


NON-STEROIDAL DRUG-INDUCED PEPTIC ULCERATION CAN WE REALLY PROTECT THE STOMACH?

Non-steroidal anti-inflammatory drugs (NSAIDs) have had a bad press in the last 5 years and are now recognized as being one of the major players in the aetiology of peptic ulceration in patients with chronic rheumatic disease requiring long term NSAID therapy [1]. However, although they are associated with an enhanced risk in elderly women on admission to hospital with an acute upper gastrointestinal bleed [2] the evidence for an association with an increased frequency of serious upper gastrointestinal complications amongst all patients taking NSAIDs in general practice is less impressive [3].

Many studies [4, 5] have shown an increased prevalence of both gastric and duodenal ulceration in osteoarthritis (OA) and rheumatoid arthritis (RA) but the mechanism of NSAID-induced gastric mucosal damage is still not entirely clear. One confounding factor is the precise role of Helicobacter pylori infection of the gastric musoca which is found more commonly in elderly patients and predisposes to NSAID-related ulcers [6]. There is also some evidence to suggest a synergistic action between an NSAID such as Indomethacin and Helicobacter in inducing gastric mucosal damage [7]. Detailed studies of gastric histology in NSAID takers have shown changes similar to those seen after gastric surgery with abnormal features such as foveolar hyperplasia, vasodilatation, oedema and lack of inflammatory cells [8]. These changes have been observed in bile reflux and with a heavy alcohol intake and have led gastroenterologists to coin the term type C or 'chemical' gastritis to describe the type of gastric mucosal damage associated with NSAIDs. The inhibition of pro-inflammatory prostaglandin release is central to the mode of action of the majority of NSAIDs and yet several studies have failed to find a correlation between gastric mucosal prostaglandin levels and gastric mucosal damage [9, 10].

A curious paradox has been observed in patients with RA on long term gold therapy in whom both the frequency of peptic ulceration and Helicobacter infection is reduced suggesting that gold compounds may have a toxic effect on this organism and thus protect against NSAID-induced gastric damage [11]. Corticosteroids which are often used in the treatment of RA have long been thought to predispose to peptic ulceration but recent reviews of the published data using meta analysis suggest that this is only the case when high doses (greater than a cumulative dose of 1000 mg for more than 1 month) are used or when they are given in combination with NSAIDs [12].

In the light of the above, can we realistically hope to protect the stomach from long term NSAID-induced...
damage? Much has been written about the advantages and disadvantages of \( H_2 \) antagonists and prostaglandin analogues as gastroprotective agents when used concurrently with NSAIDs [13] with \( H_2 \) antagonists such as ranitidine being more effective for duodenal ulcers and prostaglandin analogues such as misoprostol effective for gastric ulcers. Unfortunately all of the published data so far refer to relatively short term studies: however rheumatologists will wish to use NSAIDs and hence some form of gastric protection over a period of years. A 2-year study of ranitidine in the prevention of recurrence of duodenal ulcer in patients not taking NSAIDs reduced the rate of ulcer relapse when compared with a placebo group but when ulcer recurrence did occur it was asymptomatic in half the ranitidine-treated group [14]. This finding may have implications for patients on long term NSAIDs and analogues since these drugs may diminish the pain of peptic ulceration. Long term data for misoprostol are not yet to hand but an interim analysis of a gastroprotective study in OA and RA patients shows some promise of ulcer prevention when NSAIDs are continued [15].

Clearly the mechanisms of NSAID-induced gastric and duodenal mucosal damage are more complex than originally thought and must be considered alongside other potent risk factors such as smoking, alcohol and the nutritional status of the patient. A more judicious use of NSAIDs will help to reduce the risks of peptic ulceration for the ‘at risk’ individual along with an attempted modification of the other risk factors. Whether we will be able to protect the NSAID user’s stomach in the long term remains to be seen.

R. D. STURROCK
Centre for Rheumatic Diseases, University Department of Medicine, Royal Infirmary, 10 Alexandra Parade, Glasgow G31 2ER

REFERENCES

Editor's note
Professor Barry Bresnihan and Professor Roger Sturrock both retired from the Editorial Board of the *British Journal of Rheumatology* at the end of 1991 after many years of distinguished service. These editorials on topics of their choice commemorate their respective contributions.