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GI toxicity of celecoxib vs traditional NSAIDs

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Keywords

COX-2, coxibs, NSAID GI toxicity

Context

The discovery of a second isoform of the cyclooxygenase enzyme, COX-2, led to the recognition that COX-2 is primarily responsible for mediating pain and inflammation, whereas COX-1 provides for gastric protection and other homeostatic functions. Selective inhibitors of COX-2 (coxibs) were developed based on the hypothesis that such agents could reduce inflammation and pain with less gastrointestinal (GI) toxicity than nonselective traditional nonsteroidal antiinflammatory drugs (NSAIDs). This study tests that hypothesis in patients with rheumatoid arthritis and osteoarthritis.

Significant findings

The annual incidence of symptomatic ulcers and ulcer complications (bleeding, perforation, and obstruction) was less in patients taking celecoxib 400 mg twice daily (0.44%) than in patients taking ibuprofen 800 mg three times a day or diclofenac 75 mg twice daily (1.27%), so long as they were not taking aspirin. In patients taking low-dose aspirin (up to 325 mg/day), the occurrence of adverse GI events was lower with celecoxib than with nonselective NSAIDs, although this difference did not achieve statistical significance.

Comments

This study confirms the hypothesis that selective inhibition of COX-2 is associated with a reduction in serious GI toxicity, and demonstrates that this benefit is lost with co-administration of aspirin, an inhibitor of COX-1. The duration of therapy for analysis was limited to 6 months because of a high patient drop-out rate (43%). The fact that celecoxib therapy did not eliminate GI toxicity suggests a mechanism of toxicity unrelated to prostaglandin inhibition (such as *Helicobacter pylori*), or the

possibility that COX-2 inhibition may itself cause some GI toxicity, and that the COX-1/COX-2 paradigm is an oversimplification.

Methods

Prospective, randomized controlled trial with active comparator

References

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