Title **Gastro-duodenal Ulcers Associated with the Use of Non-steroidal Anti-inflammatory Drugs: A Systematic Review of Preventive Pharmacological Interventions**

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Aim

- To assess the effectiveness of common pharmacological interventions used to prevent upper gastrointestinal (GI) toxicity associated with non-selective non-steroidal anti-inflammatory drugs (NSAIDs)
- To compare the upper GI toxicity of cyclooxygenase-isoform type 2 (COX-2) selective NSAIDs with that of non-selective NSAIDs, with or without concomitant use of gastroprotective agents
- To compare with placebo the upper GI toxicity of the COX-2 selective NSAIDs available in Canada

Conclusions and results

Misoprostol, proton pump inhibitors, and double doses of histamine type-2 receptor antagonists (H2RAs) were shown to effectively reduce the risk of endoscopically identified NSAID-induced gastric and duodenal ulcers. Standard doses of H2RAs, however, are ineffective. While misoprostol reduces the risk of NSAID-related ulcer complications, its use is associated with significant adverse effects, particularly at higher doses.

Compared with most non-selective NSAIDs, COX-2 selective NSAIDs have a safer G I profile than other NSAIDs and are better tolerated. An exception is with the comparator diclofenac: no statistically significant differences are observed with this agent. The reduced GI complication rate due to celecoxib may be lost when it is administered with acetylsalicyclic acid; this effect has not been tested with rofecoxib. The benefit of the growing clinical use of COX-2 selective NSAIDs with added gastroprotective agents remains unclear.

Methods

A systematic review of randomized controlled trialswas conducted. The literature was searched to identify trials of prophylactic agents used to prevent upper GI toxicity and trials that assessed the GI safety of the newerCOX-2 selective NSAIDs celecoxib (Celebrex™), meloxicam (Mobicox™), and rofecoxib (Vioxx®). Two independent reviewers selected studies, rated the quality of each included trial, and extracted data.

Further research/reviews required

Testing of the clinical use of COX-2 selective NSAIDs with added prophylaxis is needed.

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