

Rheumatology Trials Review

Osteoarthritis

Rheumatoid Arthritis – Nonbiologics

Rheumatoid Arthritis – Biologics

Spondyloarthropathies

Low Back Pain

Crystal Deposition Diseases

Systemic Vasculitis

Systemic Lupus Erythematosus

Systemic Sclerosis

Osteoporosis

Sjögren's Syndrome

Antiphospholipid Antibody Syndrome

Behçet's Disease

EDITORS:

Michael Weisman, MD

Daniel E. Furst, MD

Jan Hillson, MD

Rheumatology Trials Review

Edited by:

**Michael Weisman, MD
Daniel E. Furst, MD
Jan Hillson, MD**

Studies Compiled by:

**Michael Weisman, MD
Daniel E. Furst, MD
Jan Hillson, MD**

Michael Weisman, MD

Director, Division of Rheumatology
Cedars-Sinai Medical Center
Los Angeles, CA

Daniel E. Furst, MD
Director, Arthritis Clinical Research Unit
Virginia Mason Research Center
Seattle, WA

Jan Hillson, MD
Fellow Member
Virginia Mason Research Center
Seattle, WA

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Introduction

The purpose of this volume is to inform the reader of the most recent advances in rheumatic disease therapeutics brought about by clinical trials. The authors have chosen articles in the published literature from peer reviewed journals that represent clinical studies in commonly encountered rheumatologic illnesses (such as gout, osteoarthritis, rheumatoid arthritis) as well as the unusual and less commonly encountered conditions (for example, Behçet's disease, vasculitis).

In most cases we have chosen articles that describe well controlled, blinded, placebo containing, randomized assignment clinical trials. In certain situations there could not be blinding or placebo arms in a trial; in these circumstances, the trial was included because it contained potentially useful information.

In an attempt to make this review thoughtful for the reader with a critical eye, the authors have dissected the articles with careful attention paid to the materials and methods sections. The "make or break" of a study may simply depend on the patient selection criteria or a specific outcome measure chosen, and this was emphasized in our reviews.

The conclusions drawn by the authors of this review may not be the same as put forth by the investigators in each trial. We have tried to put the study into the context of other trials in the same disease. Our goal was to tell the reader just how persuasive the evidence was for a therapeutic effect, and often it is useful to know the evidence for benefit from like or similar therapies.

It is important to remember that a trial is not the same thing as a recommendation on how to treat a particular patient. Trials are necessarily very selective in their patient populations and their outcome measures; they tell us what happens to groups of patients and not necessarily the result to be expected in a specific case. However, the authors believe that a proper interpretation of clinical trial data is essential to the understanding of therapy and the care of individual patients.

Michael Weisman, MD

Daniel E. Furst, MD

Jan Hillson, MD

Prescription and tolerability of meloxicam in day-to-day practice: Postmarketing observational cohort study of 13,307 patients in Germany

Title	Prescription and tolerability of meloxicam in day-to-day practice: Postmarketing observational cohort study of 13,307 patients in Germany.
Authors	Zeidler H, Kaltwasser JP, Leonard JP, et al.
Reference	J Clin Rheumatol 2002;8(6):305-315.
Disease	Osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and other rheumatic diseases.
Purpose	Under real world prescribing conditions, this study obtained actual use data on a large cohort of patients receiving prescriptions of a newly introduced cyclooxygenase-2 (COX-2) selective nonsteroidal anti-inflammatory drug (NSAID), meloxicam, under conditions of everyday medical practice with particular reference to patient selection and individual patient risk profiles.
Design	Large-scale prospective observational cohort study in 4000 medical practices throughout Germany shortly after the introduction of meloxicam.
Patients	13,307 patients from 2155 physicians.
Follow-up	3 months.
Regimen	Meloxicam prescriptions of 7.5 mg in 65% of patients and 15 mg in 33% of patients.

Prescription and tolerability of meloxicam in day-to-day practice: Postmarketing observational cohort study of 13,307 patients in Germany

(continued)

Results In this cohort, a substantial number of patients (12%) would be considered high-risk subjects having had a previous history of a perforation, ulcer, or bleeding. In addition, 24% had at least one concomitant cardiovascular disorder, and 26% were taking at least one antihypertensive medication. In terms of safety over this 3-month period of observation, 4 uncomplicated cases of gastric ulceration, one serious perforated gastric ulcer, and one serious ileus complication were observed related to incorrect use or incorrect dose of medication. 85% of patients reported good or very good effectiveness and 94% reported good or very good tolerability. Less than 1% (0.8%) of patients reported adverse gastrointestinal side effects related to the drug. It appears that the patients in this cohort were negatively selected for this new agent because of their prior experience with non-selective COX inhibitors as well as prior NSAID-induced toxicity and their individual risk profiles.

Conclusions Patients selected for the introduction of this new NSAID were subjects that had a significant prior history of NSAID intolerance and lack of efficacy as well as a high-risk profile for NSAID use. Despite these caveats, treatment with meloxicam at recommended dosages resulted in clinically meaningful treatment responses under real life conditions. Acceptable renal, cardiovascular, and gastrointestinal tolerability were observed; very few life-threatening or serious adverse events occurred. However, this study only evaluated patients over a 3-month period. The long-term use of this agent in this population needs further evaluation.

***Safety and efficacy of meloxicam in the treatment
of osteoarthritis***

Title	Safety and efficacy of meloxicam in the treatment of osteoarthritis.
Authors	Yocum D, Fleischmann R, Dalgin P, et al.
Reference	Arch Intern Med 2000;160:2947-2954.
Disease	Osteoarthritis.
Purpose	The purpose of the study was to evaluate the safety and efficacy of 3 doses of meloxicam (3.75, 7.5, and 15.0 mg/day) in comparison to both placebo and to an active comparator diclofenac (100 mg/day) in patients with osteoarthritis of either the knee or the hip when the prior NSAID was withdrawn.
Design	Double blind, parallel group, both placebo and active comparator controlled, multicenter study.
Patients	At least a 3 month history of osteoarthritis of the knee or hip confirmed by x-ray and clinical signs and symptoms, current NSAID user, age at least 40 years, and pain on movement in the target joint.
Follow-up	12 weeks.
Regimen	Meloxicam 3.75, 7.5, and 15 mg/day, compared to placebo and diclofenac 100 mg/day.

Safety and efficacy of meloxicam in the treatment of osteoarthritis

(continued)

Results

A total of 1091 patients were enrolled and screened at 61 study centers, 779 patients were randomized, and 774 initiated treatment. The incidence of all adverse events was comparable among all of the 3 meloxicam groups (55%–58%) and was higher than the placebo group (48%) but lower than the diclofenac group (66%). There were no significant differences in the incidence of gastrointestinal (GI) adverse events between placebo and meloxicam groups; there were significantly more GI events in the diclofenac group compared to placebo. The incidence of serious adverse events was similar among the active treated groups and slightly higher than the placebo patients. There were no statistically significant differences among the safety laboratory tests in any of the active treatment groups compared to placebo. However, there were slightly increased liver function tests noted in the diclofenac group. In terms of efficacy, all groups improved significantly from their flare state at baseline. Efficacy of the active treatment groups was evident within 2 weeks of starting drug. For the primary outcome measure at the final visit, the WOMAC, both the two higher meloxicam and the diclofenac doses were superior to placebo.

Conclusions

Meloxicam is a member of the oxicam family and is used currently worldwide in 80 countries for osteoarthritis; it demonstrates more COX-2 inhibition than COX-1 at therapeutic doses. It has a plasma elimination half-life of 20 hours, good bioavailability with once daily dosing, and has been shown to be comparable to piroxicam and diclofenac in prior studies. This study extends these evaluations and reveals that its safety profile in terms of GI side effects is better than diclofenac and similar to placebo in this short-term trial. This drug is a useful alternative to currently prescribed NSAIDs and the higher dose (15 mg) appears to be safe. However, the long-term GI toxicity needs to be further evaluated.