Efficacy and safety of piroxicam revisited: a global meta-analysis of randomised clinical trials

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CRD summary
This review concluded that piroxicam had a similar or more favourable efficacy and safety profile compared with other non-steroidal anti-inflammatory drugs. The review had a number of limitations, which mean that the authors' conclusions may not be reliable.

Authors' objectives
To evaluate the efficacy and safety of piroxicam compared with other non-steroidal anti-inflammatory drugs (NSAIDs).

Searching
The authors searched MEDLINE, BIOSIS Previews, HealthSTAR, EMBASE, the Cochrane Library, Current Contents and EBM Reviews for studies published in English between 1980 and August 2006. Search terms were not reported. Reference lists of retrieved articles were also screened.

Study selection
Parallel-group randomised controlled trials (RCTs) of piroxicam given orally (10 to 40mg/day) for more than seven days were eligible for the review. Trials had to compare piroxicam with another oral NSAID and report on pain, articular swelling, mobility, global efficacy or tolerance (overall, gastrointestinal and skin).

Included RCTs compared piroxicam with a wide range of comparators, naproxen and tenoxicam being the most common. Treatment duration ranged from seven to over 365 days; only 3% of studies lasted more than three months. About 45% of participants had osteoarthritis, 21% had rheumatoid arthritis, 17% had acute pain conditions and 10% had chronic pain.

The authors did not state how studies were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed using the 5-point Jadad scale (converted to a percentage).

The authors did not state how the validity assessment was performed.

Data extraction
Odds ratios (ORs) were extracted or calculated for dichotomous outcomes and effect sizes (weighted or standardised mean difference) for continuous outcomes. Intention-to-treat data were used where possible. Data were extracted by two independent reviewers, while data encoding was performed by a single reviewer. Quality controls were performed by random double-checking at both stages.

Methods of synthesis
Trials were pooled by meta-analysis using a fixed-effect model; a random-effects model was used if statistically significant heterogeneity (p<10% using Cochran's Q statistic) was present. The analysis focused on comparisons for which three or more RCTs were available. Publication bias was assessed by inspection of funnel plots and statistical methods.

Results of the review
Seventy-five RCTs with 33,286 participants were included. Twenty-one were rated good to excellent for quality (Jadad score 4 or 5). None of the methods used suggested the presence of significant publication bias.
**Efficacy:** Overall, piroxicam did not differ significantly from all other non-steroidal anti-inflammatory drugs (NSAIDs) combined for dichotomous global efficacy outcomes (OR 1.06, 95% confidence interval (CI) 0.96 to 1.18). Piroxicam was significantly superior to naproxen (OR 1.37, 95% CI 1.05 to 1.77; 14 RCTs). Results for specific outcomes were reported.

**Safety:** For dichotomous safety outcomes (i.e. occurrence of adverse events), piroxicam was significantly superior to other NSAIDs overall (OR 0.83, 95% CI 0.73 to 0.95) and for gastrointestinal outcomes (OR 0.74, 95% CI 0.59 to 0.93). Major gastrointestinal events were not significantly more common with piroxicam than other NSAIDs, with the exception of meloxicam (OR 2.37, 95% CI 1.13 to 4.97, five RCTs). None of the included trials reported on cardiovascular safety.

**Authors’ conclusions**
Piroxicam had a similar or more favourable efficacy and safety profile compared with other non-steroidal anti-inflammatory drugs.

**CRD commentary**
The inclusion criteria for intervention, comparators, outcomes and study design were clear. Inclusion criteria for participants were not explicitly stated and it appeared that people with any indication for NSAID treatment were included. Only RCTs were included, which was appropriate for efficacy but possibly inappropriate for the assessment of safety. The authors searched several databases but search terms were not reported, which made it difficult to assess the search strategy. Only studies published in English were included, so the review could be at risk of language bias. Unpublished studies were not sought, but publication bias was assessed by several methods and no evidence of bias was found. Validity of included RCTs was assessed using a standard scale, although results for individual quality features were not reported. Data extraction was performed in duplicate but other review methods were not reported, so the risk of reviewer errors or bias affecting the review is uncertain.

Limited details of included trials were presented. Trials were pooled by meta-analysis. Statistical heterogeneity was assessed and used to decide between fixed-effect and random-effects models. The pooled results for global efficacy and safety represent pooling of clinically heterogeneous, mainly short-term, trials with different populations and outcomes, and should be treated with caution. The absence of data on cardiovascular safety meant that the review could not give a full picture of safety issues relating to NSAIDs. Overall, the limitations of the review suggest that the authors' conclusions may not be reliable.

**Implications of the review for practice and research**
The authors did not state any implications for practice or research.

**Funding**
Chiesi Farmaceutici Italy.

**Bibliographic details**

**PubMedID**
19467328

**DOI**
10.1016/j.phrs.2009.03.021

**Original Paper URL**
http://dx.doi.org/10.1016/j.phrs.2009.03.021

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; Anti-Inflammatory Agents, Non-Steroidal /adverse effects /therapeutic use; Gastrointestinal Tract /drug effects; Humans; Middle Aged; Musculoskeletal Diseases /drug therapy; Piroxicam /adverse effects /therapeutic use; Randomized Controlled Trials as Topic; Skin /drug effects

**AccessionNumber**
12009109200

**Date bibliographic record published**
13/01/2010

**Date abstract record published**
17/02/2010

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.