May Impact Fertility in JIA Patients

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

DENVER – Chronic methotrexate therapy may harm the future fertility of girls and young women being treated for rheumatoid arthritis or juvenile idiopathic arthritis, based on preliminary findings from a prospective observational study.

“The biggest issue is that rheumatologists have become much more aggressive in their therapy for these young girls with juvenile idiopathic arthritis in the last 5-10 years. As early as 1 year of age, these girls are placed on methotrexate weekly for years and years. It’s very common for the mothers and fathers sitting in the clinic to ask this question: Is this therapy going to affect my daughter’s ability to have kids in the future?” Dr. Amber R. Cooper said at the meeting.

The study findings suggest a need to alter how physicians counsel patients and their families on this score in light of emerging evidence that long-term contraceptive therapy with methotrexate may threaten the oocyte pool, she said.

Thus far, 168 females aged 4-49 years have been recruited for the ongoing study from pediatric and adult rheumatology clinics. Every 3-4 months they undergo measurement of serum anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), inhibin B, and other indicators of ovarian reserve. In addition, transabdominal ultrasound is performed annually by sonographers blinded as to the patients’ treatment regimen in order to assess ovarian volume and antral follicle count, explained Dr. Cooper of Washington University in St. Louis.

Among the study participants, 55% have juvenile idiopathic arthritis, formerly called juvenile rheumatoid arthritis, and 43% have rheumatoid arthritis. The rest have psoriatic arthritis or undifferentiated spondyloarthropathies. The subjects’ mean age at diagnosis was 18.6 years, while at enrollment in the fertility study they averaged 25.4 years of age. Forty-three percent were on methotrexate or the related drug leflunomide, 12% were on a tumor necrosis factor (TNF) antagonist, 30% were on both, and 15% were on other agents, mainly corticosteroids, hydroxychloroquine, or sulfasalazine.

The primary study end point is change over time in AMH level, widely considered to be the best indicator of ovarian reserve. At enrollment, the median AMH level was 2.23 ng/mL in patients on methotrexate or leflunomide, 1.65 ng/mL in patients on a TNF antagonist, 2.42 ng/mL in patients on both, and 2.54 ng/mL in patients on other agents.

In a multifactorial analysis, patients on methotrexate/leflunomide were the only ones who showed a progressive decline in AMH with increasing time on therapy. In addition, patients on methotrexate or methotrexate plus another TNF biologic had significantly lower antral follicle counts than did other patients.

This preliminary finding that methotrexate may diminish ovarian reserve in patients being treated for rheumatologic diseases is biologically plausible. The drug targets rapidly dividing cells, which could include ovarian or endometrial cells, Dr. Cooper noted.

Moreover, the study findings are consistent with earlier reports by reproductive endocrinologists at Stanford (Calif.) University. The Stanford researchers found that the use of methotrexate to treat ectopic pregnancy in women being treated for infertility was associated with a significant but brief time-limited decline in oocytes retrieved when the patients subsequently underwent controlled ovarian stimulation. It took about 18 days following methotrexate -Continued on following page
Obesity Is a Barrier to Mammography Compliance

BY ESTHER FRENCH
FROM THE JOURNAL OF WOMEN’S HEALTH

Younger age, obesity, more recent health plan membership, and lower family income all lower the likelihood that a woman will complete a mammogram, reported Dr. Adrienne C. Feldstein and her associates at Kaiser Permanente Northwest in Portland, Ore. Younger age increased the likelihood that a woman would report being “too busy” to get a mammogram and that she would have more doubts about its usefulness or accuracy. Family income was a more significant variable than was race in mammogram completion, which is “consistent with findings from other studies,” they noted (J. Womens Health 2011 [doi:10.1089/jwh.2010.2195]).

In a study of 4,708 women aged 50-69 years, investigators first estimated a patient’s likelihood of completing a mammogram during a 10-month follow-up period after patients received multiple reminders over 3-4 months. Variables included age, visits to an ob.gyn. or primary care physician, race, family income, length of health plan membership, and body mass index.

In the study’s second phase, a subgroup of 540 women completed a mailed survey that identified barriers to and facilitators for mammograms by answering yes or no to provided statements such as “I’m embarrassed about having mammogram.” Their replies showed that although repeated reminders are effective, significant obstacles still remain.

Pain emerged as one of the major barriers for patients. The study cited 25% of the patients as reporting that a mammogram “causes too much pain,” and in obese patients the percentage rose to 31%.

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The relationship between pain and obesity remains unclear and could be the subject of further investigation, Dr. Feldstein said in an interview.

Meanwhile, she recommended that mammography providers explore ways to reduce pain for all patients.

“If you have the technician do the initial compression, and then the patient verbally controls the pressure from that point on, that seems to reduce the patient’s pain and still preserve the quality of the x-ray image,” Dr. Feldstein said.

The study was funded by the National Cancer Institute. Dr. Feldstein and her associates said they had no relevant financial disclosures.

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