Control of Pediatric SLE Improved Lipid Levels

BY DOUG BRUNK
San Diego Bureau

Comparison of lipid levels at different points in the course of pediatric systemic lupus erythematosus and the effect of prednisone administration revealed that the association between the two is complex, a small retrospective study demonstrated.

"The significance of our findings should be put into the context of studies which have demonstrated that levels of LDL cholesterol and HDL cholesterol, and not levels of triglycerides or total cholesterol, are the lipids that are associated with the presence of fatty streaks and raised arterial lesions in the aorta as well as with increased carotid and femoral intima-media thickness and carotid plaque formation," wrote the researchers, led by Talin Sarkissian of the division of rheumatology at the Hospital for Sick Children, Toronto. "Therefore, our findings have important implications when considering therapeutic interventions on pediatric patients with SLE" (Arthritis Rheum. 2006;54:1283-90).

The researchers obtained lipid measurements at diagnosis, and at 1, 2, and 3 years in 114 female and 25 male patients with pediatric systemic lupus erythematosus (SLE) who received care at the Hospital for Sick Children between October 1994 and April 2003. The researchers also obtained SLE Disease Activity Index scores and prednisone dosages at the same time periods. The mean patient age at the time of diagnosis was 14 years.

At the time of diagnosis, the mean levels of total cholesterol, LDL cholesterol, and triglycerides were highest, while the mean levels of HDL were lowest.

After diagnosis, "the mean total cholesterol levels decreased during year 1, then remained relatively constant, while the percentage of patients with abnormal total cholesterol values remained relatively constant," the researchers wrote. The mean LDL cholesterol levels decreased during year 1 and then remained relatively constant during years 2 and 3, they reported.

When the researchers compared the lipid levels at different prednisone doses and disease activity levels, they observed that the changes in triglyceride levels were primarily associated with changes in disease activity.

Total cholesterol levels "were higher when patients were taking high-dose prednisone as compared with when they had active SLE but were taking low-dose prednisone, but were not higher than at the time of diagnosis of SLE," the researchers wrote.

Mean HDL cholesterol levels "were significantly higher when patients were taking prednisone and the disease was inactive as compared with when patients were not taking prednisone but with active [SLE]."

Finally, mean LDL cholesterol levels "were significantly higher in patients with active disease who were taking prednisone as compared with the time when they had active disease but were not taking prednisone," the wrote.

The researchers acknowledged that a major limitation of the study is its retrospective design but concluded that the findings suggest that "control of SLE appears to improve the levels of these important lipids." ■

High Lupus Mortality in African Americans May Be Preventable

BY JONATHAN GARDNER
Contributing Writer

African Americans are two to three times more likely to die from systemic lupus erythematosus than are whites, a disparity that is higher than the risk of mortality from all causes, according to an analysis of U.S. death and hospitalization statistics.

Dr. Eswar Krishnan of the University of Pittsburgh and Helen B. Hubert, Ph.D., of Stanford (Calif.) University wrote that the greater lupus mortality risk suggests that biologic rather than socioeconomic factors may be responsible.

The study examined death statistics from the National Center for Health Statistics at the Centers for Disease Control and Prevention from 1979 to 1998. Investigators also analyzed data from the Nationwide Inpatient Sample, a database run by the Agency for Healthcare Research and Quality taken from the discharge summaries of a 20% stratified sample of hospitals in the United States from 1993 to 2002 (Ann. Rheum. Dis. 2006;[Epub ahead of print, doi:10.1136/ard.2005.040907]).

For African American women, the lupus mortality risk was 3.91 times that of white women, compared with 1.24 for death from all causes. For African American men, the lupus mortality risk was 2.4 times that of white men, compared with 1.36 for deaths from all causes.

The mean age at which women were hospitalized for lupus was 43 years for African Americans and 53 years for whites. For men, the mean age at hospitalization for lupus was 43 years for African Americans and 58 years for whites. For lupus patients who died, the mean age among African Americans was 49 years; for whites, the mean age was 64 years.

The lupus death rate increased for both African American and white women from 1979 to 1998. The death rate for African American men held steady while decreasing for white men, which resulted in an increase in the relative death risk ratio for African American men.

Insurance status did not influence relative mortality risk, suggesting that the ethnic differences may be biologic, the researchers said. Such a suggestion is supported by research indicating that African Americans are diagnosed with lupus 6 years younger than are whites on average and were more likely to show such symptoms as discoid lupus.

"Our findings have important clinical and public health implications," the investigators wrote, adding that African Americans are less likely to receive preventative health services than are whites. Therefore, many of the excess deaths among African Americans with lupus may be the result of preventable cardiovascular, infectious, and renal complications. Aggressive intervention with increased exercise, control of hypertension and hyperlipidemia, smoking cessation, and management of other risk factors may eliminate the excess mortality seen in African Americans with lupus, according to the investigators. ■

Pyoderma Gangrenosum Possible Culprit in Resistant Ulcers

BY JANE SALODOF MACNEIL
Southwest Bureau

PARK CITY, UTAH — If a leg ulcer worsens after debridement, the patient may have pyoderma gangrenosum, Dr. John Zone told physicians at a clinical dermatology seminar sponsored by Medicis.

"When a surgeon calls to say, 'we debrided, and it got bigger,' that is a hallmark of PG [pyoderma gangrenosum]," said Dr. Zone, chairman of the dermatology department at the University of Utah in Salt Lake City.

A rare skin disease caused by an intense, uncontrolled inflammatory response, PG presents with pathergy in about 20%-30% of patients, according to Dr. Zone. They develop PG at the site of a trauma, such as a needle stick, and the resulting ulcer worsens after debridement.

PG is one of a group of conditions (vasculitis, neoplastic disease, drug-induced hydroxyurea, necrobiosis lipoidica, panniculitis, and hypercoagulable state) that may cause a leg ulcer to not heal within 3 months of first-line treatment. "The most important thing in leg ulcers is keeping a differential diagnosis in place," he said.

"These people won't get better until you figure out what they have," he advised.

About 75% of PG cases are classic or ulcerative. In 50%-70% of these cases, he said PG is associated with an underlying systemic disease. Inflammatory bowel disease is the most common, followed by arthritis, hematologic disorders, hepatitis C, lupus, and sarcoidosis.

"The development of PG does not parallel systemic disease activity," he said. PG can present in a patient who has not yet developed inflammatory bowel disease, as well as in a patient who has been cured of bowel disease.

About half of PG patients have multiple lesions, and a similar proportion have multiple episodes, according to Dr. Zone.

The morphology of ulcerative PG is distinct, a tender papulopustule ulcerating within days to a week, he said, noting that it may be associated with a fever. In classic cases with acute lesions, the ulcers are purulent, painful, and violaceous with black borders that may appear necrotic, he said. They are surrounded by erythema. The ulcer may extend beneath the skin edges with tissue destruction by intense inflammatory response.

Dr. Zone recommended gastrointestinal studies in symptomatic patients. He also advised doing the following laboratory tests: a complete blood count with differential, a chemistry panel, rheumatoid factor, serum protein electrophoresis (SPEP), hepatitis B and C antibodies, and antinuclear antibody, antineutrophil cytoplasmic antibodies, and antiphospholipid antibodies.

Pulse steroids avoid the substantial side effects of standard prednisone.

DR. ZONE

Treatment needs to suppress the inflammatory tissue response locally or systematically, Dr. Zone said, recommending aggressive treatments of secondary bacterial infections.

Local wound care should be nonaggressive, however. Only gentle debridement should be used, he said. He suggested silver dressings to suppress bacterial infection and allografts or xenografts to encourage granulation tissue.

There are no controlled studies of PG therapies, according to Dr. Zone. For mild disease, he suggested superpotent topical steroids, intralesional steroids, and topical tacrolimus or pimecrolimus.

In severe cases, he said prednisone is a standard initial therapy but with substantial side effects. He said he prefers to "pulse" steroids, giving 1 g intravenous methylprednisolone once a day for 5 days. "I'm 100% sure what they got, how much they got, and when they got it," he said.

Additional options mentioned by Dr. Zone included calcineurin inhibitors, anti-inflammatory/immunosuppressive agents, tumor necrosis factor–α inhibitors, and steroid-sparing agents, in particular, cyclosporine. He cited a retrospective study in which 13 patients had complete healing with infliximab, (Am. J. Gastroenterology 2003;98:1821-6). Dr. Zone said his department also had good results but has tried the agent in only four patients.

Surgery is also an option, once the patient is immunosuppressed and inflammation is resolved, but Dr. Zone warned that there could still be a pathergic response. ■