

CELECOXIB FOR OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS (UPDATED APRIL 2005)

CLINICAL QUESTION

Is celecoxib an effective and safe treatment for pain in osteoarthritis and (OA) rheumatoid arthritis (RA)?

THE EVIDENCE

Treatment	Condition	Comparator	Relevant Results/Authors' Conclusions [#]
REVIEW ONE [†] Celecoxib ^a	Rheumatoid arthritis	Non-selective NSAIDs: Naproxen ^b (1000 mg daily) Diclofenac (150 mg) daily	Moderate evidence that celecoxib (200 mg daily) was equivalent to naproxen for all measures (OMERACT, ACR-20 index, HAQ functional disability index) at 12 weeks' follow up. Celecoxib (400 mg and 800 mg daily) was slightly more effective than naproxen at 12 weeks' (greater improvement in patient and physician global assessment (400 mg) and HAQ functional disability score [800 mg]). Celecoxib (400 mg daily) was equivalent, but not superior, to diclofenac at 24 weeks' follow up. Moderate evidence for fewer gastro-duodenal ulcers (≥ 3 mm) detected by endoscopy for: <ul style="list-style-type: none"> celecoxib (200 mg, 400 mg, 800 mg), compared with naproxen, at 12 weeks' follow up; celecoxib (400 mg), compared with diclofenac, at 24 weeks' follow up.
		Placebo	Moderate evidence for significant improvement of all measures with celecoxib (100 mg, 200 mg, 400 mg, 800 mg) at 12 weeks' follow up. Celecoxib (80 mg daily) showed no difference when compared to placebo. Moderate evidence that the risk of developing gastro-duodenal ulcers was higher with celecoxib (200 mg, 400 mg, 800 mg), but this was not statistically significant at 12 weeks' follow up.
REVIEW TWO [‡] Celecoxib ^a	Rheumatoid arthritis Osteoarthritis	Non-selective NSAIDs: Naproxen ^b (1000 mg daily) Diclofenac (150 mg daily) Ibuprofen (2400 mg daily)	Evidence that fewer gastro-duodenal ulcers were detected by endoscopy for: <ul style="list-style-type: none"> celecoxib (100 mg, 200 mg, 400 mg, 800 mg), compared to naproxen, at 12 weeks' follow up; celecoxib (400 mg), compared to diclofenac, at 24 weeks' follow up; celecoxib (400 mg), compared to ibuprofen, at 12 weeks' follow up; Celecoxib (400 mg daily) was not better than diclofenac (150 mg daily) at 12 weeks' follow up.
		Placebo	Evidence for similar rates of gastro-duodenal ulcers associated with celecoxib (100 mg, 200 mg, 800 mg daily) at 12 weeks' follow up. Celecoxib (400 mg daily) was associated with a higher incidence of endoscopic ulcers.
Summary of five independent RCTs [¶] Celecoxib ^a	Rheumatoid arthritis Osteoarthritis	Non-selective NSAIDs: Diclofenac (150 mg daily) Dexibuprofen (800 mg daily)	Evidence for similar efficacy with celecoxib 200 mg daily and dexibuprofen, at 2 weeks' follow up (one RCT). Evidence for superior dyspepsia tolerability (pain intensity and satisfaction with dyspepsia-related health) for celecoxib 800 mg daily compared to diclofenac at 4, 13, 26 and 52 weeks' follow up (one RCT).
		COX-2 inhibitors Rofecoxib ^c (25 mg daily) Nimesulide (100 mg daily)	Evidence for similar efficacy with celecoxib 200 mg daily and rofecoxib in treating signs and symptoms of OA, at one and 6 weeks' follow up. Treatments were safe and well tolerated (two RCTs). Evidence that nimesulide had a more rapid analgesic action than celecoxib 200 mg daily and rofecoxib 25 mg daily at one week follow up. Treatments were safe and well tolerated (one RCT).
		Acetaminophen (4,000 mg daily)	Evidence that celecoxib 200 mg daily was superior to acetaminophen at 14 weeks' follow up. The adverse effects and tolerability were similar (one RCT).
		Placebo	Evidence that celecoxib 200 mg daily was superior to placebo at 6 and 14 weeks' follow up. The safety profile was similar (two RCTs).

[†]Based on five **AVERAGE*** quality randomized controlled trials (RCTs), as assessed by the authors of this review, published between 1999 and 2001; [‡]Based on five RCTs (two published in 1998 and 1999 and three unpublished) that **were not assessed** for methodological quality; [#]Refer to Grading Key document for explanation of evidence grading; NSAIDs – non-steroidal anti-inflammatory drugs; [¶]Based on five independent RCTs published between 2002 and 2004 that **were not assessed** for methodological quality. [#]Refer to Grading Key document for explanation of evidence grading

ADDITIONAL NOTES

^aCelecoxib (Celebrex[®]) has market approval from Health Canada for use in the treatment of adult patients with OA and RA. In a recent trial, Celebrex[®] administered for another indication was found to raise the risk of cardiovascular problems and deaths when taken at doses of more than 400 mg daily, at 2.8 years of follow up.

The Ambassador Project was initially funded by a one time grant from the Canadian Agency for Drugs and Technologies in Health (May 2004 to April 2005) (formerly the Canadian Coordinating Office for Health Technology Assessment). The Institute of Health Economics has provided funding to continue the Project.

Health Canada recommended usage restrictions for Celebrex[®] beginning in April 2005. Celebrex[®] should not be used in patients who have had a heart attack or stroke, serious chest pain related to heart disease, or congestive heart failure. Celebrex[®] may increase the risk of cardiovascular events in patients with high blood pressure, high cholesterol, diabetes, and smoking. Also, Celebrex[®] should be prescribed and used at the lowest possible dose and for the shortest, necessary period of time.

^bNaproxen (Apo[®]-Naproxen) – preliminary data from a recent trial suggested an increased risk of heart attack or stroke in patients taking naproxen 440 mg daily compared to a placebo. Health Canada advised that patients who are taking naproxen should consult their physicians and use it according to the prescribed directions.

^cRofecoxib (Vioxx[®]) - was withdrawn from the market by Merck & Co., Inc. in September 30, 2004. After 18 months of treatment in a RCT, patients taking rofecoxib (25 mg daily) had twice the risk of heart attack and stroke, compared with those receiving placebo.

The US Food and Drug Administration and Health Canada stated that the long-term effects of other COX-2 inhibitors need to be studied to establish whether other drugs in this class have similar dangerous side effects.

IMPLICATIONS FOR PRACTICE

What we don't know:

- What is the long-term effectiveness, safety, and tolerability of celecoxib?
- Is the safety profile of celecoxib related to the dose administered?
- What is the incidence of other adverse effects such as cardiovascular problems, hypertension, and peripheral edema?
- Is celecoxib safe and effective when used in conjunction with aspirin for cardiovascular prophylaxis?
- Does celecoxib cause fewer gastrointestinal side effects compared to a combination treatment of non-selective NSAIDs and drugs, such as proton pump inhibitors or H2 antagonists that protect the gastrointestinal tract?
- What is the incidence of adverse gastrointestinal effects when celecoxib is used by patients who are older or who routinely use corticosteroids?

Research Evidence: What we know

In patients with RA and OA, evidence indicates that celecoxib:

- is as effective as non-selective NSAIDs (naproxen, diclofenac, ibuprofen, dexibuprofen) and other COX-2 inhibitors (nimesulide, rofecoxib) in relieving pain in the short term;
- is more effective than acetaminophen and placebo in relieving pain in the short term.

In patients with OA and RA, celecoxib causes fewer gastro-duodenal ulcers than non-selective NSAIDs and showed a similar gastrointestinal safety profile as other COX-2 inhibitors, acetaminophen and placebo, in the short term.

Recommendation from Clinical Ambassadors

COX-2 inhibitors are not super-NSAIDs. They only work as well as conventional NSAIDs

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April 2005

Reference: This Evidence Brief is based on results from two systematic reviews (SRs) (one **AVERAGE*** and one **AVERAGE* to POOR*** quality) and five independent RCTs that **were not assessed** for methodological quality.

Moga C, Harstall C, Tang Z. *Celecoxib for the treatment of pain in rheumatoid arthritis and osteoarthritis*. Edmonton, Alberta: Alberta Heritage Foundation for Medical Research; 2005 May. Report: Information Paper 24. Available: <http://www.ihe.ca/publications/library/>

***Quality ratings for SR:** Good ● Average ● Poor ●

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