochemical HA or polycystic ovary appearance on ultrasound).[6] In 2009, the Androgen Excess Society's (AES) new definition of PCOS is a disorder of clinical and/or biochemical androgen excess, plus either chronic oligo-anovulation and/or polycystic ovaries.[7] Other endocrinological disorders should be excluded. In spite of these definitions, the diagnosis of polycystic ovaries in adolescents can be challenging.[8]

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DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME IN ADOLESCENCE

Menstrual Disturbance

Menstrual irregularity is common in majority of girls after menarche. Nearly 85% of the cycles are anovulatory in the 1st year after menarche.[9] In adolescent girls with menstrual irregularity only 40% of them have features of polycystic ovaries on ultrasound examination.[10] Adolescent girls who have oligomenorrhea 2 years after menarche have high probability of developing PCOS.[11] And also menarche in girls with PCOS can vary widely, from early menarche before the age of 9 years to primary amenorrhea.[12] Higher androgen levels are found in women with primary amenorrhea and in overweight[13-15] or have a family history of overweight,[13] which exacerbates hyperandrogenemia. Persistence of anovulation was seen more in girls with increased body mass index (BMI).[16]

Ultrasound

In adolescent girls who are sexually not active transabdominal ultrasound is used which gives a less better picture compared to transvaginal scan. Also one of the criteria for the diagnosis of polycystic ovary is volume of the ovaries greater than 10 mL. In adolescents, normal girls also have larger volumes, so it is difficult to diagnose PCOS based on volume alone.[17] So we need higher threshold values for ovarian volume for adolescents.[18] A task force report from the Androgen Excess and Polycystic Ovary Syndrome Society recommends that normal range should be available based on age, ethnicity and body weight.[19] With the improvement in technology and with the better resolution of scan machines with transducer frequency of more than or equal to 8 MHz, the threshold for diagnosis of PCOS should be more than 25 follicles per ovary. But higher frequency scans are not available in all centers. Ovarian volume and morphology that are used for diagnosis of PCOS in adults, may be of limited value in adolescence PCOS.[17] Features of PCOS are more common in overweight or obese girls.[9]

Hyperandrogenism

Hyperandrogenism is a common clinical presentation in women. They can present with hirsutism, menstrual disturbance or infertility.[1] It can be caused by many conditions like PCOS, congenital adrenal hyperplasia, androgen-secreting tumors and Cushing's syndrome.[1,20] There is either more production of androgens or they are not converted into estrogens or they can be a combination of both in HA.[21] Modified Ferriman-Gallwey score is commonly used for evaluation of hirsutism.[22,23] In adolescents hyperandrogenemia may be a consistent marker for PCOS[24] and may represent an important symptom of PCOS.[9]

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Acne

Acne can be a feature of HA but not all girls with acne have HA.[25] It can be a normal feature for adolescents. It can affect around 70% of girls and did not associate with other features of PCOS.[17]

Hirsutism

Hirsutism in women with PCOS can be caused by increased androgen production, increased circulating free testosterone, or greater androgen activity within the pilosebaceous unit[16] and these should be addressed while treating. Hirsutism in adolescents takes longer to develop in the presence of increased androgens.[26] Acne and hirsutism can cause lot of distress to the young girls. Severity of hirsutism does not correlate well with the level of androgens.[18,27-29] Even mild hirsutism in women can be an indicator of the underlying androgen excess disorder.[30] Sometimes women with severe hyperandrogenemia may not have hirsutism.[7,31,32] Genetic counseling should be done in cases of nonclassical congenital adrenal hyperplasia where there is risk of heritable transmission.[33] The treatment of hirsutism can take longer, so women should be warned regarding this. Pharmacological treatment should aim to decrease androgen secretion and action. Physical exercise and diet are essential for the management of androgen excess and for the cardiovascular protection in women with PCOS.[7,32] Hirsutism is a chronic disorder in most cases, and the underlying disorder should be treated.[34] PCOS is a cause of hirsutism in majority of cases but others like hyperthecosis, nonclassical adrenal hyperplasia, Cushing syndrome, thyroid dysfunction, and ovarian and adrenal androgen-secreting tumors have to be ruled out.[16]

Physicians should be cautious of over diagnosing PCOS in adolescents. Adolescent girls who are obese, hirsute or having irregular menstrual cycles should be identified and followed.[16] For diagnosis of PCOS during adolescence, all three criteria (and not just two out of three) of Rotterdam consensus should be present.[16] Whenever the diagnosis is not clear they should be followed closely and diagnosis should be reconsidered.[16]

PATHOPHYSIOLOGY

Insulin resistance and HA play a key role in the pathophysiology of PCOS and insulin resistance affects 85% (75% of lean and 95% of overweight) of cases.[35] This increase in insulin leads to increase androgen production and reduces sex hormone-binding globulin (SHBG) leading to HA.[36]

LABORATORY EVALUATION

An exact criteria for diagnosis of HA was not specified by the consensus group.[37] Testosterone itself cannot confidently diagnose HA.

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There are no specific ranges for adolescent population. Free testosterone is a better marker for HA in women.[31,38,39] But there are different formulae for measuring free testosterone.[40] Serum total testosterone is commonly used for measuring HA.[37] Immunoassays are the most widespread method used to measure serum total testosterone[41] because it is easy, quicker and automation can be done. In women with PCOS where the testosterone levels are low it is less reliable.[41] Automated unextracted immunoassays can overestimate testosterone levels.[42] So extraction technique is done to remove nontestosterone androgens but by doing this it gives a low value in women who has high levels of non-testosterone androgens.[37] Mass spectrometry is the gold standard for testosterone quantitation and Endocrine Society Position statement proposed it as the preferable analytical method.[41] However, it is not widely available, lacks standardization, cumbersome and relatively expensive.[37,41] When considering the normal values for androgen levels, age and BMI were not considered. Free testosterone or the free testosterone [free androgen index (FAI)] measurement were considered[43] to be more sensitive methods to assess HA.[44] Measurement of early follicular phase serum testosterone using liquid chromatography–tandem mass spectrometry and free androgen index are important laboratory tests in the diagnosis of PCOS.[45] There is either dysfunctional production of androgens or inadequate conversion to estrogens or both in HA.[21]

Anti-Müllerian Hormone

Anti-Müllerian hormone (AMH) concentrations are a questionable surrogate marker of polycystic ovarian morphology in adolescents.[46]

FOLLOW-UP

Once the diagnosis is made by early interventions long-term complications can be prevented.[2,3] Compared to women without PCOS, women with PCOS are at higher risk of depression.[47] and at any age they are at higher risk of elevated cardiovascular disease (CVD) markers and they are magnified with obesity.[16]

TREATMENT

Main aim of treatment should be to treat the problem, maintain quality of life and prevent long-term complications. Because of the varied presentation of PCOS to different specialities, all specialists should be aware of this, and management should start at the earliest. PCOS has a negative impact on the quality of life in adolescents.[48] Some adolescent girls with PCOS find hirsutism and acne more troublesome compared to the nonvisible effects of PCOS. Obesity, hirsutism and irregular menses should be treated

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in adolescents.[16] Lifestyle modification plays a very important role in the management of women with polycystic ovaries. Weight loss through modifications in diet, exercise can decrease severity of PCOS. Adolescent girls should be educated that with restriction in calorie intake and regular physical activity, improvement in hirsutism can be seen in 40–55% of women within 6 months of weight reduction. Lifestyle's modifications should be considered as a primary line of management in these girls because they are effective and also some girls consider taking medications as a social stigma. Dieticians can be helpful in weight reduction. Medications like metformin, orlistat or bariatric surgery improves insulin resistance and reduces severity of PCOS.[49-51] Oral contraceptive pills play a very important role in the treatment of PCOS. Combined oral contraceptive pills suppress the serum levels of free testosterone and increase SHBG concentration. It improves acne, hirsutism, regularize the menstrual cycles and acts as a contraception in sexually active adolescent girls. Absolute contraindications should be considered before prescribing the oral contraceptive pills. In cases where there is estrogen intolerance, progestins can be used to prevent dysfunctional uterine bleeding. Metformin is useful in adolescent girls with glucose intolerance.[16] Metformin is very safe from a metabolic point of view especially in obese or overweight adolescents with impaired glucose metabolism, because it improves insulin sensitivity, serum triglycerides levels and BMI; however, there is no consensus on how long should this be continued. In these cases, its administration should be always associated to lifestyle modification programs.[52] For treatment of hirsutism ovarian steroid production is reduced by the use of oral contraceptive pill, which plays an important role in the treatment for PCOS.[16] Spironolactone, an antiandrogen is used alone or in combination with oral contraceptive pills to block androgen action at hair follicle.[16] Flutamide and finasteride are antiandrogens that are helpful in treating hirsutism. Topical agent like eflornithine is an irreversible inhibitor of ornithine decarboxylase is effective in decreasing unwanted facial hair. In a small minority of adolescent girls who have fertility problems, clomiphene citrate should be the treatment of choice and ovarian hyperstimulation is a major risk factor. These girls should be followed closely and they should have achievable targets to maintain their weight and diet and also group intervention is helpful. Adolescent girls with PCO tend to have psychological issues like depression, anxiety and eating disorders and they should be appropriately counseled.

CONCLUSION

Polycystic ovary syndrome in adolescence should be defined, diagnosed and followed up to improve the quality of life and to prevent short-term and long-term complications.

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