Use Echocardiograms in Fetal Heart Block

BY SALLY KOCH KUBETIN

NEW YORK — High-dose steroid therapy only rarely lessened the degree of congenital heart block in one study of 30 affected pregnancies, according to Dr. Jill P. Buyon.

In a prospective, multicenter, observational study, 30 pregnancies involving a fetus with some degree of autoimmune-associated congenital heart block were treated with 4 mg/day of dexamethasone. In all, 22 of the fetuses had third-degree heart block, 6 had second-degree heart block, and 2 had first-degree heart block. Another 10 similar pregnancies that were not treated with dexamethasone served as the control group, in which nine fetuses had third-degree heart block and one had first-degree heart block. Initial median ventricular rates, age at diagnosis, and degree of cardiac dysfunction were similar between groups, said Dr. Buyon, professor of medicine at New York University.

Although this was initially intended to be a randomized, controlled trial, that plan was not feasible, so the decision to treat with dexamethasone was made by the managing physicians.

Six deaths occurred in the group that was treated with dexamethasone, and four deaths occurred in utero, one at 15 months post partum and the other at 2 years of age.

None of the 40 fetuses experienced a reversal of third-degree block, either with therapy or spontaneously. In fetuses who were treated with dexamethasone, one in six with second-degree block progressed to third-degree block, and three remained in second-degree block at birth. After birth, one child was given a pacemaker; two others progressed to third-degree block. At birth, two babies with second-degree heart block converted to normal sinus rhythm. While one maintained sinus rhythm, the other reverted to second-degree heart block. Of the two fetuses with first-degree heart block, both converted to normal sinus rhythm at birth and maintained it throughout follow-up (Am. J. Cardiol. 2009;103:1102-6).

Among the 10 fetuses in the control group, 9 with third-degree block in utero maintained it, and 1 with first-degree block converted to sinus rhythm, Dr. Buyon said at a rheumatology meeting sponsored by the university. These findings do not preclude ever using dexamethasone in such pregnancies, she said. Physicians who elect to use dexamethasone in affected pregnancies should stop the therapy if it proves ineffective, which can be ascertained using serial echocardiograms. Physicians need to remember that every case is individual and the guidelines may be of limited applicability.

A fetus who is found to have a third-degree block of more than 1 week's duration should be followed with weekly echocardiograms and obstetric ultrasound, but no therapy, she said. When the third-degree block is shorter than 1 week in duration, the baby should be given 4 mg of dexamethasone daily for 1-2 weeks. Therapy should be discontinued if the baby's condition does not improve. However, if the baby's heart block reverses to second degree or even milder, the treating physician should consider continuing daily dexamethasone for 4-6 weeks and continuing weekly echocardiograms. ■

Disclosures: *Dr. Buyon said she had no relevant financial relationships to disclose except for support from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the American Heart Association, the Kirkland Center, the Alliance for Lupus Research, and a gift from the Lee family of Brooklyn, N.Y.*

Prolonging MTX for 1 Year Doesn't Cut JIA Relapse Rate

BY MARY ANN MOON

The continuation of methotrexate therapy for 12 months after a child with juvenile idiopathic arthritis has achieved remission did not decrease the relapse rate, compared with treatment for 6 months, according to a report in JAMA.

Longer continuation of methotrexate also failed to extend the duration of remission, said Dr. Dirk Foell of the University of Muenster (Germany) and his associates. "Therefore, it cannot be recommended that methotrexate therapy be continued in all patients for longer than 6 months after remission is induced," an approach that has been advocated even though no controlled prospective studies have examined the issue until now.

Approximately half of patients with JIA experience disease flares after they discontinue methotrexate.

The researchers assessed 364 patients who were treated at rheumatology centers in 29 countries in a randomized, prospective, open-label trial.

Patients with all subtypes of JIA were included, and all subjects had achieved remission with methotrexate therapy. The children were about 11 years old at enrollment; they had been about 5.5-6 years old at JIA onset.

Group 1 (183 children) was randomly assigned to continue the drug for 6 months, whereas group 2 (181) was assigned to continue methotrexate for 12 months. They were then followed every 3 months for at least 1 year (median follow-up, 34 months).

Approximately equal numbers of children in groups 1 and 2 had persistent oligoarthritis (30% and 23%, respectively), extended oligoarthritis (19% and 12%), polyarthritis that was negative for rheumatoid factor (30% and 45%), polyarthritis that was positive for rheumatoid factor (5% and 4%), systemic onset JIA (8% and 12%), enthesitis-related arthritis (4% and 2%), and psoriatic arthritis (6% and 2%).

The relapse rate at 1 year was about 57% in the children who discontinued methotrexate at 6 months, which was not significantly different from the rate of 56% in the group that prolonged methotrexate for 12 months. The median relapse-free intervals were 21 months and 23 months, respectively—a difference that also was not significant, the investigators said (JAMA 2010;303:1266-73). These findings were consistent across all subtypes of JIA, they added.

"Our data are of general relevance because many chronic inflammatory diseases regularly take a relapsing course," including rheumatoid arthritis, inflammatory bowel disease, and pediatric autoimmune hepatitis, Dr. Foell and his associates noted.

"In clinical practice, physicians are frequently faced with the question of what to do with patients who are clinically well after induction of remission. Physicians have to decide whether continuation of drug therapy is meaningful, because it may maintain inactive disease and induce a more stable remission" but also is likely to induce more adverse effects, they said.

The investigators found that serum concentrations of myeloid-related proteins 8 and 14 helped identify which patients in remission had subclinical disease activity and were at risk for relapse. Study subjects with levels less than 690 ng/mL were unlikely to have a disease flare during follow-up, whereas those with higher levels were at increased risk.

This finding suggests that relapses after methotrexate is withdrawn result from a local disease process that has not been completely resolved by the therapy, even though the clinical impression and standard laboratory testing both indicate that there is remission, Dr. Foell and his colleagues added. ■

Disclosures: *This study was supported by the Paediatric Rheumatology International Trials Organization, a nonprofit group, and the Deutsche Rheuma-Liga. Wyeth Pharmaceuticals funded the patients' insurance in Germany. No other potential financial conflicts of interest were reported.*

MY TAKE

When Can We Stop Methotrexate?

The most common question posed by the parents of a child with JIA who has "gone into remission" has always been, "When can we stop giving these drugs?" Any parent who has read the list of warnings and side effects included on the methotrexate package insert is understandably anxious to discontinue therapy. Findings from the research by Dr. Foell and his associates begin to answer this question. When all the patients who were diagnosed as having JIA were randomly mixed, researchers found no difference in the rate of recurrence when therapy was continued for either 6 or 12 months after remission. The significance of this interesting finding is unclear. Although the treatment groups were balanced for JIA subtypes, the researchers do not discuss which subtypes the children who flared belonged to. The investigators clearly state in the methods section that "biased results due to differences between JIA subtypes were excluded by Cox models." However, because the subtypes were evenly balanced between the two groups, this provides no information about which subgroups were most at risk.

Experienced pediatric rheumatologists have long been aware that the risk of recurrence is much higher for psoriatic arthritis and polyarthritis with a positive rheumatoid factor than for other subgroups. Unfortunately, the results for these subgroups are not separately reported. With the dramatic responses we now see with the newer biologic therapies, the questions of how and when to stop therapy become even more important.

Perhaps the most important lesson in Dr. Foell's study is that more than half of the children ultimately flared. Given that our goal is to prevent joint damage and long-term disability, does the high incidence of recurrence tell us that we should be stopping methotrexate sooner, or perhaps not stopping methotrexate at all? We need careful analysis of each of the many different diseases which masquerade as JIA—with long-term follow-up, including radiographic studies of joint damage—before we can conclude whether we are treating for too long or not long enough. Indeed, for each of the diseases lumped together as JIA, the answer may be different.

THOMAS J.A. LEHMAN, M.D., *is chief of pediatric rheumatology at the Hospital for Special Surgery in New York. He reported having no financial conflicts of interest relevant to this research.*