Tenoxicam
An Update of its Pharmacology and Therapeutic Efficacy in Rheumatic Diseases

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Tenoxicam administered orally, rectally or parenterally is an effective analgesic and anti-inflammatory agent for the symptomatic treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and various rheumatic conditions such as tendinitis, bursitis, sciatica, back pain and gouty arthritis. In clinical trials its efficacy is at least equivalent to that of other NSAIDs and it is at least as well tolerated as piroxicam and probably better tolerated than diclofenac, indomethacin and ketoprofen. Compared with many other NSAIDs, tenoxicam offers certain advantages in that it is conveniently administered once daily and dosage adjustment is not required in the elderly or in patients with renal or hepatic impairment.

Pharmacological Properties

Tenoxicam is a nonsteroidal anti-inflammatory drug (NSAID), possessing the general pharmacodynamic properties typical of this class of drugs. It is a potent analgesic, anti-inflammatory and antipyretic agent in animal models, effects which are generally believed to be mediated by the inhibition of cyclooxygenase and subsequent prostaglandin formation. Its ability to inhibit leucocyte functions, including phagocytosis and histamine release, and to promote the scavenging of oxygen radicals may contribute to its anti-inflammatory activity. Studies in animals and humans indicate that tenoxicam has a lower gastrotoxic potential than some other NSAIDs, including aspirin and diclofenac, and it was similar to piroxicam in this regard. Tenoxicam is a potent reversible inhibitor of the secondary phase of platelet aggregation but does not appear to affect fibrinolytic potential. Renal function is not normally altered during treatment with tenoxicam, although a minor decrease in creatinine clearance may occur in patients with pre-existing renal impairment, an effect generally seen with most other NSAIDs.

The pharmacokinetic profile of tenoxicam is characterised by complete absorption following oral administration, high protein binding (> 98.5%), low volume of distribution (0.12 to 0.15 L/kg), efficient penetration into synovial fluid, low systemic clearance (0.1 L/h) and long elimination half-life (60 to 75 hours), permitting once daily doses (repeated once-daily administration for 10 to 15 days being necessary to achieve steady-state). The average time to achieve peak plasma concentrations is 1 to 2.6 hours fasting and 4 to 6 hours postprandial. Tenoxicam is completely metabolised to form inactive metabolites which are excreted in urine and faeces. The bioavailability of rectally administered tenoxicam is about 80% compared with either oral or parenteral routes. The bioavailability of tenoxicam is unaffected by age, gender, renal or hepatic impairment, and rheumatic disease states.

Therapeutic Use

Tenoxicam has been well studied in the treatment of chronic rheumatic disorders such as rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Placebo-controlled trials have confirmed the analgesic and anti-inflammatory efficacy of tenoxicam in these conditions. Dose-finding studies have generally revealed that the currently recommended dosage of 20mg once daily provides the best balance between efficacy and tolerability. In long term therapy, increasing the dosage adds little therapeutic benefit with a greater risk of side effects. However, 10mg once daily may provide an appropriate maintenance dosage in Japanese patients. Therapeutic efficacy is maintained during long term treatment up to several years.

In comparative studies tenoxicam 20mg once daily was at least equivalent to usual therapeutic dosages of other NSAIDs such as piroxicam, naproxen, acemetacin, diclofenac, ibuprofen, indomethacin and ketoprofen. Tenoxicam was usually administered as tablets or capsules in these trials; however, rectal administration as suppositories or oral administration as an instant drink granulate were shown to be similarly effective (as would be predicted from their pharmacokinetic profiles). Parenteral administration may be used to provide prompt relief of severe pain in rheumatic conditions with subsequent transfer to more convenient dosage forms.

Preliminary noncomparative studies and a placebo-controlled trial indicate that tenoxicam 20 to 40mg once daily may be an effective symptomatic treatment for acute gout, although com-