

Practical Issues in NSAID and COXIB Usage

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used drugs for various acute pain situations and musculoskeletal disorders such as osteoarthritis and rheumatoid arthritis. It is estimated that around 2% to 4% of chronic NSAID user will present annually with symptomatic gastrointestinal (GI) ulcers and ulcer complications, especially bleeding. Usual clinical approaches for reducing these upper GI complications in NSAID users involve the coadministration of potent antisecretory agents such as proton pump inhibitor or misoprostol as the cytoprotective agent. Co-therapy with these drugs is recommended for those high risk NSAID users who are prone to develop GI ulcer and ulcer complications, namely those with a past history of peptic ulcer or ulcer complication, advanced age, concomitant use of anticoagulants or corticosteroids, and serious coexisting illnesses. Although NSAID-associated dyspepsia is a common complaint in those taking NSAID, itself is not a good predictor of ulcer formation.

Recent approach in minimising the GI complications of NSAIDs is based on our better understanding of the prostaglandin synthesis. NSAIDs block prostaglandin synthesis via inhibition of the cyclooxygenase (COX) enzyme. It is now evidenced that this crucial enzyme exists in at least 2 isoforms - the COX-I and COX-II. COX-II is the primary isoform at sites of inflammation and the therapeutic effect of NSAIDs is achieved with inhibition of this COX isoenzyme. On the other hand, COX-I inhibition results in the undesirable adverse effects of NSAIDs. Based on this hypothesis, one class of COX-II selective inhibitors – coxib, theoretically having better GI safety profiles, have been developed and studied. The efficacy of coxibs is shown to be comparable with that of the “conventional” NSAIDs in musculoskeletal disorders and rofecoxib is also found to be effective for symptomatic relief in acute pain syndromes. Megatrials with the two marketed coxibs, rofecoxib and celecoxib, confirming more favourable clinical GI outcomes when compared with those of the “conventional” NSAIDs, have been published recently.^{1,2} This class of newer NSAID is likely to become one important strategy in reducing NSAID-associated GI complications, though coxibs are exhibiting similar renal side effects, bearing the same contraindications, as well as having significant drug interactions such as increased warfarin anticoagulant effect with celecoxib,³ as those “conventional” NSAIDs. There are some concerns currently about the hazard of increased vascular thrombosis resulting in myocardial infarction or ischaemic stroke in patients who are prone to these events while their taking coxibs.⁴ Indeed, more data are needed before this risk could be clarified. Nevertheless, it should be emphasised that coxibs or even “conventional” NSAIDs should not be considered as substitutes for an antiplatelet agent. A proper antiplatelet agent such as aspirin, should be added in those who require antiplatelet effect for their underlying cardiovascular and/or cerebrovascular diseases. Despite the fact that coxib usage is gaining popularity in the past two years, further evaluation of this class of drug with respect to the GI safety profiles in high risk NSAID users, its efficacy in the head-to-head comparison with the present strategy of co-therapy in these individuals as well as the cost-effectiveness issue, is mandatory before the justification of its widespread use in clinical practice.

References:

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