NON-ASPIRIN, NON-STEROIDAL ANTI-INFLAMMATORY DRUGS FOR TREATING OSTEOARTHRITIS OF THE KNEE

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A B S T R A C T

Background

Osteoarthritis(OA) is the most common rheumatic disease. Simple analgesics are now accepted as the appropriate first line pharmacological treatment of uncomplicated OA. Non-aspirin NSAIDs are licensed for the relief of pain and inflammation arising from rheumatic disease.

Objective

To determine whether there is a difference in the relative efficacy of individual non-steroidal anti-inflammatory drugs (NSAIDs) when used in the management of osteoarthritis (OA) of the knee.

Criteria for considering studies for this review

We searched Medline (1966-1995) and Bids Embase (Jan-Dec, 1980-1995). The searches were limited to publications in the English language, and were last performed in November 1996. We used modified Cochrane Collaboration search strategy to identify all randomised controlled trials. The MeSH heading "osteoarthritis" was combined with the generic names of the 17 non-aspirin NSAIDs licensed in the UK for the management of OA in general practice. The search of Embase used the term "osteoarthritis" if present in the abstract, title or keywords, and was combined with the generic names of the 17 non-aspirin NSAIDs, only if they were mentioned in the title, abstract or keywords.

Selection criteria

All double blind, randomised controlled trials, in the English language, comparing the efficacy of two non-aspirin NSAIDs in the management of osteoarthritis of the knee, were selected. Only trials with subjects aged 16 years and over, with clinical and/or radiological confirmation of the diagnosis of OA knee were included. Studies which compared one "trial" NSAID with one "reference" NSAID were included provided they were non-aspirin NSAIDs available in the UK and were licensed for the treatment of OA by general practitioners. Trials which were placebo-controlled and which also involved the comparison of two NSAIDs were also included.

Data collection and analysis

The methodological design of each study was scored according to a pre-determined system. The three main outcome measures of pain, physical function and patient global assessment were chosen based on the core set agreed upon by OMERACT (Outcome Measures in Rheumatology Clinical Trials). These were used to determine the power of each trial. The equivalency of NSAID doses was calculated using the percentage of the recommended maximum daily dose. Sample size estimates for the detection of clinically relevant changes in outcome measures used in the assessment of OA knee were used for power calculations. These calculations

were performed to determine whether the trials were of a sufficient size to detect clinically relevant differences which were statistically significant. The calculations incorporate estimates of standard deviation, and minimum, median and maximum differences (delta) between drugs which are deemed to be clinically important. The number of "withdrawals due to lack of efficacy" was also selected as an outcome measure for this review. The Peto odds ratio and 95% confidence intervals were calculated where possible. The results of studies which compared the same trial and reference NSAIDs were combined where possible.

Main results

Of the 1151 trials identified by the search strategy, 22 involved knee osteoarthritis only. Sixteen of these trials fulfilled the inclusion criteria and were entered in the review. Eight NSAIDs were represented in these trials. Etodolac was represented in 11 trials. The reference NSAID in these trials was piroxicam (n=3), naproxen(n=3), diclofenac (n=3), indomethacin (n=1), and, nabumetone (n=1).

Authors' conclusions

In spite of the large number of publications in this area, there are few randomized controlled trials. Furthermore, most trials comparing two or more NSAIDs suffer from substantial design errors. From the results of this review it is concluded that no substantial evidence is available related to efficacy, to distinguish between equivalent recommended doses of NSAIDs. Had studies employed appropriate doses of comparator drug, most would have been sufficiently powerful to detect clinically important differences in efficacy. As differences in efficacy between NSAIDs have not been recorded, the selection of an NSAID for prescription for OA knee should be based upon relative safety, patient acceptability and cost.