

Review Article:

MANAGEMENT OF POLYCYSTIC OVARY SYNDROME IN ADOLESCENT

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ABSTRACT

Polycystic ovary syndrome characterized by hyperandrogen, anovulation and polycystic ovarian khronik. Manifestations of this syndrome are hirsutism, irregular menstruation, infertility, dyslipidemia, the risk of developing a type-2 diabetes mellitus and cardiovascular disease. PCOS can arise during puberty. Clinical symptoms and neuroendocrine changes in adolescents resembles PCOS in adulthood picture of PCOS, polycystic just not a requirement that must be found in PCOS adolescents. Early attention and treatment during adolescence is essential to prevent complications that may occur in the future. This paper reviewed the clinical symptoms, hormonal changes and metabolic disturbances PCOS in teenagers, how to diagnose and handling complaints that could be done for current and future prevention.

Keywords: teenagers, polycystic ovary syndrome, obesity, insulin resistance, antiandrogen, cyproteron acetic, metformin, thiazolidinedion

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrine disorder that can occur throughout the age of the woman. At first only understood a related disorder in women with infertility. But this time a teenager can indicate PCOS symptoms associated with menstrual disorders, obesity, type 2 DM and found signs hyperandrogen (hirsutism and acne). Lately, the trend of increasing prevalence (Snyder, 2005).

PCOS often manifests at the time of menarche with disorders of menstruation, so it is often considered a normal condition caused by the ripening process of the axis system of the hypothalamus, hypophysis and ovaries, as well as a lot of acne occur in adolescence, is considered something normal. Currently, if found oligomenorrhea in the first year after menarche, it is necessary to be considered, possibly PCOS symptoms. Van Hooff, conducted a survey population with the results of 45-57% girls with oligomenorrhea is part of PCOS, after clinical and laboratory examination of hyperandrogen (Mastorakos, et al, 2007). Menstrual disorders seem to be a major issue in adolescents with PCOS, but its long-term risk must be of concern such as obesity, subfertility, diabetes mellitus and was equally

likely to be a risk of endometrial hyperplasia and carcinoma (Hickey and Balen, 2003)

Therefore there are two main objectives in the handling of adolescent PCOS, the first, is to control menstrual irregularities, by having regular menstrual patients will be spared the embarrassment caused by these menstrual irregularities (Richardson, 2003). The second objective is long-term effort to avoid complications caused by obesity, insulin resistance, glucose intolerance and type 2 diabetes mellitus. All these conditions will result in lipid disorders and hypertension, which is a risk factor for cardiovascular disease emergence. Because PCOS is a long-term metabolic disorder that has significant risks in the future, then the handling of PCOS in adolescents should be associated with metabolic syndrome, especially when the girl was accompanied by obesity, acne, hirsutism and irregular menstruation. Early intervention and continuing with lifestyle modification and drug use prevention medicines is the basis of co morbidities associated with PCOS.

PATHOGENESIS OF PCOS

Polycystic ovary syndrome is a hormonal disorder of heterogeneous, with a prevalence of approximately 5% -

10% of women of reproductive age (Markie, 2001; Tweedy, 2000). Driscoll and Pugeat, said the prevalence of PCOS in adolescents even higher, namely 11-26%, with 50% of them suffer from obese (Ojanemi, 2006), while Dramusic et al, reported prevalence of PCOS in adolescents in Singapore reached 25.9% (Mastorakos, et al, 2007).

PCOS occurs in primary Hyperandrogen from testosterone overproduction theca cells derived from ovarian and adrenal glands. Hyperandrogen manifestations in women may include hirsutism, acne, hair loss in temporal and frontal, the sound becomes heavy, increase muscle mass, decreased breast size, in extreme cases, such as virilization and and clitoromegaly (Marshall: 2001).

Other important hormones involved in PCOS is insulin. Women with PCOS tend to have insulin resistance, which leads to overproduction and eventually lead to hyperinsulinemia (Azziz, 2004). Endocrine problems encountered in girls with PCOS, among others, reduction in tissue sensitivity to insulin, insulin resistance in liver and hyperinsulinemia, all of them became the basis of DM-type 2 (Lewy et al, 2001). In addition to affect glucose metabolism, insulin also affect androgen levels in the circulation. Elevated levels of circulating testosterone found in women with insulin resistance and hyperinsulinemia. High levels of androgens is caused by increased levels of insulin and lead to decreased levels of sex hormone binding globulin (SHBG), subsequently causing an increase in free testosterone levels (Azziz, 2004). Elevated levels of androgens do not only result in hirsutism, acne and male type baldness, but also cause obesity central / android. Besides central obesity worsen insulin resistance, also exacerbate the symptoms of PCOS.

Obesity, insulin resistance, hyperinsulinemia, glucose intolerance and type-2 diabetes mellitus have a major impact on overall health, especially the impact of the development into heart disease. Women with PCOS who have endocrine disorders such as mentioned above can be accompanied by increased blood pressure, increased LDL cholesterol and decrease HDL cholesterol (Sheehan, 2004). This is all a risk cardiovascular developed into a significant disease.

HOW TO DIAGNOSE

To diagnose PCOS can be a challenge, due to the appearance of clinical PCOS and vast variations can easily occur fault diagnosis (Azziz, 2004). So often happens underdiagnosed. Young women with hirsutism and irregular menstruation which must difikirkan

possibility of PCOS. Enforcement diagnosis must be based on history, physical examination and laboratory examination. Treatment must be linked with prevention efforts towards long-term complications endocrine parameters that can be used as a basis for treating complaints and clinical symptoms, which often appears in women with PCOS.

Criteria that can be widely accepted for diagnosing PCOS adolescents based on the standards that have been recognized in the year 1990, namely Consensus Conference of the National Institute on Child Health and Human Development (Ken and Legro, 2002). These criteria include chronic anovulation and hyperandrogen is not due to other endocrine disorders. Existence of polycystic ovarii is not a criteria for diagnosing PCOS adolescents as a woman of reproductive age based on 2003 Rotterdam criteria. History, physical examination and laboratory examination is needed to focus on whether a patient meets the criteria for establishing the diagnosis PCOS in teenagers.

History taking

Focused on several aspects related to menstruation, such as: a). age at menarche b). the distance between the two menstrual cycle c). menstrual quantity d). whether there dismenorhea (Markle, 2001). Girls with PCOS often during the early start of menstruation has a regular pattern, after several years of irregular menstrual pattern, not even menstruating altogether. Number of menstruation in girls with PCOS tend to be numerous and accompanied by cramping pain significantly. Goolsby, 2001, stating that the information on the development of secondary sex characteristics is important in the anamnesis. Ibanez et al, 2004, the report showed that the girl who was diagnosed with PCOS have a history of prekok puberty, puberty prekok pubic hair growth is defined as the age of 8 years (Snyder, 2005).

Family history with PCOS, and diabetes mellitus also need to be explored. PCOS have a tendency in one family in one generation, especially mothers and sisters. Family history of diabetes mellitus showed that teenagers with PCOS suffer from obesity with insulin resistance and glucose intolerance.

Physical examination

Physical examination should begin by measuring weight and height, which is used to measure body mass index (BMI). If the results of the examination must be conducted examination showed obesity a waist to hip ratio to determine whether obesity type central /

android. If the value is higher than 0.72 indicates the type of obesity.

Afterwards is showing signs of checking whether hyperandrogen, including hirsutism, acne, hair loss, deep voice that describes the circumstances and cliteromegali hyperandrogen.

Last signs of insulin resistance should be noted. Found akantosis nigrican, BMI increased with central obesity showed insulin resistance. Resistance to Acanthosis nigrican is an indicator of moderate to severe insulin.

Table 1. Clinical picture of PCOS in Adolescents

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| <ol style="list-style-type: none"> 1. Low birth weight 2. Premature puberche 3. Menstruasi irregularity (oligo-amenorrhea) 4. Hyperandrogen (hirsutism, acne, male-type baldness) 5. Obesity 6. Family history of PCOS, type 2 diabetes mellitus, premature cardiovascular disease |
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Laboratory tests

Laboratory examination is an important key to confirm the diagnosis, although clinical symptoms and physical examination is superior to diagnose PCOS. Until now, there is still no consensus on which types of tests used to diagnose PCOS. The researchers agreed that the laboratory tests should (Chang, 2004): (a) eliminate the cause of amenorrhea, such as; hipothyroidism, hyperprolactinemia and pregnancy; (b) Eliminate the cause of such hyperandrogen Congenital Adrenal hyperplasia (CAH), adrenal tumors and ovarian tumors; (c) detection of insulin resistance, glucose intolerance and lipid disorders.

Currently recommended tests are free testosterone, dihydroepiandrosterone-sulphate (DHEA-S), androstenedione, prolactin, Thyroid Stimulating Hormone (TSH), 17-hydroxyprogesterone (17-OHP) and a pregnancy test. Type examination effectively help to: (a) eliminate the serious problems that may cause these symptoms; (b) enhanced PCOS diagnosis; (c) choosing the next priority for the management and assess their effectiveness.

MANAGEMENT

PCOS treatment principles are different, depending on her age and depending on the priorities of the patient. Weight loss is recommended to all obese PCOS women,

at first, with purposes other than reducing insulin resistance, also lowering hyperandrogen. In general, ideal treatment of PCOS is to normalize the menstrual cycle, ovulation and restore fertility, reduce acne and hirsutism, improve lipid profiles and glucose tolerance, and decreased risk of cardiovascular disease (Buggs and Rosenfield, 2005). Treatment of symptoms of anovulation is restricted to control the menstrual cycle in the case of adolescent PCOS, infertility treatment, while rare, although of course the discussion about future fertility, many asked questions (Franks, 2008). Many types of treatment in PCOS decrease in ovarian androgen production and androgen action at the receptor level. Insulin Sensitizer now widely used agent for treatment of PCOS, by improving aspects of endocrine and metabolic aspects (Mastorakos et al, 2007).

Handling PCOS adolescents focused on the existing complaint, but must also be associated with long-term consequences that might occur, such as insulin resistance, glucose tolerance disorders that affect the development of a DM-type 2 and subsequently into cardio vascular diseases, it is important to diagnose and treatment of adolescent girls with PCOS. Nearly one-third more cases of PCOS in adolescents suffering from disorders of glucose tolerance (Palmert et al., 2002) Treatment is divided into three, namely hyperandrogen treatment for symptoms, for menstrual disorders, treatment of obesity and insulin resistance (Buggs and Rosenfield, 2005).

THERAPY OF HIRSUTISM, ACNE AND HAIR LOSS PATTERN

Although only symptomatic therapy, cosmetics are important, which can improve the image of adolescents with hirsutism. Topical Eflornithine HCL Cream suppress hair growth. Therapy for hirsutism among other cosmetics such as shaving and depilation chemical removal, epilation dengan wax removal and destruction of dermal papilla varied methods such as laser therapy and electrolysis. While for the treatment of baldness therapy with a combination of anti-androgen pills seem more superior combination of minoxidil (Mastorakos et al, 2007).

Combined oral contraception pill (COC)

The combination pill is the first choice for women with menstrual disorders and abnormal dermatologik caused by PCOS. The workings of the Combination Pill, suppress androgen levels, especially plasma free testosterone levels by inhibiting ovarian function. Combination birth control pills also increase the levels of SHBG and lower levels of DHEA sulfate. Androgen

levels became normal in the use of combination oral contraceptives the first month. Use of Combination Pill for 3 months to improve acne, inhibits the progressiveness of hirsutism growth and reduce the frequency of its shaving (Buggs and Rosenfield, 2005). All combinations of estrogen and progestin to give a good response to treatment in women with hirsutism, cosmetic treatment combinations. While the anti-progestin that has the properties of androgens have a better effect, and improving lipid profiles. For women who have menstrual disorders better use of the estrogen dose is higher. Pill combination with ethinyl estradiol levels of 50 mg is more beneficial for obese women. It is recommended to check back after treatment for three months, to evaluate the effectiveness of treatment and normalization of androgen levels. The use of combination pills should be forwarded to the development of mature gynecology, approximately 5 years after menarche or her weight had gone down quite significantly. In particular woman could be considered for use as a contraceptive.

Glucocorticoids

Glucocorticoids beneficial for lean PCOS women, in patients with Adrenal Functional Hyperplasi (Fah) are prominent, such as patients with high androgen levels can not be controlled by the Combination Pill, glucocorticoid use is recommended to use low doses (5-7.5 mg corticosteroid), which will reduce adrenal androgen production compared with levels of cortisol. It is recommended that the concentration of DHEA suppressed at the lower range of adult content and is not fully being suppressed. Significant glucocorticoid deficiency can be avoided by maintaining the levels of cortisol 10µg/dL or more at 8:00 in the morning or 18µg/dL hours, 30 minutes after the administration of ACTH low dose (1.0 tg).

Anti-androgens

Anti-androgens required for essential drugs to improve hirsutism. Anti-androgens work with a competitive antagonist of the androgen receptor steroid binding thus inhibiting the transformation of androgens stimulate vellus hairs become terminal. Effect of anti-androgen therapy for 9-12 months a new look, due to the growth cycle of hair length follikel. The goal of therapy is off label, for the use of anti-androgens causes the fetus pseudohermaphroditism women. Therefore, in certain cases need to consider antiandrogen contraceptive use during normal usage, this applies to all types of anti-androgens (Buggs and Rosenfield, 2005).

Spironolakton is the safest anti-androgens. Higher doses required for anti-androgen effect compared with the

effects of anti mineralokotikoid, also has properties of a weak progestin and glucocorticoid. Effective enough to reduce androgen-third of the initial score hyperandrogen (Ferriman-Gallwey system). Recommended starting dose of 100 mg twice a day, until reaching a maximum effect, then reduced to 50 mg twice daily as maintenance dose. Spironolakton should be used for patients wanting improvement of hirsutism, the use of the above dose is generally well tolerated, but the possibility of hyperkalemia limit its usefulness, therefore contra indications for patients with abnormalities in the adrenal, liver and kidney insufficiency. Hyperkalemia risk for a woman when using ACE inhibitors, potassium supplements, NSAIDs every day, potassium-sparing diuretics, heparin or similar drugs. Therefore, the electrolyte balance must always be monitored. Use single sipronolakton have irregular bleeding tendency, so it is used in pill form of contraception.

Another anti-androgen therapy can be used is ciproteron acetic hirsutism, flutamide and Finasteride. Cyproterone is an anti androgen progestational acetic having weak anti gukokortikoid. Available in combination with estradiol in birth control pills etynil combination. More specific antiandrogen Flutamide with similar effectiveness spironolakton and CPA, is used more limited because of toxic effects hepatoselluler. Flutamide may increase ovulation in women with PCOS, thus feminizing effects on male fetuses, then the application by contraceptive pills. Finasteride is a 5- α -reductase inhibitor, a little less effective than other anti-androgens for the treatment of hirsutism.

THERAPY OF MENSTRUAL DISORDERS

Progestin

Often irregular menstrual oral progestins can be given 50-10 mg daily for 7-10 days. This progestin causes withdrawl (bleeding funny?) In some patients, but there are some patients who did not give a response caused by anti-estrogen effect of androgens on the endometrium. Progestin treatment could not normalize androgen levels and reduce hirsutime. In adolescents perimenarche which gives a good response to the progestin may be continued up to six menstrual cycles to detect spontaneous. Some side effects may be due to the use of progestin is complained of depression, swelling and breast pain. Also need to be informed to the patient, that is not a progestin oral contraceptives.

Combined oral contraceptive pill (COC)

Bleeding Uterus Dysfunction can be treated with

progestin, but if the PUD requires heavy treatment with estrogen. Estrogen can be given in the form of combination pills, one tablet 3-4 times daily for seven days. Every birth control pills can be used, but it is suggested that contains estradiol 50 mcg ethynil, awaited the next withdrawal Combination Pill used to prevent recurrence of PUD.

Combination birth control pills can reduce the amount of bleeding up to 50% in cases of menorrhagia. However, if the bleeding does not stop then we have to find other factors, until the suspicion of malignancy. There are several potential losses on the use of combination pills for the case of PCOS in adolescents, is the cessation of growth. Combination birth control pills, especially third generation contraindication in patients with venous thrombosis risk of an eye. In patients who have migraines often best avoided, even if not able to be with good explanations and chosen with low estrogen levels. Long-term use of fertility Combination Pill still not clear, generally after the cessation of birth control pills will be followed by phase combination of amenorrhea, estrogen, high doses used in early adolescence may increase risk of infertility.

GnRH

Used to suppress gonadotropin secretion in cases that do not tolerate Combination Pill. Treatment with GnRH must be accompanied by a low dose of estradiol as an add back therapy (50 tg estradiol) for keeping vaginal lubrication, and ensure bone growth during adolescence.

Insulin Sensitizing Agents (ISAs)

ISA hyperandrogenpada improve ovulation and PCOS by lowering insulin levels, as discussed below.

THERAPY OF OBESITY AND INSULIN RESISTANCE

Treatment of obesity improve ovulation and reduce androgen levels in patients with PCOS, and this should be a priority even though initial weight reduction therapy is effective in patients with PCOS, but the implementation is very difficult.

Table 2. Overview of treatment options in young PCOS

Treatment of hyperandrogen symptoms • Inhibition of androgen production in the ovaries ✓ Combined oral contraception pill ✓ GnRH analogues • Inhibition of androgen action ▪ Anti -androgen (cyproterone acetate, flutamid, spironolactone) ▪ 5α-reductase inhibitor (finasteride)
Treatment of menstrual disorders ❖ Progestine ❖ Combined oral contraception pill ❖ GnRH ❖ Insulin Sensitizing Agent
Treatment of obesity and insulin resistance ➤ Weight loss by diet and exercise ➤ Metformin ➤ Thiazolidinedion

Oral metformin is a proven biguanida well as diabetes therapy, antihyperglycemik which work by inhibiting the production of glucose in the liver and increase insulin receptor. Insulin concentrations would decrease and followed by subsequent phenomena of reduction of

androgen levels and LH and increased SHBG. Metformin was also able to work directly on the cell theka reduce androgen production (Homburg and Lambalk, 2004). While thiazolidinediones work by enhancing insulin sensitivity through increased

mobilization of fat from the bloodstream. The effectiveness of both drugs was also reported in patients with no indication of insulin resistance (Buggs and Rosenfield, 2005). Metformin is useful in cases of PCOS adolescents, because in addition to suppress appetite and also stimulates weight loss. The recommended starting dose of 500 mg before dinner, and raised 500 mg per week until reaching the maximum dose of 2000 mg. Thiazolidinedione Troglitazone one faction has withdrawn from the market in the USA and the United Kingdom due to hepatotoxic risks. While the new generation of pioglitazone and rosiglitazone appear more secure and profitable in women with PCOS. However these drug classes have a tendency to increase body weight.

CONCLUSIONS

PCOS should be considered in adolescent girls with hirsutism, irregular periods and obesity. Linking and treating PCOS in adolescents is very important, because they can reduce the metabolic syndrome and chronic anovulation associated with an increased risk of endometrial hyperplasia and malignancy becomes.

Free testosterone levels higher than normal levels of adult women is recommended screening tests. PCOS should be removed from other hyperandrogen disorders that require specific therapy, such as virilizing tumors, non-classic CAH, Cushing's syndrome and hiperprolactemia.

Reduction of insulin resistance should be a therapeutic target in one adolescent PCOS. Weight loss and lifestyle modifications are important and always accompanies the main treatment, according to a priority for the adolescent. Metformin has been used widely with good results and few side effects.

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