

Non-Steroidal Anti-Inflammatory Drugs for Pain: A Review of Safety

Context

Non-steroidal anti-inflammatory drugs (NSAIDs) play an important role in pain management for clinical conditions such as headaches, menstrual disorders, post-operative pain, spinal and soft tissue pain, rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis.

Technology

NSAIDs reduce pain by blocking cyclooxygenase (COX) enzymes needed to produce prostaglandin. There are two forms of the enzyme: COX-1 and COX-2. Traditional NSAIDs, called “non-selective NSAIDs,” block both forms. NSAIDs that target only the COX-2 form are called “COX-2 selective NSAIDs” or “COX-2 inhibitors.”

Celecoxib (Celebrex) is the only COX-2 inhibitor currently available in Canada.

Issue

Based on their mechanism of action, COX-2 inhibitors are thought to be safer than non-selective NSAIDs in terms of gastrointestinal (GI) bleeding. However, COX-2 inhibitors are associated with an increased risk of major cardiovascular events such as heart attacks and strokes. The COX-2 inhibitor rofecoxib (Vioxx) was removed from the Canadian market in 2004 for this reason. Generic versions of celecoxib will soon be available in Canada.

A review of the comparative safety of NSAIDs will help inform decisions on their use for the management of pain.

Methods

A limited literature search was conducted of key resources, and titles and abstracts of the retrieved publications were reviewed. Full-text publications were

evaluated for final article selection according to predetermined selection criteria (population, intervention, comparator, outcomes, and study designs).

Key Messages

- The COX-2 inhibitor, celecoxib, appears to be associated with:
 - a cardiovascular risk similar to diclofenac and ibuprofen, and a higher risk than naproxen
 - a GI bleeding risk similar to diclofenac, and a lower risk than ibuprofen and naproxen.
- Among non-selective NSAIDs:
 - diclofenac may be associated with a higher cardiovascular risk than ibuprofen or naproxen
 - naproxen may be associated with a lower cardiovascular risk than diclofenac, ibuprofen, or indomethacin.
- Interpret these results with caution as:
 - study durations were short (generally less than three months)
 - studies used different NSAID doses.

Results

The literature search identified 275 citations, with an additional 8 articles identified from other sources. Of these, 13 were deemed potentially relevant and 6 met the criteria for inclusion in this review — 5 systematic reviews and 1 health technology assessment.

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