Allopurinol Desensitization Effective in Select Patients

BY KERRI WACHTER
Senior Writer

Destin, Fla. — Oral desensitization appears to be a safe and effective alternative for patients who are allergic to allopurinol and who cannot take other urate-lowering drugs for gout, Adel G. Fam, M.D., reported at a rheumatology meeting sponsored by Virginia Commonwealth University.

While 1%-3% of patients experience a pruritic maculopapular rash in response to allopurinol, severe allopurinol hypersensitivity syndrome (AHS) occurs in only about 0.4% of patients, said Dr. Fam, a professor of rheumatology at the University of Toronto.

Dr. Fam suggested that allopurinol desensitization be considered in gout patients with any of the following circumstances:

- Renal impairment, which renders uricosuric drugs ineffective.
- Underexcretion hyperuricemia; and al- legy, intolerance, or contraindications to both probenecid and sulfinpyrazone.
- Overproduction/overexcretion hyper- uricemia, which coupled with uricosurics can increase the risk of renal stones.
- History of transplantation, renal insuf- ficiency, and severe and debilitating gout.
- The patient requires prevention of ma- gnetic resonance imaging an indispensable tool for use

MRI Tool of Choice For Diagnosing RA, Expert Says

BY KERRI WACHTER
Senior Writer

Destin, Fla. — The advent of disease-modifying drugs has made magnetic resonance imaging an indispensable tool for diagnosing and monitoring patients with rheumatoid arthritis, Charles G. Peterfy, M.D., said at a rheumatology meeting sponsored by Virginia Commonwealth University.

MRI already is the tool of choice for use in clinical trials. Now, meeting sponsor clinical practice to incorporate this superior tech- nology, said Dr. Peterfy, a radiologist spe- cializing in musculoskeletal imaging, and chief medical officer of Synarc Inc., which specializes in radiology services for clinical trials. Radiographs have a number of shortcomings. Not only are they relatively insensitive for predicting disease pro- gression and bone erosion, they are not ac- curate for measuring cartilage loss or for visualizing the synovium.

MRI can provide information on synovi- tis, tendinitis, and bone edema (or osteitis), all of which improve the predictive accura- cy, particularly the negative predictive value. “The absence of these findings on MRI is a very powerful predictor that this patient is not going to progress,” Dr. Peterfy said at the meeting, also sponsored by the Inter- national Society for Clinical Densitometry.

MRI of synovitis correlates with histopathology. Doppler ultrasound, PET imaging and “has been found to be more sensitive than clinical examination for swelling and tenderness,” he said.

There are MRI techniques that allow the visualization of preerosive osteitis, which is key because osteitis can progress very rapidly, said Dr. Peterfy, who also is on the advisory board for MagneVu, the maker of portable MRI units. According to one study, baseline osteitis can predict func- tional disability at 5 years. A number of studies have demonstrated that MRI detects erosions earlier than x-rays, said Dr. Peterfy. In fact, one study demonstrated the ability of baseline MRI to predict bone erosions as much as 2 years later.

The development of a semiquantitative scoring system—such as the Rheumatoid Arthritis MRI Score (RAMRIS), developed by the European League Against Rheuma- tism—Outcome Measures in Rheumatoid Arthritis Clinical Trials (EULAR)/ACT—should help standardize the use of MRI to monitor the progression of RA. This system incorporates erosions, os- teitis, and synovitis to assess disease changes. The group recently published an MRI atlas intended to improve the performance and generalizability of the MRI scoring system (Ann. Rheum. Dis. 2005;64 [suppl. 1]:s33-s55).

History and Rationale for Use

In the medicinal system of the Ashan-inka Indians of Peru, the human being is made up of body and spirit—flesh (nati- sa) and “deepest being” (úmay), according to Klaus Kelpler, who stud- ied the Ashaninka during nine trips to the Amazon rain for- est (J. Ethnopharmacol. 1999;64:23-34). According to the Ashaninka, disrup- tions in communica- tion between body and spirit are a result of anxiety and preparations of powerful plants (saventaro) that are inhabited by good spirits can eliminate these disruptions and restore health and harmony. One of these plants is Uncaria tomentosum, or uña de gato (cat’s claw), so called be- cause of its distinctive curling hooks. A decoction of sliced root bark boiled in water is used in traditional Peruvian medicine to treat numerous inflamma- tory disorders, ulcers, and infections.

Mechanisms of Action

Various hypotheses have been proposed to account for the purported clinical ef- fects of cat’s claw. One group of inves- tigators has reported that the most likely mechanism for cat’s claw’s effects is immunomodulation via suppression of tumor necrosis factor-α (TNF-α) syn- thesis. The in vitro suppression ranges from 65% to 85% (Free Radic. Biol. Med. 2000;29:71-8).

Another group of researchers re- cently proposed that cat’s claw’s effects also derive from enhancement of DNA repair and immune cell responses through regulation of the nuclear tran- scription factor-β (NF-β), which con- trols nuclear events that protect the cell from apoptosis and also controls proin- flammatory cytokine production (J. Ethnopharmacol. 2005;96:577-84).

In fact, a double-blind trial of an extract from the cat’s claw vine to treat various maladies. Two small clinical studies have suggested that the herb may double the benefits in rheumatoid arthritis and osteoarthritis.

Peruvian Indians have long used preparations made from the cat’s claw vine to treat various maladies.

Clinical Studies

A double-blind trial of an extract from U. tomentosum (Krállendorn capsules, made by Immortal Pharmaka GmbH, Volders, Austria) was recently conduct- ed among a group of 40 patients with rheumatoid arthritis being treated at Innsbruck (Austria) University Hospital. All patients had active disease and had been treated with sulfasalazine or hy- droxychloroquine for at least 6 months; they were on stable doses of the drugs. Nonsteroidal anti-inflammatory drugs and daily doses of prednisolone up to 10 mg/day were permitted in the study. Patients were randomized to receive one capsule (20 mg) of the plant extract or placebo three times per day for 24 weeks. During the next 24 weeks, all pa- tients were allowed to switch the placebo.

At the end of the first phase of the study, the number of painful joints had decreased by 53.2% in the active extract group vs. 24.1% in the placebo group. J. Rheumatol. 2002;29:678-81). Statisti- cally significant differences also were seen in the number of tender joints and duration of morning stiffness in the treat- ment group, but not in the placebo group, at 24 weeks compared to baseline. No changes were seen in other para- metrics, including, among patients, as- sessment of disease activity, subjective assessment of pain, and laboratory markers, except for an increase in rheumatoid factor in the placebo group. By the end of the second phase of the study further significant improvements in the number of tender joints and du- ration of morning stiffness were seen among patients initially randomized to the extract group. Patients initially ran- domized to placebo also had signifi- cant improvements in the number of painful and swollen joints once they were switched to the active extract. They also reported decreased pain in- tensity, disease activity, and duration of morning stiffness, although these dif- ferences did not reach statistical signifi- cance. There was a nonsignificant de- crease in rheumatoid factor in this group. One patient in the extract group withdrew because of gastritis, and one patient in the placebo group withdrew because of diarrhea. No serious side ef- fects were reported.

Cat’s claw has also been evaluated for use in knee osteoarthritis. In a multi- center, double-blind, placebo-controlled randomized to receive 100 mg of freeze-dried cat’s claw or placebo daily for 4 weeks. The cat’s claw group had significant improvements in pain associ- ated with activity and in patient and physician assessment of disease activi- ty. Improvements were seen as early as week 1 and continued throughout the trial (Inflamm. Res. 2001;50:442-8).

The authors observed a reduction in PGE_{2} production, which they attrib- uted to an inhibition of cyclooxyge- nase-2 expression. They wrote, “Of par- ticular interest in the treatment of arthritis is the ability of cat’s claw not only confer benefit to the joints but also negate the side effects of NSAIDs on the stomach and intestine.”

—Nancy Walsh

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