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DAILY HIGHLIGHTS
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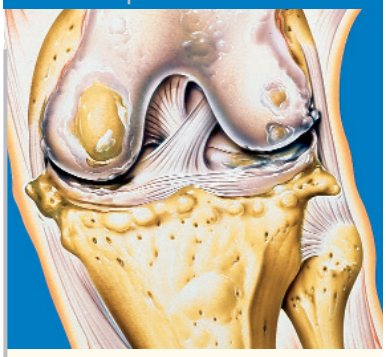

COX-2 inhibitor safer and as effective as NSAIDs in OA

SAN FRANCISCO—The COX-2 inhibitor celecoxib causes fewer upper gastrointestinal (GI) complications than conventional nonsteroidal anti-inflammatory drugs (NSAIDs) when used for the treatment of osteoarthritis (OA). When given at doses of either 200 or 400 mg daily, the drug is also as effective as NSAIDs.

Gurkirpal Singh, MD, professor of medicine immunology and rheumatology, Stanford University Medical School, and his colleagues analyzed results from the Successive Celecoxib Efficacy and Safety Study. The double-blind, randomized study of patients with knee, hip, and hand OA showed that, compared with diclofenac 100 mg daily and naproxen 1,000 mg daily, celecoxib reduced GI complications by 75% ($p < .008$).

Of the 13,274 patients in the study, 4,393 received celecoxib 200 mg daily; 4,407 were taking celecoxib 400 mg daily; 905 were given naproxen; and 3,489 were in the diclofenac group. Efficacy of the drugs was measured according to a pain visual analog scale and the Western Ontario and McMaster Universities Osteoarthritis Index. Scores for both measures were comparable for all groups.

—David Wild

New Arthritis Pain Guidelines Unveiled

SAN FRANCISCO—Acetaminophen is the drug of first choice for patients with mild osteoarthritis (OA) pain, according to the first evidence-based guidelines for managing arthritis pain.

COX-2 inhibitors should be used as first-line agents for moderate-to-severe pain unless a patient is at increased risk of gastrointestinal (GI) complications or renal disease, according to the guidelines, which were developed by the American Pain Society.

Members of the guideline development panel presented details of the guidelines. The formal guideline document, *Guidelines for the Management of Pain in Osteoarthritis, Rheumatoid Arthritis, and Juvenile Chronic Arthritis*, will be released in early 2002.

In addition to a complete history and physical examination, treatment of people with arthritis should include an initial comprehensive pain assessment as well as ongoing assessment of pain and functional status. Pain assessment should focus on the type and quality of pain, source of pain, pain intensity, location and duration, and the effect of pain on lifestyle.

The goal of pain assessment is not only to describe a patient's pain, but also to assess the comprehensive biological, psychological, and social factors that could influence perception of pain and the strategy for coping with pain.

The guidelines state that the patient's self-report should be the primary method of pain assessment whenever possible. Behavioral observations and physiological measurements may provide additional information, and could be the primary source of pain assessment for nonverbal children and nonverbal and cognitively impaired adults.

When arthritis is persistent or severe, physicians should perform a comprehensive assess-

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Electronic risk-assessment accurate

SAN FRANCISCO—Now nonsteroidal anti-inflammatory drug (NSAID)-related gastrointestinal (GI) perforations, ulcerations, and bleeding (PUB) in rheumatoid arthritis (RA) sufferers can be predicted electronically using a defined set of easily measured patient characteristics. According to a new study of patient information collected from databases, individuals can be accurately assessed as being at risk for these particular adverse events.

Lead investigator Gerald Levy, MD, rheumatologist at the Bellflower Medical Center, Bellflower, California, and his colleagues found that all but one of the risk factors identified were associated with a higher incidence of PUBs. Steroid use, age, diagnosis of RA, previous use of GI med-

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Better Clinical Response to Infliximab in Etanercept-Naïve Patients

SAN FRANCISCO—Patients with rheumatoid arthritis (RA) are more likely to respond to infliximab (INF) therapy if they have not previously been treated with etanercept (ETA). According to a questionnaire-based study, however, the initial functional improvement wanes after the first 6 months, independent of concomitant methotrexate (MTX) use.

RA patients receiving INF at the on-site ambulatory infusion unit of the Hospital for Special Surgery, Weill Medical College of Cornell University, New York, were asked to complete questionnaires on their RA history, treatment, and functional disability (on the multidimensional Health Assessment Questionnaire [mdHAQ]) at baseline and every 2 months thereafter. They were also questioned about their adverse events related to between-infusion INF treatment.

The investigators, led by Yusuf Yazici, MD, compared response to treatment, adverse events, and discontinuation rates in etanercept-naïve (ETA-N) and etanercept-failed (ETA-F) patients.

The team had previously demonstrated a significant improvement in measurements of functional disability among RA patients with long-standing disease within the first 6 months of INF treatment, regardless of concomitant use of MTX as well as a higher rate of early discontinuation of INF when MTX was not used (*Ann Rheum Dis* 2001;60(S1):122).

Eighty-eight patients (77 women and 11 men with an average age of 61 years) were treated with INF at the infusion unit between January 2000 and April 2001. Their average length of RA was 13.4 years. Thirty-seven (42%) were ETA-F patients. There was no difference in age, disease duration, or number of failed disease-modifying antirheumatic drugs (DMARDs) between ETA-F and ETA-N patients. Subjects had failed to respond to an average of two DMARDs prior to their INF treatment.

Forty-two (48%) patients did not receive concomitant MTX (MTX-NR) because of a history of adverse events with MTX, an allergy to it, or because they refused the drug. The baseline characteristics of the MTX-NR and those receiving MTX (MTX-R) were similar with respect to disease duration and age. Sixteen ETA-F and 10 ETA-N patients were excluded from the analysis because of insufficient data.

There was no significant difference in number of adverse events between the 31 ETA-F and 46 ETA-N patients. After an average of 6.7 months of follow-up, 66% (40 of 61) of subjects experienced a total of 96 adverse events over 648 infusions. Moreover, 60% of MTX-NR patients (16 of 27) experienced 46 adverse events compared with 71% (24 of 34) of MTX-R patients who experienced 50 adverse events ($p = .51$). Most of these adverse events were minor, and none resulted in INF discontinuation. INF treatment was discontinued in 36% of MTX-R subjects (15 of 42) and in 26% (12 of 46) of MTX-NR subjects.

As shown in the Table, ETA-N patients had a significant improvement in morning stiffness and also demonstrated a trend toward improvement in mdHAQ and pain scores. However, no significant improvement was seen in ETA-F patients. Three ETA-F patients did respond to INF. Scores on the modified HAQ also improved significantly in both MTX-R and MTX-NR patients. After an average of 10.6 and 9.7 months, respectively, mdHAQ scores for 17 MTX-R patients improved from an average of 1.03 to 0.92. Those for the MTX-R patients changed from 0.98 to 1.03.

"Our clinical experience demonstrates a better clinical response to INF among ETA-naïve patients," noted the investigators in their poster presentation of these results. "These results may reflect a population of refractory RA patients with more severe disease and who are generally difficult to manage, or who are non–anti-TNF responders."

The scientists also found that functional improvement in RA patients receiving INF treatment waned after the first 6 months of therapy, regardless of whether these subjects were receiving concomitant MTX.

"These findings may be due in part to patient characteristics—specifically, long-standing RA and multiple DMARD failure—or our small sample size," the investigators concluded. "Continued follow-up of this cohort should demonstrate whether MTX is a necessity for all patients receiving INF; it will also provide a better risk-benefit assessment of INF used alone."

— *Shoshana Frei*

TABLE: RESPONSE BEFORE AND AFTER INFLIXIMAB TREATMENT IN ETANERCEPT-FAILED (ETA-F) AND ETANERCEPT-NAÏVE (ETA-N) PATIENTS

Treatment Group		Modified Health Assessment Questionnaire	Pain on Visual Analog Scale (mm)	Morning Stiffness (minutes)
ETA-N	PRE	1.15 ± 0.67	51.0 ± 29.8	80.8 ± 71.7
	POST	0.91 ± 0.66	40.5 ± 29.4	41.7 ± 56.7
	P VALUE	.16	.17	.02
ETA-F	PRE	1.04 ± 0.5	58.4 ± 23.9	79.0 ± 72.7
	POST	1.02 ± 0.4	55.3 ± 23.4	58.6 ± 67.5
	P VALUE	.89	.67	.33

New Arthritis Pain Guidelines Unveiled *continued from page 1*

ment, including an evaluation of the biological, psychological, and social factors that may be contributing to pain, as well as assessment of the overall impact on pain and function.

"Because pain is a major cause of disability in persons with arthritis, assessment of functional status should be included in pain assessment," said guideline panel member Karen L. Kerr, MSN, RN, of the Children's Hospital of Michigan in Detroit.

Treatment recommendations

Cognitive behavior therapy (CBT) should be used to reduce pain and psychological disability and enhance self-efficacy and coping, Kerr told listeners at an afternoon conference on Monday. Analgesic and anti-inflammatory medications should be used concurrently with CBT and nutritional, physical, and educational intervention.

Traditional nonsteroidal anti-inflammatory drugs (NSAIDs) should be considered only for patients who do not respond to therapy with acetaminophen or COX-2 inhibitors, and only after risk analysis is done to determine the risk for significant NSAID-induced GI complications, Kerr stated. If such risk factors exist, a prophylactic drug, such as a proton pump inhibitor, should be prescribed along with traditional NSAIDs.

For patients with knee OA that is unresponsive to acetaminophen, traditional NSAIDs, or COX-2 inhibitors, or those who cannot take these drugs, injection of hyaluronic acid into the knee can be considered at any time during the illness.

For patients with RA receiving disease-modifying antirheumatic drug therapy, acetaminophen should be used concomitantly for mild pain. For patients in more severe pain, with or without inflammation, a COX-2 inhibitor should be used concurrently unless the patient has clear risk factors for exacerbation of GI complications or renal disease.

When selecting pain medication, clinicians need to consider efficacy of treatment, adverse effects, dosing frequency, cost, and patient preferences. Treatment needs to be tailored to the patient.

Such is the case with COX-2 inhibitors. Panel co-chair Lee S. Simon, MD, associate professor of medicine at Harvard Medical School in Boston, observed: "If you've got a high-risk patient with a lot of hypertension and edema and congestive heart failure, I probably wouldn't choose rofecoxib. If they have a sulfonamide allergy, I wouldn't choose celecoxib."

For many patients, it is important to treat the anticipation of pain, and celecoxib could offer an advantage in this regard. Celecoxib, but not rofecoxib, can be taken twice daily, which may provide a psychological comfort to some patients. "It makes the patients feel more in control," said Dr. Simon, associate chief of medicine at the Beth Israel Deaconess Medical Center in Boston.

— Jody Charnow

Electronic risk-assessment accurate *continued from page 1*

ications, and previous hospitalization for GI problems were all related to a higher rate of GI bleeding ($p < .001$).

The investigators examined data collected electronically for patients who filled a prescription for NSAIDs between July 1, 1999, and March 31, 2000. The study included 303,211 patients taking NSAIDs for at least 8 months.

—DW

Joint distraction superior to debridement for severe OA

SAN FRANCISCO—Clinical outcome is better with joint distraction than with arthroscopic debridement in the treatment of severe ankle osteoarthritis (OA). A new, controlled study found that joint distraction provided greater improvement in pain, function, and clinical condition.

Although previous studies have shown the clinical benefits of joint distraction (see, for example, *Osteoarthritis & Cartilage* 1999;7: 474-479), this is the first closed, controlled study to examine the effects on severe knee OA. The method prevents mechanical contact of the articular surfaces while maintaining intra-articular intermittent fluid pressure during walking.

Joannes W. J. Bijlsma, MD, of the University Medical Center, Utrecht, the Netherlands, and his colleagues conducted the randomized study, which included nine patients who underwent joint distraction and eight who had debridement of the ankle joint. After 1 year, the distraction group patients had an average 49% reduction in pain compared with 20% reduction in the debridement group. Function increased by 52% versus 24% with distraction compared with debridement, and clinical condition improved by 61% versus 12%. Moreover, radiographic joint space width increased after distraction, while decreasing after debridement.

—DW

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