Weight Loss Key to PCOS, Insulin Management

BY TIMOTHY F. KIRN
Sacramento Bureau

VAIL, COLO. — Weight loss can go a long way toward improving the effects of hyperandrogenism in the adolescent with polycystic ovary syndrome, Dr. Patricia S. Simmons said at a meeting sponsored by the American Academy of Pediatrics.

"In the obese patient, this can be all she needs," said Dr. Simmons, a past president of the North American Society for Pediatric and Adolescent Gynecology. "If their weight normalizes, usually their insulin levels and secondary hyperandrogenism will too."

Polycystic ovary syndrome (PCOS) can be associated with a different pathophysiology in different individuals, said Dr. Simmons, a professor of pediatrics at the Mayo Clinic, Rochester, Minn. About 2%-3% of the general female population has PCOS, and it is present in about 53% of adolescents with chronic anovulation and amenorrhea.

One of the condition's hallmarks, hyperinsulinemia, is present in about 20% of adolescents with PCOS. Those individuals are more often obese, but that is not always the case. And in those individuals, the hyperinsulinemia helps drive the hyperandrogenism, which is why weight loss and improving insulin sensitivity can help, Dr. Simmons said.

Though in overweight individuals, weight loss alone may be treatment enough, others may also require drug therapy. The first-line drug for adolescents is an estrogen/progestin oral contraceptive, she said. The progestin inhibits luteinizing hormone, which leads to decreased androgen production by the ovaries, and the inhibition of adrenal androgen production. The estrogen elevates serum hormone-binding globulin, which further inhibits the effects of androgen.

Over the long term, this therapy protects the endometrium from the dysplasia and cancer associated with PCOS.

The oral contraceptive that many experts recommend is the one with ethinyl estradiol and drospirenone, because that progestin is actually an anti-androgen structurally similar to spironolactone, which itself is used as a treatment for PCOS in conjunction with an oral contraceptive, Dr. Simmons said. Though common, this is not supported by data.

Oral contraceptive therapy also improves acne, makes menstruation more regular, and stops the progression of hirsutism.

"It's an easy thing to prescribe with great confidence," Dr. Simmons added.

The diagnosis of PCOS in the adolescent can be difficult, especially since one would like to identify it early and begin addressing some of the long-term health impacts.

Oral contraceptives, however, do not influence insulin levels, hence the necessity for weight loss in overweight PCOS patients.

The use of oral glycemic agents in children and adolescents has not been rigorously studied and is recommended for use only in selective cases, she said, adding "We don't use them unless we have clearly defined need."

Dr. Simmons has no conflicts of interest to report. ■

Society Calls for Standardization Of Labs Measuring Testosterone

BY JANE ANDERSON
Contributing Writer

Laboratory proficiency testing for testosterone should be based on the ability to accurately and precisely measure a sample containing a known concentration of testosterone, not upon agreement with peers using the same method, a panel of endocrinologists concluded in a new Endocrine Society guideline on testosterone measurement.

In "Utility, Limitations and Pitfalls in Measuring Testosterone: An Endocrine Society Position Statement," which was published online in the Journal of Clinical Endocrinology and Metabolism, the panel urged physicians ordering and using androgen assays to know the type and quality of the assay that is being used, along with the properly established and validated reference intervals for that assay (J. Clin. Endocrinol. Metab. 2007;92:405-13).

The AACE has hyperandrogenism guidelines and menopause guidelines that include androgen assessment.

DR. PETAK

The panel also noted that, in the absence of other information, direct assays perform poorly at low testosterone concentrations such as those found in women, children, and hypogonadal men, and therefore should be avoided. The guideline summarizes and evaluates the laboratory methods in use currently to measure testosterone.

In the October issue of the Journal of Clinical Endocrinology and Metabolism, the Endocrine Society issued a strong word of caution on the topic of androgen therapy with a new clinical practice guideline that recommends against diagnosing and treating androgen deficiency in women. That guideline cites the "lack of a well-defined clinical syndrome" and the "lack of normative data on total or free testosterone levels across the lifespan" as reasons against making the diagnosis (J. Clin. Endocrinol. Metab. 2006; 91:3697-710).

Dr. Andre Guay, director of the Center for Sexual Function at the Lahey Clinic in Peabody, Mass., admitted that "the measurement of total testosterone leaves a lot to be desired." But he added that the androgen therapy guidelines "don't emphasize the clinical point that before a clinician should treat, there needs to be [both] some biochemical measure of low androgen and the proper clinical symptoms. We don't treat with only a testosterone level or with a symptom alone."

However, Dr. Neil Goodman, professor of medicine at the University of Miami, argued that inaccurate results aren't useful to clinicians. "If we can't measure the test accurately, then how are we going to know if someone is deficient?" he asked, "If you send a woman's blood to five different labs, you're going to get five different answers."

Dr. Goodman said that endocrinologists and the companies that make the laboratory instruments to measure testosterone are moving toward adopting a standard, which will likely be tandem mass spectrometry.

American Association of Clinical Endocrinologists (AACE) President Dr. Steven Petak said that testosterone testing using radioimmunoassay "can be adequately standardized for detection of hyperandrogenism in women, providing the laboratory normal ranges have been adequately determined based on women without hyperandrogenic symptoms and with normal cycles by basal body temperature charts." Dr. Petak noted that AACE has published guidelines pertaining to hyperandrogenism as well as menopause guidelines that include androgen assessment along with caveats pertaining to the measurement of androgens.

The Endocrine Society's position statement on measuring testosterone was chaired by Dr. William Rosner and included Dr. Richard Auchus, Dr. Ricardo Azziz, Dr. Patrick Sluss, and Dr. Hershel Raff. ■

Metabolic Syndrome, Adrenal Steroid Levels Linked in Blacks

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Increased levels of adrenal steroids appear to contribute to metabolic syndrome in African Americans, Dr. Theodore A. Kotchen said at a meeting of the American Heart Association Council for High Blood Pressure Research.

"We speculate that the finding of a relatively high plasma aldosterone and low plasma renin activity in hypertensive African Americans may represent a forme fruste or mild variant of the spectrum of disorders that we refer to as primary aldosteronism," said Dr. Kotchen, professor of medicine at the Medical College of Wisconsin, Milwaukee.

The prevalence of hypertension in African Americans is among the greatest in the world. Their hypertension-related cardiovascular event rates are also high.

To examine the relationship between adrenal steroids—specifically, aldosterone and cortisol—and metabolic syndrome risk factors in African Americans, Dr. Kotchen and his coinvestigators studied 182 hypertensive and 215 normotensive African Americans aged 18-55 years in an inpatient clinical research unit. Roughly half were women. All subjects had temporarily discontinued antihypertensive and lipid-lowering medications weeks beforehand.

The mean plasma aldosterone value of 8.4 ng/dL in hypertensive subjects was significantly higher than the 6.3 ng/dL in normotensives. Both late-night and early-morning salivary cortisol levels were significantly higher in hypertensive individuals as well.

In contrast, plasma renin activity was inversely related to blood pressure, indicating that the increase in aldosterone in hypertensive African Americans isn't renin mediated.

Overall, 17% of study participants met criteria for metabolic syndrome. Plasma aldosterone levels were significantly higher in those with metabolic syndrome than in those without it.

Moreover, both aldosterone and blood pressure were significantly correlated with each of the individual elements of metabolic syndrome: waist circumference, cholesterol, triglycerides, body mass index, low HDL cholesterol, plasma insulin, and insulin resistance. In other words, hypertensive subjects as well as those with higher plasma aldosterone had greater waist circumference, more insulin resistance, and more unfavorable lipid profiles.

Based upon these observations, Dr. Kotchen offered the following speculation: Environmental and perhaps genetic factors contribute to the development of central obesity, which triggers increased activity of β-hydroxysteroid dehydrogenase in visceral adipose tissue. This enzyme converts metabolically inactive cortisone into active cortisol, which promotes adipogenesis and adipose tissue hypertrophy in target tissues, creating a vicious cycle that leads to further increases in cortisol.

Elevated cortisol levels result in hyperinsulinemia and insulin resistance. And there is evidence from animal and in vitro studies to suggest that elevated insulin stimulates aldosterone production through a renin-independent mechanism.

Alternatively, it's possible that fatty acids present in adipose tissue stimulate aldosterone production independent of insulin's actions. In any case, the increased aldosterone promotes sodium retention, resulting in both elevated blood pressure and a reduction in renin secretion, Dr. Kotchen explained. ■