Comparison of Etodolac and Piroxicam in Patients with Osteoarthritis of the Hip or Knee

A Prospective, Randomised, Double-Blind, Controlled Multicentre Study†

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Summary

The efficacy and safety of etodolac and piroxicam were compared in patients with osteoarthritis of the hip (n = 111) or knee (n = 160). Special emphasis was placed on clinical gastrointestinal adverse effects.

271 patients participated in this 8-week prospective, multicentre, randomised, double-blind trial. Efficacy was measured by patient’s and investigator’s assessment of key parameters after 4 and 8 weeks of treatment compared with baseline. Tolerability was evaluated by patients’ complaints at each visit (adverse events) and laboratory tests performed before and at the end of treatment.

After 4 and 8 weeks of treatment and at the end of treatment, patients’ and investigators’ assessments were significantly improved from baseline in both groups. There were no statistically significant differences between the groups in any efficacy assessment at any observation. In the etodolac group 30% reported adverse events, compared with 46% in the piroxicam group (p < 0.01). In the study, 20% in the etodolac group and 29% in the piroxicam group reported gastrointestinal adverse events (not significant). Clinically significant falls in haemoglobin occurred in 22% of patients with no significant difference between the 2 groups.

In conclusion, the study indicated that etodolac 600mg per day was as effective as piroxicam 20mg per day in the treatment of osteoarthritis. Etodolac produced adverse events in a significantly smaller number of patients than piroxicam. No significant differences were found between etodolac and piroxicam with respect to incidence of clinical gastrointestinal adverse events.

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Osteoarthritis (OA) is a widespread, slowly developing disease, with a high prevalence which increases with age. In a large study of a Dutch community, the maximum age-specific prevalence of severe radiological OA of the hip was 3.7% for men and 10.4% for women. Similarly, radiological OA of the knee reached a maximum age-specific prevalence of 8.5% for men and 29.9% for women.[1]

Although the primary disorder of idiopathic OA is probably noninflammatory, inflammation and pain are common complications of the disease, making nonsteroidal anti-inflammatory drugs (NSAIDs) important in the pharmacological treatment of OA.[2] NSAIDs have proven to be efficient in relieving the signs and symptoms of OA, but with a marked variability in patient response to therapy.[3]

Treatment with NSAIDs is associated with a high incidence of symptomatic complications of primarily gastrointestinal origin, which leads to discontinuation of therapy in up to 10% of patients with rheumatic diseases treated with NSAIDs.[4] These symptoms may sometimes be relieved simply by switching therapy from one NSAID to another, emphasising the unpredictability of the interaction between patient and NSAID medication.[3, 4] Similarly, endoscopic and micro-bleeding studies have shown that asymptomatic complications such as gastroduodenal erosions, ulcerations, and bleeding are quite common, while patients complaining of gastrointestinal symptoms frequently present without objective gastrointestinal lesions.[4]

Epidemiological evidence suggests that NSAID use is associated with at least a 3-fold increase in risk of upper gastrointestinal bleeding or ulceration.[5-8] Despite these adverse effects NSAIDs remain among the most commonly prescribed drugs, and the economic consequences of dealing with the gastrointestinal adverse effects of NSAID use are staggering.[8]

Etodolac, a relatively new NSAID with analgesic and antipyretic activity, is characterised by a tetrahydropyranoindol nucleus. Etodolac has been shown to provide symptomatic relief in the treatment of OA.[9, 10] Results from clinical trials and postmarketing surveillance studies have established a favourable tolerability profile of etodolac[9-11] with an incidence of adverse effects other than dyspepsia and abdominal pain similar to that of placebo.[11]

Piroxicam 20mg per day is an effective NSAID and a frequently selected treatment for OA.[12] The present study was designed to compare the efficacy and tolerability of etodolac 600mg per day and piroxicam 20mg per day in the treatment of patients with OA of the hip or knee, with special emphasis on the incidence of clinical gastrointestinal adverse effects.

**Patients and Methods**

**Patient Selection**

Patients with radiologically proven OA of the hip or knee, showing at least 2 of the following conditions: 1) weight-bearing pain, 2) joint stiffness, 3) pain on motion, who gave their informed consent, were recruited to participate in a double-blind, randomised study. The patients were men and women 40 years of age or over. The women enrolled were not pregnant or breast-feeding, and women of childbearing age were required to use contraception.

Patients were excluded if they had impaired renal or liver function; a history of gastrointestinal bleeding or peptic ulcer disease; inflammatory joint disease; allergy towards aspirin or other NSAIDs. Patients who were receiving lithium; H2-antagonists; anticoagulants; systemic or intra-articular corticosteroids within the previous 2 months; penicillamine, gold, immunosuppressive drugs or cytotoxic agents within the previous 6 months were not eligible for the study. Patients with OA in more than one joint were classified and evaluated according to the most affected joint.

**Study Design**

This was a prospective, multicentre, randomised, double-blind, double-dummy, outpatient study