More Research Is Needed on Aromatase Inhibitors in PCOS

BY MARY ELLEN SCHNEIDER
New York Bureau

PHILADELPHIA — The jury is still out on whether aromatase inhibitors could offer an alternative to clomiphene in the treatment of infertility associated with polycystic ovary syndrome, based on results in two small clinical trials.

Aromatase inhibitors are on the horizon, Dr. Andrea D. Coviello said at Endocrinology in the News, sponsored by Boston University, INTERNAL MEDICINE NEWS, and FAMILY PRACTICE NEWS. Although they have been approved for use in breast cancer, they are still experimental for ovulation induction. Instead of blocking the receptors centrally in the hypothalamus and the pituitary, aromatase inhibitors completely block estradiol production. Like clomiphene, aromatase inhibitor drugs are used during the follicular phase, she said.

There are significant concerns about fetal development problems in babies conceived by women who were using aromatase inhibitors.

The rationale for moving to aromatase inhibitors is that this class of drugs is thought to have fewer antiestrogenic side effects, including a lower risk of ovarian hyperstimulation syndrome and a lower risk of multiple gestation. But there are also significant concerns about fetal development problems in the babies conceived by women who were using aromatase inhibitors, explained Dr. Coviello, of the Endocrinology, Diabetes, and Nutrition Section, Boston University School of Medicine.

A definitive study that would help physicians assess how aromatase inhibitors stack up to clomiphene has yet to be done. The available data are derived from very small studies, she noted.

In a prospective, randomized trial of 74 patients, researchers did not find a significant difference in pregnancy rates between women who received clomiphene and those who received the aromatase inhibitor letrozole (Fertil. Steril. 2006;86:1447-51). However, the researchers found significantly lower estrogen levels in the letrozole group on the day of human chorionic gonadotropin administration, Dr. Coviello said.

Another study, published online, compared the efficacy of letrozole and clomiphene among women who had failed to ovulate when taking 100 mg/day of clomiphene citrate (Fertil. Steril. 2008 January [Epub doi:10.1016/j.fertnstert.2007.08.044]). Sixty-four patients were randomized to receive either 7.5 mg/day of letrozole or 150 mg/day of clomiphene. The researchers found that letrozole had better ovulation and pregnancy rates compared with clomiphene. However, those results came as no surprise because the women in the study were clomiphene resistant, Dr. Coviello said. So although it showed that letrozole is not inferior in terms of ovulation, it failed to make the case that aromatase inhibitors outperform clomiphene.

Dr. Coviello stated she had no financial conflicts of interest to disclose. INTERNAL MEDICINE NEWS, FAMILY PRACTICE NEWS, and this newspaper are published by the International Medical News Group, a division of Elsevier. ■

Cardiac Events in LQTS Plunge After Menopause

BY BRUCE JANCIN
Denver Bureau

CHICAGO — The high cardiac event rate in women with long QT syndrome drops dramatically post menopause, according to a registry analysis.

This finding suggests that estrogen is a major contributor to arrhythmic events in women with long QT syndrome (LQTS), Jehu S. Mathew reported at the annual meeting of the American College of Cardiology.

If this indeed proves to be the case, the clinical implications could be profound. Planned future observational studies will look at LQTS patients who are on antiestrogen therapy—tamoxifen or aromatase inhibitors—for prevention of breast cancer. If their cardiac event rate turns out to be substantially lower than expected, it could open the door to a whole new form of cardiovascular preventive therapy in the extremely high-risk population of women with heritable LQTS, added Mr. Mathew, a fourth-year medical student at the University of Rochester (N.Y.), in an interview.

"The potential impact of those therapies on women with long QT syndrome is astounding if estrogens are actually implicated in their cardiac event risk," he observed.

Mr. Mathew reported on 1,624 women aged 20-70 years who were enrolled in the International Long QT Syndrome Registry, including 560 who were postmenopausal. The risk of the combined end point of syncope, LQTS-related sudden death, or aborted cardiac arrest was 94% lower in the postmenopausal group.

The impact of menopause was particularly striking in women with the LQT2 genotype. Their annual combined event rate was 11.86/year before menopause and 1.91/year after menopause.

Among women with a QTc interval of 500 msec or more, the event rate was 9.68/year before menopause and 2.35/year afterward. And among women with a history of syncope before age 20, the event rate was 8.21/year prior to menopause, compared with 2.26/year postmenopause.

The genesis for this study examining the influence of menopause on cardiac events in LQTS was prior work establishing that females have a substantially higher cardiac event rate than have males with LQTS and that women with LQTS have a higher event rate during the first 9 months post partum—a period of hormonal flux—than they do during pregnancy. ■

Lamotrigine Aids Pain, Depression In Women With Chronic Pelvic Pain

BY KERRI WACHTER
Senior writer

BALTIMORE — The anticonvulsant lamotrigine shows promise for reducing pain and improving mood symptoms associated with chronic pelvic pain, particularly in women with the vulvovaginal subtype.

In a study of 43 women with chronic pelvic pain, researchers at the University of North Carolina found that treatment with lamotrigine resulted in significant reductions in total pain, overall pain intensity, and depressive symptoms at 8 weeks, compared with baseline.

There were slightly greater reductions in those measures at 12 weeks that achieved significance. The study, which was presented as a poster at the annual meeting of the American Psychosomatic Society, was funded by GlaxoSmithKline Inc., maker of Lamictal (lamotrigine).

Dr. Samantha Meltzer-Brody of the department of psychiatry at the University of North Carolina, Chapel Hill, and her colleagues recruited women from a tertiary care clinic. Participants had to have pelvic pain for at least 6 months. Women were excluded if they had active systemic disease or substance abuse, pelvic surgery in the previous 6 months, or initiation/change in psychiatric medications in the previous month.

After baseline assessments, the women were titrated up to a therapeutic dosage of 400 mg/day lamotrigine over 8 weeks. This dosage was continued for weeks 8-12. Patients then were slowly discontinued from the drug over a 2-week period. A total of 31 women completed the 8-week titration phase and 21 completed all 12 weeks of treatment. Patients completed the McGill Pain Scale at each visit. Patients were also administered the Hamilton Depression Rating Scale.

The women completing 8 weeks of treatment were aged 41 years on average and were predominantly white (95%). The average dosage in that period was 340 mg/day. Most of the women had the vulvodynia/vulvar vestibulitis syndrome subtype (17). The remaining women were evenly split between diffuse abdominal pain (7) and neuropathic pain (7).

The researchers also analyzed the data by chronic pelvic pain subtype. Those with the vulvovaginal pain subtype (VVS) had significant reductions in McGill total pain and visual analog scale overall pain intensity scores at weeks 8 and 12. They also had a significant reduction in Hamilton Depression Rating Scale scores at 12 weeks. However, the investigators noted in the poster that "VVS patients have better mental health and decreased rates of sexual and/or physical abuse history compared to women with other chronic pelvic pain subtypes." ■

Urinary Incontinence Is Not More Severe With Bacteriuria

SAVANNAH, GA. — Urinary incontinence symptoms do not appear to be more prevalent or more severe in women with bacteriuria, based on a study of 530 urogynecology patients seen at one institution.

Dr. Mary P. Fitzgerald, of the obstetrics and gynecology department at Loyola University in Chicago, and her colleagues conducted a chart review of all new urogynecology patients seen from March to December 2004. Scores from the Urogenital Distress Inventory (UDI6) and Medical, Epidemiological, and Social Aspects of Aging (MESA) incontinence questionnaires were available. Urine cultures had been obtained by catheterization. Significant infection was considered to be present if at least 10,000 colonies of uropathogen were present.

Of the 530 patients, 62 (12%) had positive cultures, Dr. Fitzgerald reported in a poster session at the annual meeting of the Society of Gynecologic Surgeons. UDI6 and MESA scores were compared between women with and without positive cultures. Uropathogen antibiotic sensitivities were compared with those of the general hospital population at that time.

Uropathogens included *Escherichia coli* (43), *Klebsiella pneumoniae* (13), *Proteus mirabilis* (4), Group B *Streptococcus* (1), and *Citrobacter freundii* complex (4). Antibiotic resistance profiles of the uropathogens were similar to those found in the general hospital population.

"We suggest that incontinence may not be a reliable symptom of bacteriuria in women attending a female urology/urogynecology clinic," the researchers wrote.

Dr. Fitzgerald reported that she had no relevant financial relationships.

—Kerri Wachter