Modest Weight Loss Is of Little 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.

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. ■

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