Neonatal Lupus Study Seeks Pregnant Women

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Intravenous immune globulin has been suggested as a possible therapy for preventing congenital heart block caused by neonatal lupus, and early data from a study of the treatment indicate that further study is warranted.

Of five women with a previous fetus affected by neonatal lupus—who thus are at increased risk of having a baby with congenital heart block—who were enrolled at press time in the Preventive IVIG Therapy for Congenital Heart Block (PITCH) study, three had given birth to babies without congenital heart block following IVIG treatment, one was still undergoing treatment but showed no fetal echocardiographic evidence of congenital heart block, and one had not reached 12 weeks' gestation and therefore had not begun treatment, principal investigator Dr. Jill Buyon said during an informational teleconference on the study. At least 19 total patients are needed to adequately power this open-label first- phase of the PITCH study, which is sponsored by New York University and the Alliance for Lupus Research, said Dr. Buyon, professor of medicine and vice chair of the department of rheumatology at New York University.

An additional 35 patients will be needed for the second phase of the study, which will proceed if fewer than 3 of the 19 women in the first phase have children with second- or third-degree heart block.

Neonatal lupus can affect babies of mothers with SSA/Ro and SSB/La autoantibodies, and can appear as a transient rash that disappears by the time the baby is about 6 months old, or, in rare cases, as a transient abnormal blood or liver condition. In some cases, however, congenital heart block occurs in affected fetuses, causing permanent heart damage and fetal death.

The risk of congenital heart block is about 2% in a first pregnancy for women with anti-Ro and anti-La antibodies, but the risk jumps to 20% in subsequent pregnancies in women who have had a previous child with congenital heart block or neonatal lupus-related rash, coinvestigator Dr. Deborah Friedman of St. Barnabas Medical Center in Livingston, N.J., said.

Since no therapy has been successful for the treatment of complete heart block, the focus has shifted to prevention of the condition, which appears to occur because of scarring of the conduction system that results from inflammation triggered by the mother's antibodies.

The scarred heart beats extremely slowly, and 20% of affected babies die—most of them within 2 weeks and in utero. Surviving babies almost always require permanent implantation of a pacemaker.

Giving IVIG to at-risk mothers was suggested as a potential preventative therapy because it has the potential to lower maternal antibody levels, thereby reducing fetal exposure, and also to influence effector mechanisms in the fetus itself. Furthermore, IVIG has been shown to be safe in pregnancy, Dr. Buyon noted.

Having a total of 19 women enrolled in the first phase of PITCH will provide adequate power to demonstrate a reduction of risk from 20% to 5% in women with a previously affected child. Patients will receive 400 mg/kg IVIG every 3 weeks for a total of five treatments from weeks 12-24 of pregnancy.

IVIG will be considered efficacious and worthy of further study if fewer than six women in phase II of PITCH have a child with advanced heart block.

Participants should be aged 18-50 years, have a current intrauterine pregnancy of less than 12 weeks, and have circulating SSA/Ro and/or SSB/La antibodies. Participants also should have a previous child with congenital heart block of any degree, which has been documented by EKG and/or echocardiogram; with confirmed characteristic lupus rash; or with congenital heart block and rash.

Women with rheumatic disease can participate if they aren't taking more than 20 mg/day of prednisone. Other exclusion criteria include conditions that would contraindicate the use of IVIG such as a prior serious IVIG infusion reaction, known IgA deficiency, intolerance of volume load, and nephrotic syndrome. Those with a fetus with structural lesions that could cause congenital heart block also are excluded.

Those interested in enrolling patients in PITCH should refer to ClinicalTrials.gov identifier NCT00460928, and should contact research administrator, Lena Geffrard, by calling 212-263-2255 or sending an e-mail to geffrl01@med.nyu.edu. ■