Infertility Studies Support Anastrozole, Letrozole

Christopher S. Sipe, M.D., lead investigator of the anastrozole study, said in an interview that he believes enough data exist for physicians to start prescribing aromatase inhibitors for infertility patients, but that few will without an indication for infertility from the Food and Drug Administration. “I think you can still use it, but I don’t think a lot of people will with the medicolegal aspects in the field,” said Dr. Sipe of the department of ob-gyn, at the University of Iowa Hospitals and Clinics, Iowa City.

The anastrozole trial recruited 50 couples from the University of Iowa Infertility Treatment Center. Patients with tubal factor infertility or severe male factor infertility were included. Women were randomized to receive 1 mg of anastrozole or 100 mg of clomiphene citrate on cycle days 3 through 7, followed by a single injection of 75 IU of purified FSH on days 7 through 11. On day 12, ultrasound and measurements of serum estradiol were initiated and performed every other day if needed. FSH injections continued until a follicle greater than 18 mm was observed and the patient received 10,000 U of human chorionic gonadotropin. IUI followed 36 hours later. Overall, the cancellation rate was 16% and the pregnancy rate 18% with nine pregnancies achieved. Though the pregnancy rates of 16% with anastrozole and 20% with clomiphene were similar, Dr. Sipe said the trial was too small to draw conclusions.

Women who took anastrozole before undergoing IUI had a pregnancy rate comparable overall with those treated with clomiphene and IUI.

“This study did not have enough patients to look at the multiple pregnancy rates—you need 1,200 patients or so that is what we are thinking,” Dr. Sipe said.

Perhaps the most provocative finding was in women with polycystic ovary syndrome. Anastrozole produced more follicles overall with those patients suggesting the aromatase inhibitor could produce fewer multiple births.

Infertility Work-Up Should Include Examination With TVL, Expert Says

London — The modern infertility work-up should include a transvaginal hydrosalpingoscopy to visualize the tubes and ovaries, said Stephan Gordits, M.D., of the Leuven (Belgium) Institute for Fertility and Embryology.

He pioneered transvaginal hydrosalpingoscopy (TVL) in 1998 (later, another group named the procedure “fer-toscopy”) and said he’s simple abandoned tubal assessment by hysterosalpingoscopy (HSG).

Whereas the HSG can explore tubal patency only, “with TVL you have a more complete exploration of the patient,” he told this newspaper.

Speaking at the annual congress of the International Society for Gynecologic Endoscopy, Dr. Gordits explained that TVL can evaluate both the tube and its outside of a patient’s reproductive organs and can evaluate adhesions and endometriosis by incorporating hysteroscopy and transvaginal hydrosalpingoscopy, salpingoscopy, and tubal patency testing.

TVL can be done in an ambulatory setting, under local anesthesia, and requires only an oocyte aspiration room, rather than a full operating theater. The procedure is performed with the insertion of a needle transvaginally into the pouch of Douglas followed by infusion with saline. An endoscope can be introduced, allowing visualization of the outside of the uterus, the ovaries, and the distal part of the fallopian tubes. The scope can be introduced a few centimeters into the distal end of the fallopian tube for evaluation of the ampulla and the inside of the distal tube. A biopsy can reveal the presence of normal cilia movement.

At the same time, a hysteroscope can visualize through the cervix, allowing evaluation of the inside of the uterus, and infusion of dye through the fallopian tubes to assess their patency. The presence of saline makes adhesions and subtle endometriotic lesions flat, allowing for easier identification. The procedure is often masked under the high intraabdominal pressure of laparoscopy,” Dr. Gordits said.

Although it’s primarily a diagnostic procedure, TVL can be used to perform adhesiolysis, treat mild to moderate endometriosis, and drain ovaries in patients with polycystic ovarian disease.

Unlike Dr. Gordits, Jacques Donnez, M.D., he believes there is still a place for HSG in the fertility work-up—and the combination of HSG and TVL might offer the most thorough tubal assessment.

Although TVL can visualize a few centimeters of the inner distal fallopian tube, and evaluate patency by confirming spillage of dye infused through the cervix, it offers no other information about the status of the proximal tube, said the professor and head of gynecology at Catholic University of Louvain in Brussels.

“You can see if the dye is not going through, but if this happens you have no idea of the location of the blockage or if there is some diverticuli or anomalies in the proximal tube,” he said in an interview. “HSG currently the only procedure for this because they had fewer symptoms or less severe symptoms—probably had more premenopausal estrogen.”

Smoking, Estrogen Bad Combination for Alzheimer’s

By Michele G. Sullivan

Miami Beach — The risk of Alzheimer’s disease declines by almost half among postmenopausal nonsmokers who use estrogen therapy, but nearly doubles among those who both smoke and use estrogen therapy, Rosebud O. Roberts, M.B., said in a poster presented at the annual meeting of the American Academy of Neurology.

Dr. Roberts, an epidemiologist at the Mayo Clinic, Rochester, Minn., also found that early estrogen therapy might be a predictor for Alzheimer’s in postmenopausal women; in contrast, estrogen therapy taken later in life appears to be more protective. But these conclusions may have more to do with premenopausal estrogen levels than postmenopausal estrogen therapy, she said in an interview.

“What I suspect is that smoking may lead to lower estrogen levels premenopausally, which could lead to brain neurons that are less viable and more likely to die early. Those who initiate therapy earlier probably have less [endogenous] estrogen, and more symptoms, while those who initiate therapy at a later age—because they had fewer symptoms or less severe symptoms—probably had more premenopausal estrogen.”

She and her associates conducted a case-control study that included 216 women with natural menopause who developed Alzheimer’s disease during 1985-1989. They were compared with 210 cognitively intact controls who had similar ages and menarche and menopause.

A similar percentage of women in both groups used estrogen therapy for at least 6 months (11.6% of cases, 14% of controls). Of the 54 women on estrogen, the 25 with Alzheimer’s started estrogen therapy earlier than the 29 controls (50 years vs. 53 years), and had a shorter lag time between menopause and the initiation of estrogen therapy (1 year vs. 4 years). Estrogen users had a 20% reduced risk of Alzheimer’s disease, but this was not statistically significant.

The investigators did see significant differences in estrogen therapy and the risk of Alzheimer’s disease between men and women, however. The odds ratio of Alzheimer’s was 1.93 in smokers who used estrogen therapy and only 0.54 in nonsmokers who used estrogent therapy. In women who used estrogen therapy of more than 3 years duration showed a significant protective effect, reducing the risk of Alzheimer’s by almost 70%.

“It is in women who don’t smoke where we see the beneficial effects of [estrogen therapy],” she said.