Modest Weight Losses Fail to Benefit in PCOS

BY JEFF EVANS
Senior Writer

Overweight women with polycystic ovary syndrome may need to lose more than 5% of their weight to see improvement in inflammatory markers, reported Lisa J. Moran of the University of Adelaide (Australia) and her colleagues.

At the end of an 8-week, prospective study of the effect of dieting on metabolic risk factors and inflammatory markers, 15 women with polycystic ovary syndrome (PCOS) and 17 women without PCOS lost weight (mean of 3.9 kg [4%] vs. 4.5 kg [4.7%], respectively) and reduced fasting insulin and triglyceride to similar levels. But significantly more women with PCOS had insulin resistance (IR) after weight loss than did women without PCOS.

The metabolic benefits conferred by weight loss may be contingent on reduction on a key level of abdominal or visceral abdominal fat.

Women with PCOS tended to have higher levels of the inflammatory markers interleukin-6 (IL-6) and tumor necrosis factor–α (TNF-α) after weight loss than did those without PCOS, and none of the women in either group had a reduction in the markers' levels after weight loss, according to Ms. Moran and her associates (J. Clin. Endocrinol. Metab. 2007;92:2944-51).

The lack of a reduction in those inflammatory markers in all patients was "surprising," even though the investigators expected a similar response between groups given their comparable reductions in weight and waist circumference.

"The metabolic benefits conferred by weight loss, specifically reductions in IR, may therefore be contingent on reduction on a key level of abdominal or visceral abdominal fat," they wrote.

But in a post hoc analysis, women who had below-median C-reactive protein (CRP) levels at baseline had significantly higher increases in adiponectin—which is thought to have insulin-sensitizing, antiatherogenic, and anti-inflammatory properties—and greater reductions in triglycerides after weight loss, regardless of PCOS status. "This suggests that subjects with an adverse inflammatory profile may demonstrate less favorable metabolic improvements after weight loss," the researchers wrote.

The lack of differences in response to weight loss between the groups could mean that the participants in the study were "not representative of the general population where differences in cardiovascular risk profiles are commonly observed between women with and without PCOS." Therefore, in cases "where women with PCOS display an elevated cardiovascular risk profile in association with elevated inflammatory markers, a greater degree of weight loss [more than 5%] may be required to achieve metabolic benefits similar to subjects without PCOS," Ms. Moran and her coinvestigators wrote.

The need for greater weight loss in PCOS to reduce inflammatory markers "may be related to the elevated IR commonly observed in PCOS," the researchers wrote, because PCOS-associated IR is "predominantly associated with postreceptor defects in insulin signaling and is thus metabolically distinct from obesity-associated IR." It has been suggested that "obesity-associated increases in TNF-α and IL-6 reduce adiponectin expression and thus insulin sensitivity," making it possible that "adiponectin, IL-6, and TNF-α may not be involved in the mediation of IR in PCOS."

On the other hand, IR in women with PCOS "may require a greater reduction in weight, abdominal or visceral adiposity, and androgens to be ameliorated," the researchers noted.

"It is possible that despite the similar waist circumferences, differences in visceral abdominal fat existed between subjects with and without PCOS. This could account for the differences in fasting insulin and HOMA [homeostatic model assessment] and the differential effect of weight loss on CRP in PCOS in this study," the investigators wrote. But they thought it more likely that alterations in IR "are primarily responsible for mediating changes in cytokines and adipocytokines with weight loss."

Both groups of women, all of whom were white, had an average body mass index of about 35 kg/m^2. The patients were aged in their low- to mid-30s.

The investigators noted that besides a lack of a measurement of the ratio between the high- and low-molecular-weight forms of adiponectin, an additional weakness of the trial included not controlling for age and menstrual cycle stage. ■

Metformin May Help Reduce Acne in Polycystic Ovary Syndrome Patients

BY MARY ELLEN SCHNEIDER
New York Bureau

TORONTO — A 6-month treatment regimen of metformin can help reduce the prevalence and degree of acne in women with polycystic ovary syndrome, according to Dr. Susanne Tan and her colleagues.

The researchers treated 100 women with polycystic ovary syndrome (PCOS) and acne papulopustules with a weight-adapted dose of metformin for 6 months. The degree of acne fell from a mean of 1.5 to 0.9 and the prevalence dropped from 100% at baseline to 72% after 6 months of treatment.

The mean age of the women who participated in the study was 28 years, and they had a mean body mass index of 31.8 kg/m^2. Dr. Tan of the University Hospital Essen, in Germany, and her colleagues defined PCOS according to the Rotterdam criteria, while degree of acne was rated by the number of lesions per half of the face.

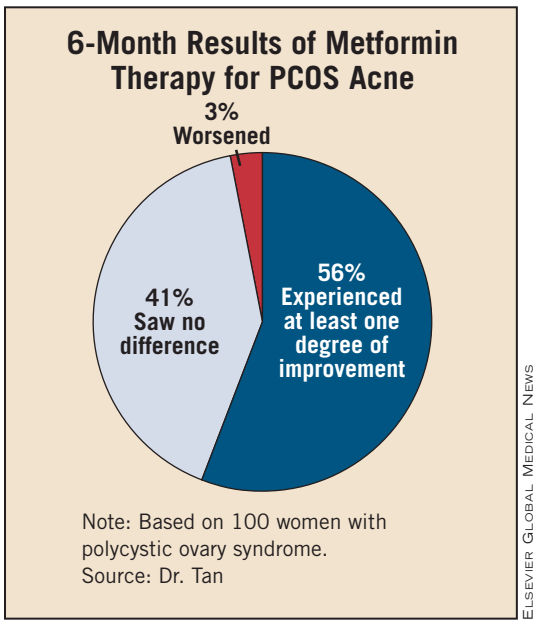
The findings were reported in a poster presentation at the annual meeting of the Endocrine Society.

Women with 1-10 lesions were considered to have degree I acne, those with 11-20 lesions had degree II, and those with 21-30 lesions had degree III. At baseline, 55% of participants had degree I acne, 39% had degree II acne, and 6% had degree III.

Hyperandrogenism and chronic anovulation were assessed at baseline and after 6 months through physical exam and blood testing, the researchers wrote.

After metformin therapy, 56% of women in the study experienced at least one degree of improvement in their acne. About 41% saw no difference, and 3% worsened, according to the study. After 6 months of treatment with metformin, there was a statistically significant decline in some PCOS symptoms, such as high BMI, amenorrhea, and acne.

There was no statistical difference in hirsutism or alopecia from baseline, Dr. Tan and her colleagues noted. ■



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Testing for Hyperandrogenism in Hirsute Women Not So Reliable

BY MARY ELLEN SCHNEIDER
New York Bureau

TORONTO — Finding the right test to screen for hyperandrogenism in hirsute women can be difficult because of a lack of reliability among affordable assays, Dr. Robert L. Rosenfield said at the annual meeting of the Androgen Excess Society.

Testing for hyperandrogenism is generally recommended when hirsutism is moderate or severe (a score of greater than 15 on the Ferriman-Gallwey scale) or if there is any degree of hirsutism accompanied by risk factors for virilizing neoplasm or polycystic ovary syndrome.

Total testosterone should be the initial screening assay, since testosterone is the major circulating androgen. However, testing is not clearly better than clinical judgment if laboratory validity is not ensured, as is often the case, said Dr. Rosenfield, professor of medicine and pediatrics at the University of Chicago.

Ideally, free testosterone would be measured, but this assay is less standardized than total testosterone assays, he said. As a result, the reliability of the assay in general laboratories is less consistent. A free testosterone determination by a specialty laboratory is indicated for patients with risk factors for tumor or polycystic ovary syndrome, even if the initial total testosterone is normal, he said.

Follow-up is an important part of the management of a mildly hirsute patient with no central obesity and no menstrual dysfunction, Dr. Rosenfield said. If a patient with mild hirsutism develops other associated symptoms, she can be tested then, he said. But overtesting is not cost-effective and can yield both false-positive and false-negative results. Dr. Rosenfield receives research support in the form of grants from the U.S. Public Health Service and Quest Diagnostics, maker of a testosterone assay.

The Endocrine Society also recently weighed in on the issue of measuring testosterone (J. Clin. Endocrinol. Metab. 2007; 92:405-13). In a position paper released in February, the Endocrine Society recommended that laboratory proficiency testing be based on the ability to accurately measure a sample containing a known concentration of testosterone, not simply on agreement among peers using the same method.

The position statement concluded that free testosterone is the most useful, clinically sensitive marker of hyperandrogenemia in women when calculated using high-quality testosterone and sex hormone–binding globulin assays with well-defined reference intervals.

In an effort to advance the field, the Endocrine Society and the Centers for Disease Control and Prevention are collaborating on the establishment of standards to validate the performance of laboratory assays of serum testosterone levels. The CDC's work is supported through a partnership between the CDC Foundation and Solvay Pharmaceuticals Inc. ■