Postsurgery Gout Attack Risk Factors Identified

BY DENISE NAPOLI
Assistant Editor

The risk for a postsurgical gout flare is greatest in patients with high presurgical serum urate levels, patients who've had cancer surgery, and in those who did not receive presurgical colchicine, according to a study.

Dr. Eun Bong Lee of the Seoul (South Korea) National University and colleagues looked at 67 patients who had a postsurgical gout attack and 67 who did not. All had prior histories of gout (Ann. Rheum. Dis. 2007 Nov. 12 [Epub doi:10.1136/ard.2007.078683]).

In an interview, Dr. Lee said "the postsurgical gout attack develops within 14 days after the surgery," although the mean in this study was 4 days.

Lower extremity joints were affected in 65 of the 67 patients (97%) with a postsurgical gout flare. The most common site was the first metatarsophalangeal (MTP) joint (42 patients, or 63%). The ankle was the second most commonly affected joint (21 patients, 31%), followed by the knee (15 patients, 22%). In all, 14 patients had an additional lower-extremity joint affected. Upper-extremity involvement occurred in only nine patients.

Overall, about half (33) of patients had only one affected joint; 22 patients had two; 8 patients had three; and only 2 patients each had four or five.

In multivariate analysis, the authors reported that cancer surgery was performed on 60% of gout attack patients versus 34% of controls, a significant difference. "Cancers, especially hematologic malignancies, are known to cause hyperuricemia and gout because of high rates of cellular turnover," wrote the investigators.

Presurgical serum uric acid levels greater than or equal to 9 mg/dL were also significantly correlated with an attack. This was "the most important risk factor," and "the risk of attack increased in proportion to presurgical uric acid levels," the added.

In an interview, Dr. Kenneth Saag, director of the center for education and research on therapeutics of musculoskeletal disorders at the University of Alabama at Birmingham, who was not affiliated with the study, said assessing a gout patient's presurgical urate levels isn't common practice, and shouldn't be. "Knowing the serum urate is only partially related to the likelihood of postsurgical gout. The level of serum urate is not something that can be managed in the perioperative period, anyway."

A lack of colchicine prophylaxis before surgery was also tied to a significant risk of attack. But Dr. Saag, urged caution. "Some patients have kidney dysfunction, and colchicine is not an unequivocally safe medicine."

"[Postsurgical gout attacks] can prolong the hospital stay. Surgeons aren't particularly eager to send patients home after surgery if they can't walk or are in severe pain. Sometimes gout can cause fevers which can be confused with postoperative infection," said Dr. Saag. On the other hand, "the treatments for gout can compromise healing. Sometimes, if a steroid like prednisone is used to manage gout, that may impair wound healing."

Dr. Lee said his team had no financial disclosures in relation to this study. ■

Diacerein Found Safe, Effective For Reducing OA Pain Symptoms

BY DENISE NAPOLI
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Diacerein is safe and effective for reducing osteoarthritis-associated pain, and its effects persisted for at least 3 months after treatment was stopped in a randomized, double-blind, placebo-controlled, multi-center study.

The anthraquinone derivative is approved for use in several European countries but not in the United States.

An intent-to-treat analysis was carried out on 165 patients randomized to receive 50-mg diacerein capsules (82 patients) or placebo twice daily for 3 months. Most patients had bilateral knee OA, and most were taking nonsteroidal anti-inflammatory drugs. The majority were female and the mean duration of OA was 6.5 years (Arthritis Rheum. 2007;56:4055-64).

Unpublished international guidelines likely will approve the use of diacerein for OA pain.

DR. ALTMAN

The two primary end points were the percentage change in baseline pain as recorded on a 100-mm visual analog scale (VAS) in section A of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and change in score on the total WOMAC from baseline to the fifth month.

"Diacerein showed statistically significant superiority over placebo (*P* less than .0001) for the primary efficacy criterion," wrote Dr. Karel Pavelka, of Charles University, Prague, and his associates. Changes in pain on a 100-mm normalized scale were "already significantly different in favor of diacerein at month 2" and the level of pain "decreased further in the diacerein group by the end of treatment (month 3) ($P = .0006$) and persisted at this level not only at months 4 and 5 … but also at month 6."

The absolute change in pain at month 3 for the treatment group was 21.6 mm, versus 9.4 mm in the placebo group. At month 5, the treatment group change persisted, at 23.3 mm, versus 9.5 mm in the placebo group.

The other primary end point—change on the total WOMAC—"was also significantly different (*P* less than .0001) compared with placebo at month 5," wrote the investigators. The total WOMAC score at baseline was 1,251 and 1,183 in the diacerein and placebo groups, respectively. The diacerein group's score dropped to 834 at month 3 versus 982 in the placebo group, and diacerein patients had a total score of 733 at month 6 versus 1,011 for placebo patients ($P = .0045$ at month 3 and P less than .0001 at month 6).

A former consultant for Negma, a French company that marketed the drug, Dr. Roy Altman said in an interview that the drug was put before the Food and Drug Administration several times in the last decade. But the "shifting sands" of the agency's clinical trial data requirements prevented the drug from ever gaining approval. (A representative from the FDA's Center for Drug Evaluation and Research would not comment on drugs that had not been approved.)

The Osteoarthritis Research Society International's new therapeutic guidelines are likely to give "approval for diacerein for OA, but not a high recommendation," according to Dr. Altman, a visiting professor in the division of rheumatology of the University of California, Los Angeles.

The study was supported by a joint grant from TRB Chemedica International SA and Glynn Brothers Chemicals AG, two Switzerland-based companies. ■

Responses to Ustekinumab in PsA Significant and Sustained

BY NANCY WALSH
New York Bureau

BOSTON — Inhibition of two key immunoregulatory cytokines known to be involved in the pathogenesis of psoriasis and other autoimmune diseases led to significant improvements in psoriatic arthritis, judging from data from a new study, Dr. Alice B. Gottlieb reported at the annual meeting of the American College of Rheumatology.

Interleukin (IL)-12 and IL-23 play important roles in coordinating innate and adaptive immune responses, binding via the p40 subunit to the IL-12 receptor β1 on the surface of T cells and natural killer cells. Among the functions of IL-12 in psoriasis are T-cell differentiation and the facilitation of T-cell homing to the skin (Cell Immunol. 2007;247:1-11).

The drug ustekinumab now has also been evaluated in active psoriatic arthritis (PsA) in a multicenter, double-blind study that included 146 patients randomized to receive the active treatment at weeks 0, 1, 2, and 3, followed by placebo at weeks 12 and 16, or placebo at weeks 0, 1, 2, and 3 followed by the active treatment at weeks 12 and 16. They were then followed through week 36.

The primary end point was the percentage of patients achieving a response on the American College of Rheumatology (ACR) 20 scale at week 12. Patients in the active treatment group received four subcutaneous doses of either 63 mg (n = 59) or 90 mg (n = 17) of ustekinumab. This inconsistency in dose resulted from a change in preparation of the drug during the study, said Dr. Gottlieb, of the Tufts–New England Medical Center, Boston.

At baseline, the swollen joint count was 12, and the tender joint count was 22. Approximately 20% of patients were on concurrent methotrexate, and half were on concurrent NSAIDs, but none was taking oral corticosteroids. At week 12, 42% of patients in the ustekinumab group had achieved the primary end point, compared with 14% of patients in the placebo group.

By week 36, patients initially randomized to ustekinumab had not received any active treatment for 32 week—yet three-quarters maintained an ACR 20 response. "You do not see this with any of the anti–[tumor necrosis factor] agents," Dr. Gottlieb said.

Moreover, patients who initially received placebo but then were crossed over to the active treatment group at week 12 also went on to have rapid and sustained responses, she said.

A higher proportion of patients in the active treatment group also reached ACR 50 and ACR 70 responses. A total of 25% and 11% of patients in the ustekinumab achieved these levels of response, compared with 7% and 0% of those in the placebo group.

The decrease from baseline on the Health Assessment Questionnaire disability index at week 12 was greater in the ustekinumab group (mean change –0.31), compared with the placebo group (–0.04).

A total of 52% of patients receiving the active treatment achieved a PASI 75 result at week 12, as did 6% of those receiving placebo. The 85% of patients with at least 3% body surface area psoriasis involvement who received ustekinumab had a greater decrease in the Dermatology Life Quality Index (mean change –8.6), compared with those who received placebo (–0.8). All of these differences were statistically significant.

There were no serious adverse events through week 12 in the active treatment group, whereas in the placebo group there was one report of myocardial infarction, one of gastric ulcer hemorrhage, and one of chest pain. There were no problems with abnormal laboratory values through week 12, nor were there any cases of tuberculosis or serious opportunistic infections, she said.

Dr. Gottlieb disclosed that she has received research grants and consulting fees from Centocor Research and Development Inc., which funded the trial and makes ustekinumab. ■