Study: Hormone Tx May Raise Ovarian Ca Risk

BY MARY ANN MOON

All hormone therapy—regardless of the formulation, estrogen dose, progestin type, dose regimen, route of administration, or duration of use—appears to raise the risk of ovarian cancer, according to a report.

If the association between HT and ovarian cancer proves to be causal, it would mean that as many as 5% of such malignancies could be attributable to the treatment. "Even though this share seems low, ovarian cancer remains highly fatal, so accordingly this risk warrants consideration when deciding whether to use [HT]," said Lina Steinrud Mørch of Copenhagen University and her associates (JAMA 2009;302:298-305)

They assessed ovarian cancer using data from the Danish Sex Hormone Register Study, a national 10-year cohort study of nearly 1 million Danish women. Ms. Mørch and her colleagues restricted their analysis to the 909,946 women who were perimenopausal or postmenopausal at baseline in 1995. This included 575,883 women who had never used HT and 334,063 who had. Among the current users of HT, nearly half had been taking the hormones for more than 7 years.

A total of 3,068 incident ovarian cancers developed during the study period, including 2,681 that were epithelial tumors. Compared with women who had never taken HT, those who had showed a relative increase of 30%-58% in their risk of developing ovarian cancer, according to Ms. Mørch and her colleagues. The risk did not differ significantly by duration of use, with women who took HT for up to 4 years showing similarly increased risk as those who took it for 5 years or more. Similarly, women who took estrogen alone had approximately the same risk as did those who took combined estrogen plus progestin.

Women who took cyclic HT had increased risk similar to that in women who took continuous HT. And ovarian cancer risk was elevated regardless of HT dosage and whether HT was delivered by oral tablet, patch, or gel.

"If the difference in risk between never users and current users is due to hormone therapy, these results imply that use of HT resulted in about 1 extra case of ovarian cancer for roughly every 8,300 women taking HT each year," the investigators wrote.

In commenting on the study, Dr. Wulf Utian, executive director of the North American Menopause Society, said, "The possibility of a very slight increase in ovarian cancer risk [with HT] should be added to the risk-benefit discussion" between the doctor and the patient. Women who have severe vasomotor symptoms negatively affecting their quality of life are likely to take the risk, he added.

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DR. UTIAN

Although Dr. Utian said the Scandinavian figures are probably "as reliable as you can get in a public health system," he said the investigators included in the progestin category drugs that are not progestins such as cyproterone acetate, an antiandrogen, and raloxifene, a selective estrogen receptor modulator (SERM).

"What they've got here is fruit salad. They've got all different kinds of products lumped together, and they haven't adequately broken them out," he said. Of the progestins that were specified, norethisterone acetate, the one most widely used in the study, was significantly associated with an increased risk of ovarian cancer; however, medroxyprogesterone acetate and levonorgestrel were not associated with an increased risk of ovarian cancer.

In addition, the investigators did not specify the type of estrogen used in their study, he noted. This contrasts with the Women's Health Initiative, a randomized, controlled study that found that Premarin (conjugated estrogens) does not increase ovarian cancer risk.

Dr. Utian reported no conflicts of interest relevant to the European drugs used in the study, but said he has consulted for several pharmaceutical companies that make estrogen products, including transdermal estrogen and SERMs. Ms. Mørch reported no conflicts of interest. Dr. Øjvind Lidegaard, an associate in the Danish study, reported receiving a grant from Schering AG, Berlin, to cover research expenses and has received fees for speeches from Schering Denmark and Novo Nordisk. ■

Felicia Rosenblatt Black contributed to this report.

BMI Tied to Depression in PCOS

BY JOYCE FRIEDEN

WASHINGTON — Women with polycystic ovary syndrome who have a high body mass index or poor body self-esteem are more likely to be depressed, according to results from a study of 67 untreated PCOS patients.

Depression is very common in PCOS patients, with previous studies showing depression rates of 35%-50% in PCOS patients compared with 12%-14% in the general female population, said Lisa Pastore, Ph.D., of the department of obstetrics and gynecology at the University of Virginia, Charlottesville, at the annual meeting of the Androgen Excess and PCOS Society. Prior research also has shown neither the degree of hirsutism nor that of acne are related to body self-esteem in PCOS patients, she added.

Eligibility criteria for the current study included a diagnosis of PCOS using the National Institute of Child Health and Human Development criteria, age 18-43 years, weight less than 250 pounds, and at least one menses in the past 6 months but no more than eight periods in the most recent 12 months without hormonal intervention. Exclusion criteria included use of metformin or hormones in the prior 60 days, current pregnancy or breastfeeding in the prior 30 days, acupuncture treatment for ovulatory disorders in the prior 30 days, and any bleeding disorder.

The mean age of study participants was 27 years; 54% were single. Overall, 39% of participants were normal weight, 12% were overweight, and 49% were obese; 27% were of minority ethnicity.

Study participants were asked to rate each of 35 items, including body parts and functions, on a 5-point Likert scale with possible responses ranging from 1 (very negative feelings) to 5 (very positive feelings).

Respondents also completed the Quick Inventory of Depressive Symptomatology–Self Report, which includes 16 items used to assess depressive episodes or major depressive disorders. Areas covered include sad mood, self-criticism, suicidal ideation, decreases or increases in appetite and weight. Participants self-reported frequency and severity of symptoms over the previous 7 days, rating severity on a scale of 0-3.

Patients underwent chemiluminescent immunoassay of total testosterone and testing for dehydroepiandrosterone sulfate and sex hormone binding globulin (SHBG). Mathematically derived free testosterone also was calculated.

Respondents' total testosterone ranged from 19 ng/dL to 161 ng/dL with a mean of 62 ng/dL. SHBG ranged from 2 nmol/L to 86 nmol/L with a mean of 31 nmol/L. Free testosterone ranged from 3 pg/mL to 45 pg/mL with a mean of 13 pg/mL. Nearly half of the patients in the study were depressed; 70% of those had mild depression, according to Dr. Pastore, the study's lead author.

The study was consistent with an association between depression severity and body esteem among PCOS patients after the researchers controlled for age, education, and BMI. Higher BMI also was correlated with depression, although body self-esteem was an independent predictor of depression in both lean and obese women.

In addition, although none of the androgens was predictive of depression severity, "there was some curvilinear relationship," with depression severity lowest among patients with very high or very low free testosterone levels, Dr. Pastore said.

The study was funded by the National Center for Complementary and Alternative Medicine and the National Center for Research Resources. Dr. Pastore disclosed no conflicts of interest. ■

Zygote Screening May Improve Outcome in IVF

BY KATE JOHNSON

AMSTERDAM — A new genetic screen of zygotes performed a few hours after in vitro fertilization has advantages over conventional preimplantation genetic screening, particularly in patients with a very poor prognosis, based on results of the first clinical application of the procedure.

Although preimplantation genetic screening (PGS) allows examination of only about half of the chromosomes in a 3-day embryo, the new technique, known as comparative genomic hybridization (CGH), can evaluate all chromosomes in newly fertilized oocytes (zygotes), Elpida Fragouli, Ph.D., reported at the annual meeting of the European Society of Human Reproduction and Embryology.

Her study of CGH in 82 women with a very poor prognosis shows an ongoing pregnancy rate of 20%, including three deliveries.

"This is exceptional considering the extremely poor prognosis of the women involved," said Dr. Fragouli of the University of Oxford (England). "This represents a doubling of the usual pregnancy rate for people who fall into this category, which is otherwise, at best, under 10%, and at worst, 0."

The women were an average of 41 years old, with histories of implantation failures and multiple unexplained spontaneous abortions, she said.

Using CGH, Dr. Fragouli and her associates found chromosomal abnormalities in 64% of 473 screened zygotes, including abnormalities in chromosomes that are not examined in conventional PGS. "With standard screening, 39% of these abnormalities would not have been detected, and 16% of abnormalities would have been incorrectly diagnosed as normal."

Only healthy zygotes were allowed to mature, resulting in 73 embryos, which were transferred to 35 patients.

The CGH technique is considered less invasive than regular PGS, because it does not require a day 3 biopsy of embryonic cells, which some experts consider damaging to the embryo. Instead, CGH involves the removal and examination of polar bodies, which are by-products of fertilization and not necessary for embryo development.

Dr. Fragouli did not declare any conflicts of interest. ■