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Title **Cyclooxygenase-2 Selective Non-Steroidal Anti-Inflammatory Drugs (Etodolac, Meloxicam, Celecoxib, Rofecoxib, Etoricoxib, Valdecoxib and Lumiracoxib) for Osteoarthritis and Rheumatoid Arthritis: A Systematic Review and Economic Evaluation**

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Aim

To review the clinical and cost effectiveness of cyclooxygenase-2 (COX-2) selective nonsteroidal antiinflammatory drugs (NSAIDs) for osteoarthritis (OA) and rheumatoid arthritis (RA).

Conclusions and results

The COX-2 selective NSAIDs examined in this report (ie, etodolac, meloxicam, celecoxib, rofecoxib, valdecoxib, etoricoxib, and lumiracoxib) were found to be similar to nonselective NSAIDs for the symptomatic relief of RA and OA and to provide superior gastrointestinal (GI) tolerability (most evidence is in patients with OA). Although COX-2 selective NSAIDs offer protection against serious GI events compared to nonselective NSAIDs, the amount of evidence for this protective effect varied considerably across individual drugs. The volume of trial evidence with regard to cardiovascular safety also varied substantially between COX-2 selective NSAIDs. Increased risk of myocardial infarction (MI) compared to nonselective NSAIDs was observed among those drugs with greater volume of evidence in terms of exposure in patient-years. Subgroup analyses of clinical and complicated upper GI events and MI events related to aspirin use, steroid use, prior GI history, and *Helicobacter pylori* status were based on relatively small numbers and were inconclusive. Economic modeling shows a wide range of possible costs per quality-adjusted life year (QALY) gained in patients with OA and RA. Costs per QALY varied if individual drugs were used *in standard-* or *high-risk* patients, the choice of nonselective NSAID comparator, and whether NSAID was combined with a proton pump inhibitor (PPI). When the model was run using ibuprofen or diclofenac combined with a PPI as the comparator, the results changed substantially, with the COX-2 selective NSAIDs looking generally unattractive from a cost-effectiveness standpoint. See Executive Summary link at www.hta.ac.uk/project/1383.asp.

Recommendations

This report summarizes the best available evidence and discusses its implications, but does not make recommendations about policy or clinical care.

Methods

Systematic reviews of randomized controlled trials and a model-based economic evaluation were undertaken. Electronic databases were searched up to November 2003. Industry submissions to the National Institute for Health and Clinical Excellence in 2003 were also reviewed. Meta-analyses were undertaken for each COX-2 selective NSAID compared with placebo and nonselective NSAIDs.

Further research/reviews required

With reduced costs of PPIs, future primary research needs to compare the effectiveness and cost effectiveness of COX-2 selective NSAIDs relative to nonselective NSAIDs with a PPI. Direct comparisons of different COX-2 selective NSAIDs, using equivalent doses that compare GI and MI risk are needed. Pragmatic studies that include a wider range of people, including the older age groups with a greater burden of arthritis, are also necessary to inform clinical practice.

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