

Nonsteroidal Anti-Inflammatory Drugs, Cyclooxygenase Inhibitors, and the Risk of Gastrointestinal Complications

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Although control of inflammation and pain in such conditions as osteoarthritis has improved greatly through the widespread use of nonsteroidal anti-inflammatory drugs (NSAIDs), a price has been paid. The price can be expressed in dollar terms, but is more properly a price paid in trading the inflammation and pain of the underlying diseases being treated by the NSAIDs, for the medical complications of the NSAIDs themselves. These complications are primarily gastrointestinal (GI) in nature, and include the development or exacerbation of peptic ulcers and gastritis, and complications of these conditions such as bleeding, perforation, and obstruction.

The magnitude of the problem is surprisingly large. Annually in the United States, NSAID-associated ulcer complications are estimated to lead to more than 100,000 hospitalizations and 16,500 deaths.¹ The annualized incidence rate in NSAID users of symptomatic ulcers ranges from 2% to 4% and of ulcer complications ranges from 1% to 2%.^{1,2} In the United States, the annual direct medical costs of these GI adverse events are approximately \$4 billion.^{1,2} The risk of ulcer complications, such as bleeding, is greatest in patients with comorbid conditions and in the elderly.

While the mechanisms underlying the adverse effects of NSAIDs on the GI tract have not all been elucidated and placed in order of importance for specific complica-

tions, they certainly include both a propensity to irritate the gastric mucosa and a deleterious (at least as regards GI disease) effect on platelet function.

Advances in our understanding of basic cell biology and the pharmacology of NSAIDs have led to the development of a new generation of anti-inflammatory agents, which act in a more targeted fashion. These agents inhibit the subtype of cyclooxygenase (COX-2) that is involved in the inflammatory pathway, while having no effect on the subtype (COX-1) that is thought to be responsible for the GI and platelet effects, and thus should exert a selective, more uncompromisingly beneficial action.

Elucidation of the effects of these new agents on the rate of actual GI complications of NSAID use requires a good deal of study. The uncertainty that exists stems from the hazards of translating a theoretical benefit based on pharmacological considerations into the complex world of sick patients with multiple risk points for the development of GI problems. For example, the role of *Helicobacter pylori* infection and NSAID-related GI complications need further examination. Nonetheless, much data are now available to address the question of whether these new agents do, indeed, provide clinically meaningful advantages in the quest for ever safer and more effective means of controlling inflammatory conditions.

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The articles and the interview that follow explore the topics introduced above in greater depth. The topics are based on presentations delivered during a symposium held May 19, 2001, in Atlanta. This supplement has been critically reviewed by faculty of the Johns Hopkins School of Medicine and other institutions for the purpose of summarizing the information and making it accessible to a broad audience of professionals.

... REFERENCES ...

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