ARTHRITIS CAPSULES

Epidemiology was the word of the day in a sampling of posters presented at the annual meeting of the American College of Rheumatology. Below are three posters that received a lot of attention at this year's meeting. The report on heart failure risk in rheumatoid arthritis was one of this year's blue ribbon–winning posters.

RA Severity Predicts Heart Failure

The risk for new-onset heart failure in patients with RA is greatest in patients with the most severe disease, Dr. Soko Setoguchi of Brigham and Women's Hospital in Boston and her associates reported. The research involves 8,483 patients whose RA was diagnosed by a rheumatologist and who were enrolled in the CORRONA (Consortium of Rheumatology Researchers of North America) registry. Patients were followed from the time of registry enrollment until Dec. 15, 2006, or death, whichever happened sooner. Patients' mean age was 59 years, 75% were female, 93% were white, 15% were current smokers, and their mean body mass index was 29 kg/m^2. Although none had heart failure at enrollment, some had other cardiovascular risk factors, including coronary artery disease (5%), hypertension (28%), hyperlipidemia (9%), and diabetes (6%). In all, 26 cases of new-onset heart failure were confirmed by the rheumatologists' medical records (a primary outcome), and 33 were reported only by the physician on a follow-up CORRONA form (secondary end point). Findings from Cox proportional hazard regression show that overall markers of RA severity were associated with the risk for heart failure. After multivariate analysis, the strongest indicators were scores on the modified Health Assessment Questionnaire that indicated limited function (hazard ratio, 2.8; 95% confidence interval, 1.6-4.9), extra-articular manifestation (HR, 1.2; 95% CI, 0.5-2.7), and steroid dose greater than 7.5 mg (HR, 4.1; 95% CI, 1.5-10.7). The study was funded by CORRONA.

Women's RA Risk Is Twice Men's

The lifetime risk for RA has remained "remarkably stable" during 1945-1995, according to Cynthia S. Crowson and her associates from the Mayo Clinic in Olmsted, Minn. For men, the lifetime risk is 1.8%; for women, it ranges from 3.4% to 3.7%. This stability occurred despite a gradual decrease in the incidence of RA from 1955 to the mid-1980s. More recently, women are experiencing an increased incidence, whereas that of men remains steady. The investigators used participants in the population-based incident cohort of Olmsted County who fulfilled the 1987 ACR criteria for RA between 1995 and 2005. These findings come from Poisson regression analyses performed to calculate the observed incidence rate in each sex. Calling the lifetime risk "significant" and women's higher lifetime risk "substantial," the investigators noted an additional worry in their poster: The lifetime risk may be even higher in some subgroups with high-risk genotypes. This research was funded by the National Institutes of Health.

Uveitis Incidence Established in AS

Noninfectious uveitis is more than 20 times more common in patients with ankylosing spondylitis than in the general population, judging from findings presented by Shelagh M. Szabo of Oxford Outcomes in Vancouver, B.C., and colleagues. Using longitudinal physician billing data from Quebec province, the investigators calculated that 7,663 people were diagnosed with AS between 1998 and 2006 (the AS 1 group); another 3,006 people were diagnosed with AS during that time period and were seen for a related visit at least once during the next year (AS 2). The AS 1 group was designed to maximize sensitivity and the AS 2 group to maximize specificity. The AS 1 patients may have had milder disease. The investigators used a 1% random sample of unaffected individuals from Quebec (the population of which was 7.6 million in 2006) as the control group. The crude 10-year incidence of noninfectious uveitis in the AS 1 patients was 368 cases per 10,000 persons; for the AS 2 group, it was 482 cases per 10,000 persons; in the control group, the incidence was 21 cases per 10,000 persons. The standardized incidence ratio (SIR) for uveitis development during the study period was 18.04 for those in AS 1 vs. the controls. The SIR was 23.88 for those in the AS 2 group vs. controls. Age played a significant factor in incidence, with those in the 20- to 39-year-old age group having the largest risk. In the AS 1 group, the uveitis incidence was 53 cases per 1,000 persons in those aged 20-39 years vs. 33 per 1,000 for those aged 40-59 years, and 8 per 1,000 for those aged 60 years or older. In the AS 2 group, the uveitis incidence was 69 per 1,000 persons in those aged 20-39 years vs. 40 per 1,000 persons for those aged 40-59 years, and 13 per 1,000 for those aged 60 years or older. Several of the researchers were employed by Abbott Laboratories.

—Sally Koch Kubetin

Biologics and Pregnancy: Insights From the OTIS Study

BY AMY ROTHMAN SCHONFELD

PHILADELPHIA — Women with rheumatic disease who took etanercept during pregnancy were three times more likely to have a child with a major malformation than was a disease-matched comparison group, judging from interim results from a small sample.

Most of the malformations were isolated, and no patterns of birth defect were apparent, according to Christina Chambers, Ph.D., who presented the findings from the Autoimmune Diseases in Pregnancy Project being conducted by the Organization of Teratology Information Specialists (OTIS) at the annual meeting of the American College of Rheumatology.

"Although outcomes were presented for these pregnancies, I always caution health care providers and patients that these are ongoing studies with a target sample size that is intended to have sufficient power to answer our research questions. For that reason, we have not performed any formal interim statistical analysis nor have we adjusted for differences between groups, such as maternal smoking or folic acid use, that may affect pregnancy outcomes," said Dr. Chambers of the department of pediatrics and family and preventive medicine at the University of California, San Diego.

OTIS is a prospective observational cohort study with the purpose of evaluating the effects of autoimmune diseases and their treatment on pregnancy outcomes and fetal development. Recruitment began in 2000 and is projected to continue through 2015. Current recruitment stands at 944, with a goal of 1,500.

Pregnant women are typically enrolled in the study before they reach 20 weeks of gestation. To be enrolled, the women must have current diagnoses of rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriasis and psoriatic arthritis, or Crohn's disease. Many participants are referred by their rheumatologists to the OTIS coordinating center, where they undergo multiple interviews and review of their symptom management. After birth, the infants are followed for up to a year, during which time they are assessed by their pediatricians, undergo blinded dysmorphological examination by OTIS physicians, and are photographed.

"Evaluating pregnancy outcomes following medication exposure is a not a situation that lends itself to conducting a randomized controlled trial for obvious ethical reasons," said Dr. Chambers. Although the literature contains case reports, the OTIS project is designed to give clinicians the evidence-based information they need to counsel patients who are pregnant or considering becoming pregnant.

At the time of this progress report, outcome was available for 115 women with RA who had been exposed to etanercept, compared with 55 disease-comparison controls. Outcome was available for 42 women with RA who were exposed to adalimumab, compared with 58 disease-matched women and 84 healthy controls. The percentage of live births was higher in those treated with etanercept, compared with those with similar rheumatic diseases (92% vs. 85%), and fewer spontaneous abortions occurred in the etanercept-treated group (4% vs. 11%). There were no ectopic pregnancies in either group. One stillbirth was reported in the etanercept cohort and none in the controls. Preterm deliveries were more common in women who were taking etanercept (23% vs. 13%).

Of the major malformations among all pregnancies enrolled in OTIS, 12% (14 of 114) were reported in the etanercept group, compared with 3.8% (2 of 53) in the disease-matched controls.

The defects included displaced stomach with epispadias and congenital eye defect; ventricular septal defect with peripheral pulmonic stenosis; pyloric stenosis; hypospadias; ventricular septal defect with patent foramen ovale and patent ductus arteriosus; volvulus; patent foramen ovale; atrial septal defect with patent ductus arteriosus; microcephaly; congenital hypothyroidism; and an unspecified heart defect. Three abnormalities—Noonan syndrome, Turner syndrome, and Down syndrome—were genetic or chromosomal. No cases of the malformation patterns VATER or VACTERL were found.

"Typically we would see a specific pattern of malformation with a medication that truly causes defects, but our results indicate that most of the defects were isolated with no apparent patterns," Dr. Chambers said.

'Firm conclusions await the accumulation of target sample size' needed for multivariate analysis.

DR. CHAMBERS

For those exposed to adalimumab, the percentage of live births was lower in those receiving the drug (88%) compared with those with similar autoimmune illnesses (93%) and healthy controls (92%). The rate of spontaneous abortions also was higher in the adalimumab-treated cohort (12%) compared with the disease-matched (5%) and healthy (1%) cohorts. There were no ectopic pregnancies or stillbirths in the drug-treated group.

Preterm delivery was higher in both the adalimumab-treated (14%) and disease-matched comparison (17%) groups, compared with healthy controls (4%). Mean birth weight was approximately 300 g less in term infants whose mothers had received adalimumab, compared with healthy controls, but similar to term infants in the disease-matched comparison group. Rates of major malformations were similar (4% to 5%) in all groups and within the range of expected numbers in the general population, said Dr. Chambers.

"Firm conclusions await the accumulation of target sample size for adalimumab and etanercept and multivariate analysis.

"It is important to recognize that many differences between medication-exposed and comparison groups can be accounted for by other maternal risk factors, and so until these are addressed in multivariate analysis, we are dealing with very preliminary results. We also will be evaluating minor anomalies, 1-year growth, and developmental screening data," Dr. Chambers said. ■