Metformin May Improve Metabolic Parameters

BY DIANA MAHONEY  New England Bureau

BOSTON — Treatment with metformin significantly improves body mass index (BMI) and waist circumference in women with polycystic ovary syndrome and metabolic syndrome, according to researchers at the Ewha Womans University College of Medicine, Seoul, South Korea, and colleagues.

The 113 women in the study had a mean age of 26 years and a 15% prevalence of metabolic syndrome (MS), which is lower than what has been reported in studies of PCOS patients in the United States (45%-46%) and Germany (31%). The prevalence of MS is about 4% in the general urban population of age-matched Korean women and about 6% in American women aged 20-39 years (Diabetes Res. Clin. Pract. 2007;77[suppl. 1]:S243-6).

Of the five components of the diagnosis of metabolic syndrome as per the National Cholesterol Education Program Adult Treatment Panel III, 45% of the women had a high-density lipoprotein cholesterol level of less than 50 mg/dL, 24% had a waist circumference greater than 80 cm, 20% had high systolic blood pressure (130 mm Hg or more) or high diastolic blood pressure (85 mm Hg or more), and 20% had triglyceride levels of at least 150 mg/dL. In addition, 13% had fasting glucose levels of at least 110 mg/dL. Compared with those without MS, those with MS had a higher body mass index, waist girth, systolic and diastolic blood pressures, fasting glucose, fasting and post–glucose load insulin levels, triglycerides, and free testosterone levels.

The prevalence of MS was 31% in women who entered into our clinical studies, we determined the BMI cut-off value corresponding to a waist circumference of 88 cm,“ the researchers said. The average period from initiation of metformin therapy to the most recent assessment for the study population was 31 months. The data for those who were lipid lowering or antihypertensive therapy during follow-up were analyzed up until the beginning of such therapy, said Dr. Cheang. The investigators assessed baseline and follow-up metabolic syndrome parameters using a two-sided student’s paired t test and observed a significant difference with baseline, follow-up values for BMI, diastolic blood pressure, and high-density lipoprotein level. The latter finding suggests that the pathogenic link between hyperinsulinemia and luteinizing hormone together could induce the changes that lead to polycystic ovary morphology, such as ovarian stroma and theca interna hyperplasia, and could contribute to menstrual dysfunction in adolescent girls, she said. For this reason, Dr. Bak and colleagues hypothesized that identifying the subset of adolescent girls with polycystic ovary morphology who may be more severe in those with MS,“ he said in an interview. Even young women with PCOS and MS,“ they said. Some correlations of irregular menstrual cycles and the presence of normal fasting plasma glucose tolerance testing relative to normal-weight girls with similar ovarian changes.” The latter finding suggests that the measure of insulin with the OGTT should be considered in all obese girls with irregular menstrual cycles, even in the presence of normal fasting plasma glucose“ in order to implement the proper early therapy against hyperinsulinemia,“ said Dr. Bak. Early intervention is important, she said, because the correlation between hyperinsulinemia and PCOS-like ovarian changes in this population suggests that hyperinsulinemia in adolescent girls could have a significant effect on their fertility.

“Insulin resistance is most likely the pathogenic link between PCOS and MS,” they said. Some data suggest women with PCOS and MS have higher rates of hyperandrogenemia, low serum sex hormone–binding globulin, and anacanthosis nigricans, than do those without MS. That “may reflect more severe insulin resistance” in PCOS women with MS.

Insulin Resistance More Severe in PCOS With Metabolic Syndrome

I n women with polycystic ovary syndrome, insulin resistance may be more severe in those with metabolic syndrome than in those without it, according to data from a cross-sectional study of women with PCOS.

Even young women with PCOS should be screened for metabolic disturbances to more effectively prevent cardiovascular events later in life, wrote Dr. Hwi Ra Park of the Ewha Womans University College of Medicine, Seoul, South Korea, and colleagues. "The prevalence of MS is about 4% in the general urban population of age-matched Korean women and about 6% in American women aged 20-39 years (Diabetes Res. Clin. Pract. 2007;77[suppl. 1]:S243-6)."

The findings were limited by the study’s retrospective design, Dr. Cheang said. "As information was not being collected specifically for this study, certain parameters may have been available for all patients."

The time between patient visits was inconsistent, and there was a possibility of selection bias because the clinic from which the patient pool was collected specializes in PCOS care, she said. According to study coauthor Dr. John E. Nestler, chair of the university’s division of endocrinology and metabolism, previous studies have shown that treatment with metformin, coupled with diet and exercise, improves ovulation and lowers androgen levels in PCOS patients. The latter finding suggests that the pathogenic link between hyperinsulinemia and luteinizing hormone “together could induce the changes that lead to polycystic ovary morphology, such as ovarian stroma and theca interna hyperplasia, and could contribute to menstrual dysfunction in adolescent girls,” she said. For this reason, Dr. Bak and colleagues hypothesized that identifying the subset of adolescent girls with polycystic ovary morphology who may be more severe in those with MS, “he said in an interview.

An ovary with the cysts (in black) that form in polycystic ovary syndrome.

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Metabolic Disorders

BY DIANA MAHONEY  New England Bureau

BOSTON — Adolescent girls with polycystic ovary syndrome have severe hyperinsulinemia after glucose stimulation, and the degree of insulin elevation is correlated with obesity, a study has shown. The findings emphasize the role of obesity and hyperinsulinemia in the pathophysiology of polycystic ovary syndrome, Dr. Marianna I. Bak said at the Fifth Annual World Congress on the Insulin Resistance Syndrome.

Hyperinsulinemia directly influences the ovary function by potentialization of [luteinizing hormone] secretion and, as a consequence, may lead to increased ovarian androgen production, “Dr. Bak of the Medical University of Warsaw said. It has been suggested that hyperinsulinemia and luteinizing hormone together could induce the changes that lead to polycystic ovary morphology, such as ovarian stroma and theca interna hyperplasia, and could contribute to menstrual dysfunction in adolescent girls, she said. For this reason, Dr. Bak and colleagues hypothesized that identifying the subset of adolescent girls with polycystic ovary morphology who may be more severe in those with MS, “she said in an interview.

Even young women with PCOS and MS, “they said. Some correlations of irregular menstrual cycles and the presence of normal fasting plasma glucose tolerance testing “in order to implement the proper early therapy against hyperinsulinemia, “she said. Dr. Bak. Early intervention is important, she said, because the correlation between hyperinsulinemia and PCOS-like ovarian changes in this population suggests that hyperinsulinemia in adolescent girls could have a significant effect on their fertility.

“In all of the studied ovaries, we observed small subcapsular follicles and increased stromal thickness,” Dr. Bak reported. She noted, however, that the degree of advanced morphological changes was differentiated based on BMI status. “In 50% of the obese girls, the stromal score was moderately increased [compared with the normal BMI group] and in 30% it was markedly increased,” she said. All of the girls had biochemical features of various degrees of hyperandrogenemia, and all had normal fasting glucose regardless of their BMI. In addition, although the degree of insulin elevation was increased in both groups, “insulin levels during [OGTT] were markedly higher in obese girls relative to normal BMI subjects,” said Dr. Bak. In fact, “the obese girls had a threefold higher frequency of prediabetes based on oral glucose tolerance testing relative to normal-weight girls with similar ovarian changes,” the researchers said. The latter finding suggests that the measure of insulin with the OGTT should be considered in all obese girls with irregular menstrual cycles, even in the presence of normal fasting plasma glucose “in order to implement the proper early therapy against hyperinsulinemia,” she said. Dr. Bak. Early intervention is important, she said, because the correlation between hyperinsulinemia and PCOS-like ovarian changes in this population suggests that hyperinsulinemia in adolescent girls could have a significant effect on their fertility. —Jeff Evans

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Insulin Resistance More Severe in PCOS With Metabolic Syndrome