Biologics Increase Risk of Postoperative Infection

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SAN ANTONIO — Rheumatoid arthritis patients who are on tumor necrosis factor–inhibitor therapy have a fourfold greater risk of developing deep postoperative infections, according to a Johns Hopkins University review of patients who had undergone orthopedic procedures.

The findings, although not definitive, suggest that these agents should be stopped before surgery, Jon T. Giles, M.D., said at the annual meeting of the American College of Rheumatology.

Based on each agent's half-life, Dr. Giles recommended that etanercept be discontinued 2 weeks before surgery, infliximab 8 weeks before surgery, and adalimumab 4 weeks before surgery.

"In addition, we recommend avoidance of TNF inhibitors for 2 weeks after surgery," he said.

Even without adding the biologics, patients with rheumatoid arthritis already have a higher risk of postoperative infection, noted Dr. Giles of Johns Hopkins University, Baltimore. Compared with a 1% rate of infection among people in the general population undergoing orthopedic procedures, infection rates among rheumatoid arthritis patients are two- to fourfold higher.

Dr. Giles's investigation involved 91 RA patients who had undergone a bone or joint surgical procedure in a Johns Hopkins clinic during a 5-year period from the beginning of 1999. Half of those patients had large joint arthroplasty procedures, and the rest were divided between fusion or resection procedures with no implanted materials and small joint procedures.

Among the 35 patients identified to be on biologic therapy at the time of surgery, seven developed early, deep, postoperative infections, including two cases of osteomyelitis, three cases of septic arthritis, and two cases of paraspinal abscess. There were three infections among the 56 patients not taking a biologic.

Patients on TNF-inhibitor therapy had an unadjusted 4.4 odds ratio for developing infection, compared with those patients not on the biologics; after adjustments for age, gender, and disease duration, the odds ratio rose to 4.6. After adjustment for prednisone use, diabetes, and presence of rheumatoid factor, the odds ratio was 5.3.

Given the study's small numbers, it could not be determined if the risk of infection varied by the type of surgery, site of surgery, or particular biologic agent used. ■

Remicade Label: Severe Hepatic Reactions Added

A small number of patients using infliximab (Remicade) have had very severe hepatic reactions, according to a revision of the package prescribing information.

In announcing the new safety information, the Food and Drug Administration and Centocor Inc. said there have been 35 cases of severe hepatic reactions in patients using infliximab reported in postmarketing data and 3 cases reported in clinical trials.

The reactions have included acute liver failure, jaundice, hepatitis, and cholestasis. Some cases were fatal or resulted in liver transplantation. They occurred from 2 weeks after starting therapy to more than a year after initiation. A causal relationship with infliximab has not been established, but treatment with the biologic can induce autoantibodies and autoimmune hepatitis has been diagnosed in some of the cases.

According to the warning, patients with signs of liver dysfunction should be evaluated. If jaundice or elevations in liver enzymes (greater than 5 times the upper limit of normal) occur, the biologic should be stopped and an investigation undertaken.

In clinical trials, mild to moderate elevations in liver enzymes were noted, without progression to severe hepatic injury.

In addition to the hepatic-reaction warning, Centocor added a warning that patients receiving infliximab may be at an increased risk of developing pneumonia, based on data from clinical trials data in rheumatoid arthritis patients.

Infliximab is approved for rheumatoid arthritis and Crohn's disease; in December, it was approved for ankylosing spondylitis.

—Timothy F. Kirn