CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Polycystic Ovary Syndrome

BY NEIL S. SKOLNIK, M.D., AND CHARISSA MYERS, M.D.

Polycystic ovary syndrome, with a prevalence of approximately 7%, is a common, important, and often underrecognized condition.

Although definitions vary, PCOS is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. Obesity often results in hyperinsulinemia, which may contribute to decreased levels of sex hormone–binding globulin (SHBG), increased circulating androgen, and increased androgen production. Obesity may exacerbate the clinical manifestations of PCOS, but not all women with PCOS are obese.

Diagnostic Criteria

The three following diagnostic criteria are commonly referenced for PCOS:

► **NIH criteria.** Hyperandrogenism and menstrual abnormalities (amenorrhea or oligomenorrhea) must be present.

► **Rotterdam criteria.** Ultrasonography of polycystic ovaries is an important component of the diagnosis of PCOS (12 or more follicles, 2- to 9-mm diameter, or increased ovarian volume greater than 10 cm^3). This testing has been criticized for increasing the number of PCOS diagnoses and subjecting women without PCOS to unwarranted management.

► **Androgen Excess Society criteria.** Hyperandrogenism (whether present clinically or in serum) must be present.

History and physical should include medications, onset of androgen excess, menstrual history, family history, blood pressure, body mass index, waist circumference, signs of hyperandrogenism (acne, clitoromegaly, body hair distribution, balding), and signs of insulin resistance (acanthosis nigricans, obesity). Lab assessments should include fasting lipids, fasting glucose, 2-hour oral glucose tolerance test, total testosterone (free testosterone and SHBG), as well as thyroid-stimulating hormone, prolactin, and 17-hydroxyprogesterone.

If Cushing's disease is suspected, obtain a 24-hour urinary free-cortisol excretion test or low-dose dexamethasone suppression test. Use pelvic ultrasonography to evaluate for polycystic ovaries and endometrial abnormalities.

Clinical Manifestations

Clinical manifestations include menstrual dysfunction, infertility, hirsutism, acne, androgenic alopecia, insulin resistance, and metabolic syndrome. Long-term sequelae include an increased risk of type 2 diabetes, cardiovascular disease, and endometrial cancer.

Differential Diagnosis

Diseases to consider in patients with the clinical manifestations listed above are thyroid disease, exogenous androgens, primary ovarian failure, and prolactin disorders. In addition, be aware of rare disorders that can cause symptoms similar to PCOS, including Cushing's syndrome, androgen-secreting tumors of the ovaries or adrenals, and nonclassical congenital adrenal hyperplasia.

Weight Loss With PCOS

Weight loss in obese women with PCOS produces increases in SHBG, decreased circulating-androgen levels, resumption of menses, and improved pregnancy rates. Weight loss also decreases hirsutism, insulin resistance, and lipid levels. Weight loss that occurs by lifestyle modifications, pharmacologic agents (such as orlistat), and gastric bypass have shown similar effects.

PCOS and Diabetes Risk

There is a two- to fivefold increased risk of diabetes in women with PCOS. Women with PCOS should be screened with a fasting-glucose level and a 2-hour glucose level after a 75-g glucose load. Metabolic syndrome (defined as blood pressure greater than 130/85, waist circumference greater than 35 inches, fasting glucose greater than 100 mg/dL, HDL cholesterol less than 50 mg/dL, and triglycerides greater than 150 mg/dL) affects nearly 33% of women with PCOS. Although there are insufficient data to recommend insulin-sensitizing pharmacological agents prophylactically, the Diabetic Prevention Program trials showed a decreased risk of developing type 2 diabetes in women with PCOS when lifestyle modifications or metformin (1,500-2,000 mg/day) were used by those with impaired glucose tolerance.

Cardiovascular Disease Risk

There is no well-documented evidence of increased risk of cardiovascular events in women with PCOS. However, given the increase in cardiovascular risk factors, their cardiovascular risk should be periodically assessed. These risks can be reduced through exercise, caloric restriction, weight control, and possibly by introducing statins and insulin-sensitizing agents.

Menstrual Dysfunction

Combination low-dose hormonal contraceptives are the primary treatment for menstrual dysfunction. They work by suppressing luteinizing hormone and androgen secretion by the ovaries and increasing circulating SHBG. Progestin-only contraceptives or intrauterine devices prevent endometrial cancer in women with PCOS and can be used as an alternative. There is an increased risk (50%-89%) of abnormal bleeding.

Although not FDA approved for treating menstrual abnormalities, insulin-sensitizing agents are associated with improved ovulation and glucose tolerance, and decreased circulating androgen levels by increasing SHBG.

Ovulation Induction in PCOS

Clomiphene citrate is the first-line agent that is recommended to induce ovulation, followed by either laparoscopic ovarian surgery or exogenous gonadotropins. Ovulation induction carries the risk of ovarian hyperstimulation, multiple births, and hypertensive disorder. Gonadotropins carry a lesser risk of ovarian hyperstimulation but an increased risk of multiple births. Aromatase inhibitors have been proposed to be similar to clomiphene, with higher implantation rates, less risk of multiple pregnancies, and a shorter half-life. Although metformin has been suggested, success rates are not as high as with clomiphene – although some studies show increased success rates when metformin is combined with clomiphene.

Treating Hirsutism

Topical eflornithine is the only FDA-approved treatment for hirsutism; it has a 60% improvement rate after 6 months. Some nonrandomized studies have shown improvement with hormonal contraceptives, especially when they are combined with spironolactone (an androgen receptor antagonist). Antiandrogens have been used empirically and are often combined with oral contraceptives because of their teratogenic effects. There is no evidence indicating that metformin improves hirsutism. Mechanical hair removal (by shaving, waxing, plucking, electrolysis, or laser) is often the treatment of choice.

Bottom Line

PCOS is characterized by a combination of hyperandrogenism, insulin resistance, menstrual dysfunction, polycystic ovaries, infertility, hirsutism, acne, androgenic alopecia, and metabolic syndrome. The most effective intervention for PCOS appears to be lifestyle management, with a goal of exercise and weight loss. Further treatment is geared toward symptom relief and reduction of long-term cardiovascular risk.

Reference

ACOG Practice Bulletin No. 108: Polycystic Ovary Syndrome. Obstet. Gynecol. 2009;114:936-49.

DR. MYERS *is a chief resident in the family medicine residency program at Abington Memorial Hospital.* DR. SKOLNIK *is an associate director of the family medicine residency program at Abington (Pa.) Memorial Hospital.*

Cure Rates Similar for Mesh/No Mesh Prolapse Repair

BY ROBERT FINN

FROM THE ANNUAL MEETING OF THE AMERICAN UROGYNECOLOGIC SOCIETY

LONG BEACH, CALIF. – A randomized controlled trial found no advantage for vaginal prolapse repair using mesh colpopexy compared with no-mesh repair, said Dr. Andrew I. Sokol of Washington (D.C.) Hospital Center.

After a mean follow-up of 14.7 months in this study of 65 women, 96% of women having mesh colpopexy with Prolift and 92% of women undergoing vaginal colpopexy without mesh were free of bulge symptoms; 25% of the mesh group and 22% of the no-mesh group experienced recurrent prolapse beyond the hymen. Neither of these differences was significant.

A total of 38% of women in the mesh group, compared with 30% of women in the no-mesh group, achieved optimal scores (stage 1 or below) on the pelvic organ prolapse quantification (POP-Q) scale, a difference that was not significant.

On the other hand, the vaginal mesh erosion rate was relatively high at 15.6%, and the data safety monitoring board terminated the study early because of this, Dr. Sokol said at the meeting.

In addition, there were three reoperations for erosion and three reoperations for prolapse among patients in the mesh group, compared with no reoperations in the no-mesh group, a significant difference.

In October 2008 the Food and Drug Administration issued a formal notification on reported complications from mesh use. Recognizing the high complication rate, mesh manufacturers have developed lighter-weight and mixed composite meshes.

The study included 65 women who were at POP-Q stages 2-4 uterovaginal or vaginal prolapse and who desired vaginal reconstructive surgery; the mean age in both groups was 64 years.

The study was supported by research grants from the AUGS Foundation and the MedStar Health Research Institute. Ethicon Women's Health and Urology donated the Prolift mesh kits for this study.

Dr. Sokol stated that he had no conflicts of interest. ■