A Double-Blind Study Comparing Nimesulide with Naproxen in the Treatment of Osteoarthritis of the Hip

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Summary

120 patients, aged between 45 and 87 years, with a history of osteoarthritic disease of at least 12 months' duration and unilateral or bilateral hip pain, were randomly allocated to treatment with either nimesulide (100mg twice daily) or naproxen (500mg twice daily) for 4 weeks. Nimesulide was associated with a statistically significant improvement in the primary efficacy variable - pain intensity at rest - compared with baseline (mean improvement 71% at week 2, 80% at week 4; p < 0.01), and a significant concomitant improvement in the number of night awakenings, pain on active and passive movement, morning stiffness and impairment of articular mobility on active and passive movement. The global clinical efficacy of nimesulide at the end of treatment was rated as good/fair by ≥ 85% of patients and doctor. For all the efficacy variables assessed, there was no statistically significant difference between treatment with nimesulide or naproxen. Four adverse events were reported in each treatment group; they were mild/moderate in intensity and predominantly gastrointestinal in nature. The results of this study confirm that nimesulide is clinically effective and a suitable alternative to naproxen for the short term treatment of patients with osteoarthritis of the hip.

Osteoarthritis is a chronic, progressive articular disorder characterised by pain, a reduction in joint mobility and, in some patients, inflammation. The prevalence of this most common joint disease rises with increasing age and occurs in approximately 85% of 75- to 79-year olds. In this setting, surgical intervention is an option for patients with severe and debilitating disease, while pharmacotherapy is principally palliative and directed at symptomatic relief. Simple analgesics are useful in patients with mild disease, although nonsteroidal anti-inflammatory drugs (NSAIDs) are the mainstay of therapy, particularly in patients with joint inflammation. Nimesulide is an NSAID structurally characterised by a sulfonanilide functional group. It has demonstrated clinically significant anti-inflammatory, analgesic and antipyretic activity in a variety of painful inflammatory conditions, including those associated with osteoarthritis, musculoskeletal injury, cancer, thrombophlebitis, postoperative trauma and gynaecological disorders. Compared with other NSAIDs, nimesulide is a selective inhibitor of inflammatory prostaglandin synthesis.
addition, various nonprostaglandin mechanisms have been postulated to explain its therapeutic effects. Indeed, nimesulide has been shown to possess a variety of pharmacological properties, including free radical scavenging and the inhibition of histamine release and activity, neutrophil myeloperoxidase, cartilage degradation (through metalloprotease synthesis inhibition), phosphodiesterase type IV, platelet activating factor synthesis and tumour necrosis factor-α.\textsuperscript{[4,6]}

This double-blind trial was designed to further assess the efficacy of nimesulide (100mg twice daily) in the short term treatment of patients with osteoarthritis of the hip. The NSAID naproxen (500mg twice daily) is a standard drug used in the treatment of osteoarthritis and was selected as the comparative agent. The study was conducted using a double-dummy technique.

Patients and Methods

Patients

Male and female patients with a history of osteoarthritic disease of at least 12 months’ duration and unilateral or bilateral hip pain were eligible for enrolment in this study. Patients with diffuse osteoarthritic pain were eligible only if the hip was the main source of all subjective and/or objective symptoms.

All patients had active disease. Clinical diagnosis of the condition was confirmed by x-ray of the affected joint during the preceding 12 months and the presence of pain of moderate to severe intensity.

Patients with a known hypersensitivity to any NSAID, those with a history of peptic ulceration or gastrointestinal bleeding in the preceding 12 months, and patients who had received oral, intrarticular or systemic corticosteroids up to 2 weeks prior to study commencement were excluded. Patients with clinically significant gastrointestinal, hepatic and/or renal impairment, those with other systemic inflammatory diseases, and pregnant or lactating women were also excluded.

The concurrent administration of anti-inflammatory analgesic or muscle relaxant drugs was not permitted, and NSAID therapy was withdrawn at least 7 days prior to study commencement. The occasional use of paracetamol (up to 3g daily) as a rescue medication for pain relief was permitted.

At study entry the clinical history of each patient was recorded and an objective clinical examination performed that included documentation of the following: general and local conditions, joint function and pain provoked by movement, unilateral or bilateral localisation of the hip due to osteoarthritis, distant or recent history of osteoarthritis disease, other disorders and/or concurrent treatment.

All patients gave informed consent to participate in this investigation. The study was conducted in compliance with the recommendations of the Declaration of Helsinki as revised in Venice (1983) and Hong Kong (1989).

Study Treatment

Eligible patients were randomly allocated to receive nimesulide 100mg twice daily or naproxen 500mg twice daily for 4 weeks; the maximum permitted variation in the duration of treatment was ± 5 days. The double-blind design of this study was accomplished using a double-dummy technique. The code for each medication package was supplied in a sealed envelope to be opened at the end of the trial. It was unnecessary to reveal the identification of the study medication for any patient during the course of the trial.

Efficacy Variables

Efficacy variables were assessed at baseline (week 0) and after 2 and 4 weeks of treatment (± 3 days) by clinical examination and review of patients’ diaries.

The primary end-point, spontaneous diurnal pain at rest, was rated by the patient on a 10cm visual analogue scale (VAS) [0cm = no pain, 10cm = unbearable pain] and on an arbitrary 4-point scale (0 = no pain, 3 = marked pain). Other variables assessed by the patient were pain provoked by active and passive movement (10cm