Tips for Predicting High-Risk Pregnancies in SLE

ARTICLES BY
M. ALEXANDER OTTO

FROM THE INTERNATIONAL CONGRESS ON SYSTEMIC LUPUS ERYTHEMATOSUS

VANCOUVER, B.C. — Monthly monitoring by rheumatologists of every pregnancy in every woman with systemic lupus erythematosus may be unnecessary, according to Dr. Michelle Petri.

A relatively small list of criteria can distinguish high-risk pregnancies in women with systemic lupus erythematosus (SLE)—ones that carry a higher likelihood of miscarriage, extreme prematurity, and SLE flare—from others, and signal the need for intensive monitoring by obstetricians and rheumatologists, Dr. Petri said at the meeting.

At present, however, there is little effort to make such distinctions, so most SLE pregnancies are subjected to monthly visits to rheumatologists and obstetricians, and, starting at week 26, weekly monitoring by obstetricians.

That's not always necessary; women are subjected to needless anxiety and hospital resources are wasted, Dr. Petri said.

Based on the Hopkins Lupus Cohort, a database that has been tracking several thousand patients with SLE over the past 25 years, Dr. Petri and her colleague, Duke University rheumatologist Megan Clowse, have identified those factors that truly put women and fetuses at risk during SLE pregnancies.

Pregnancy and the postpartum period are hard on the kidneys of women with SLE, though organ involvement elsewhere in the body tends to lessen, said Dr. Petri, professor of rheumatology at Johns Hopkins University, Baltimore.

"Proteinuria from active lupus significantly increases, and this continues even after delivery," she added.

Therefore, pregnant women with lupus nephritis truly do need close monitoring. Dr. Petri recommended monthly urine protein-creatinine ratios to detect a worsening of the condition and the need for treatment.

In terms of fetal health, the risk of miscarriage doubles if, at the first pregnancy visit, a woman is proteinuric, thrombocytopenic, or hypertensive, or has a history of antiphospholipid syndrome.

The risk triples if two or more of these conditions are present, Dr. Petri said. The presence of antithyroid antibodies also increases the risk of miscarriage.

In addition, active SLE, especially if accompanied by anti–double-stranded DNA antibody or low complement levels, predicts extreme prematurity. Autoimmune thyroid disease also appears to be associated with preterm birth.

Screening for the various factors, "we can predict at the first pregnancy visit if there's going to be a poor outcome," Dr. Petri said.

If the risk factors are present, monthly monitoring by a high-risk obstetrician, followed by weekly monitoring at week 26, are appropriate to gauge if, and when, a rescue delivery is needed. ■

Vitamin D Repletion in SLE Requires at Least 2,000 IU Daily

FROM THE INTERNATIONAL CONGRESS ON SYSTEMIC LUPUS ERYTHEMATOSUS

VANCOUVER, B.C. — A daily dose of at least 2,000 IU of vitamin D is required to elevate serum 25-hydroxyvitamin D levels above 30 ng/mL, the minimum threshold for optimal immune health, according to Dr. Diane Kamen, a rheumatologist at the Medical University of South Carolina in Charleston.

The conclusion is based on an open-label, phase I study of vitamin D repletion in 18 black patients with lupus.

Starting from a baseline mean 25-hydroxyvitamin D (25[OH]D) level of 13.3 ng/mL, six patients received 800 IU vitamin D once daily; six received 2,000 IU once daily; and six received 4,000 IU once daily.

VITALS

Major Finding: Five of six black lupus patients who were given 2,000 IU vitamin D daily repleted serum 25-hydroxyvitamin D to 30 ng/mL or more at 3 months.

Data Source: A phase I study of 18 patients.

Disclosures: The study was funded by the National Institutes of Health. The principal investigator said she had no disclosures.

After 12 weeks, 67% (four patients) in the 800-IU group, 83% (five) in the 2,000-IU group, and 67% (four) in the 4,000-IU group repleted to 30 ng/mL or greater. In the 4,000-IU group, levels in 33% (two patients) rose above 40 ng/mL. That level was not reached at the lower doses.

The results are important, Dr. Kamen said in an interview. Although there is growing awareness that such high doses of vitamin D are needed to restore 25(OH)D levels in patients with autoimmune disease, the rheumatology literature still contains recommendations for doses of 600-800 IU/day.

"That's just not going to cut it; 2,000 IU a day is the minimum effective dose for repletion," especially if patients avoid the sun to prevent lupus flares, Dr. Kamen said.

Rheumatologists "need to know to recommend those higher doses, and to monitor levels" of 25(OH)D to make sure they are maintained, she said.

The 18 patients were enrolled from the Gullah, a population of blacks living on the Sea Islands of South Carolina and Georgia, in whom there is a high incidence of lupus. An earlier Gullah study found that 43% of 187 subjects had 25(OH)D levels below 10 ng/mL; in some, levels were undetectable. Lower levels correlated with higher SLEDAI scores and higher anti-dsDNA antibody levels, Dr. Kamen said.

The mean age in the phase I study was 44 years; mean prednisone dose 4.3 mg/day; and mean SLEDAI score 2.4. In all, 17 of 18 of the subjects were women, 50% (9) took hydroxychloroquine, and 50% (9) were anti-dsDNA antibody positive. Compliance with the treatment regimen was 99%, by pill count. The doses were very well tolerated and safe, Dr. Kamen said.

Although 2,000 IU per day elevated 26(OH)D levels in most patients to at least 30 ng/mL, there's debate about whether target blood levels should be higher in lupus patients. "We know that 30 ng/mL is the minimum accepted as normal," Dr. Kamen said, noting that secondary hyperparathyroidism can begin below that level. "We also know [healthy] sun-exposed people tend to live closer to 60 ng/mL. The debate is over if the target should be 30, 40, 50, or 60," she said.

"I tell my patients at high risk for conditions influenced by vitamin D, such as osteoporosis and inflammatory conditions, that we want them to stay between 40 and 60 ng/mL," she said, but "it's a gray zone" that awaits further research.

Levels of 25(OH)D are known to be low in lupus patients, but no one can say for sure whether that is a cause or a consequence of the disease, or if it results from the medications used to treat it, such as prednisone and hydroxychloroquine. ■

Urinary Retention in SLE? Think Gray Matter Myelitis

FROM THE INTERNATIONAL CONGRESS ON SYSTEMIC LUPUS ERYTHEMATOSUS

VANCOUVER, B.C. — Fever and urinary retention without obstruction in a patient with active systemic lupus erythematosus should be considered a medical emergency and treated immediately with high-dose intravenous corticosteroids, according to recent findings from Johns Hopkins University.

Those signs signal gray matter myelitis and spinal cord ischemia, and high-dose corticosteroids can prevent a cord infarct and permanent paraplegia, Dr. Michelle Petri said.

Rheumatologists at the school have identified two previously unrecognized forms of myelitis in SLE patients: gray matter myelitis and white matter myelitis.

Both are longitudinal and likely to span three vertebral segments; the nomenclature refers to the type of spinal cord tissue affected.

Gray matter myelitis leads to rapid onset of permanent paraplegia and urinary incontinence in as little as 4 hours. Because it usually presents with acute urinary retention, it is often misdiagnosed and mistreated as a bladder infection.

But the "patient is announcing ischemia of the spinal cord and needs high-dose corticosteroids and to be admitted," said Dr. Petri, professor of rheumatology and director of the lupus center at Johns Hopkins in Baltimore.

If the syndrome—and how to treat it—was more widely recognized, "hundreds of young women would be saved from permanent paralysis," she said.

"When you have to place a catheter because the patient cannot urinate, treatment [with 1,000 mg IV methylprednisolone] should start," Dr. Julius Birnbaum, the lead investigator on the project and a rheumatologist and neurologist at Johns Hopkins, said in an interview after the conference.

VITALS

Major Finding: Of 11 SLE patients with gray matter myelitis, a newly recognized form in SLE, 10 presented with urinary retention and fever and were treated for bladder infections; the mistake likely led to permanent paraplegia.

Data Source: Retrospective study of 22 patients.

Disclosures: The investigators said they had no disclosures. The study was funded by the National Institutes of Health.

"The overall message is, don't wait to provide treatment," he said.

Gray matter myelitis, which the team considers a vasculopathy, presents with lower motor neuron signs: flaccidity and hyporeflexia, in addition to urinary retention and fever (Arthritis Rheum. 2009;60:3,378-87).

On the other hand, white matter myelitis presents with upper motor neuron signs: hyperreflexia and spasticity. The onset is more gradual, antigravity strength is more likely to be preserved; attacks are less severe; and disability comes from repeated episodes that eventually lead to paralysis, in some cases.

It is more likely an antibody-driven phenomenon; white matter myelitis shares features with neu-

Continued on following page