

Some PCOS Therapies Can Lower CVD Risk

BY SHERRY BOSCHERT

SAN FRANCISCO — Metformin, some oral contraceptives, and possibly statins used to treat polycystic ovary syndrome can decrease the associated cardiovascular risk, while other oral contraceptives increase cardiovascular risk, studies suggest.

Dr. Andrea Dunaif summarized the data on cardiometabolic risk in the treat-

ment of polycystic ovary syndrome (PCOS) at a meeting sponsored by the American Diabetes Association.

“We treat women with PCOS with insulin sensitizing drugs, but we also frequently treat them to regulate their menstrual periods with oral contraceptives,” explained Dr. Dunaif, professor of endocrinology at Northwestern University, Chicago.

Previous evidence that estrogen ther-

apy can increase triglyceride levels and that certain oral contraceptives can exacerbate insulin resistance raised concern that oral contraceptives may have adverse metabolic consequences in women with PCOS.

One study randomized 48 hirsute women with PCOS to 6 months of treatment with a common oral contraceptive (Yasmin, or Yaz) containing 3 mg of drospirenone and 20 mcg of ethinyl

estradiol or the same therapy plus either metformin 1,500 mg/day or cyproterone acetate (12.5 mg/day, 10 days per cycle), a progesterone that is not used in the United States but is used in other countries (Fertil. Steril. 2009 Nov. 19 [doi: 10.1016.j.fertnstert.2009.10.016]).

Insulin sensitivity improved in patients on Yasmin alone or Yasmin plus metformin but significantly worsened with Yasmin plus cyproterone acetate in the open-label trial, Dr. Dunaif said.

A separate open-label trial randomized 100 overweight women with PCOS to 6 months of oral therapy with 35 mcg of ethinyl estradiol and 2 mg of cyproterone acetate (a formulation known in Europe as Diane-35), a low-dose oral contraceptive regimen (20 mcg of ethinyl estradiol and 100 mcg of levonorgestrel) plus the antiandrogen drug spironolactone 50 mg b.i.d., or metformin 1 g b.i.d.

Each of the treatment arms showed similar, significant improvements in PCOS symptoms and menstrual cycle length.

Insulin resistance improved significantly in the metformin group, but insulin resistance and arterial stiffness worsened in the ethinyl estradiol/cyproterone acetate group (Diabetes Care 2007;30:471-8).

“Cyproterone acetate looks to be a bad actor in these studies,” Dr. Dunaif said.

Several studies of metformin therapy in women with PCOS have shown that the drug can improve risk factors for cardiovascular disease such as endothelial dysfunction, she noted.

Compared with placebo, 12 weeks of metformin significantly decreased arterial stiffness and improved endothelial function in 30 women with PCOS in a randomized, double-blind crossover trial (J. Clin. Endocrinol. Metab. 2010;95:722-30).

Most recently, “statins are showing promise” in women with PCOS by decreasing androgen levels and improving insulin sensitivity, Dr. Dunaif added.

One prospective trial randomized 136 women with PCOS to treatment with simvastatin, metformin, or a combination of the two drugs for a period of 3 months.

Improvements in insulin sensitivity were greater with simvastatin than with metformin or with the combination, while testosterone levels decreased significantly and comparably in all groups (J. Clin. Endocrinol. Metab. 2009;94:4938-45).

“This is something to look out for in the future, to see more data on the role of statins in the treatment of women with PCOS,” she said.

PCOS has been associated with multiple cardiometabolic risk factors including increased risk for type 2 diabetes. Indirect evidence suggests that the relative risk for MI may be increased sevenfold in women with PCOS, Dr. Dunaif said. ■

Disclosures: Dr. Dunaif has been a consultant for Bristol-Myers Squibb Co., which makes metformin.