CLINICAL CONSEQUENCES OF CYCLOOXYGENASE INHIBITION ON THE UPPER AND LOWER GASTROINTESTINAL TRACT

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NSAIDs are widely used in the treatment of different musculoskeletal diseases. The use of NSAIDs has been found to be associated with significant morbidity and mortality from both the upper and the lower gastrointestinal tract. Patients taking NSAIDs have an increased risk of serious gastroduodenal events, including gastroduodenal symptomatic ulcers and gastrointestinal complications, by between 2.5 and 5-fold as compared with individuals not taking NSAIDs. No less than 25% of patients that use NSAIDs also develop dyspepsia which may be the main reason for stopping NSAID use. Factors that increase the risk of these serious gastroduodenal ulcer events in NSAID users include a history of ulcer or ulcer complications, advanced age (≥ 65 years), and the use of high-dose NSAIDs, more than one NSAID, anticoagulants, or corticosteroid therapy. In addition, low-dose aspirin is largely prescribed for the prevention of cardiovascular events. Low-dose aspirin has also been associated with increased risk of gastroduodenal ulcer bleeding when compared to patients not using aspirin. In clinical practice, more than 20% of patients suffering from different rheumatic conditions that need NSAIDs are on low-dose aspirin regimes, a condition that put patients at high risk. The cyclooxygenase-2 (COX-2)-selective NSAIDs are regarded as having approximately one-half the associated risks of serious gastrointestinal events compared with non-specific NSAIDs. However, this favourable GI safety profile occurs in the absence of concomitant aspirin therapy and has to be balanced against the known cardiovascular risks of COX-2 selective NSAIDs. In order to reduce the risk of NSAID-induced gastrointestinal toxicity, the first approach should be focused on modifiable risk factors which include, among others, the prescription of the lowest effective dose of the safest NSAID agents and for the lowest possible period of time. If possible, the combination of NSAIDs with aspirin, non-aspirin anti-platelet agents or anticoagulants should be avoided. For those patients with risk factors who need NSAIDs, PPI co-therapy is an option that will reduce the incidence and risk of peptic ulcer and ulcer complications. Coxib therapy alone is another therapeutic alternative, but a PPI co-therapy may be advisable in patients taking also low-dose aspirin or those with a bleeding ulcer history. Furthermore, the benefits on the GI tract and the risks of CV events with all these strategies have now to be considered in the individual patient. COX-2 inhibition may be a better approach in patients with lesions from the lower GI tract.

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