What do we do about Helicobacter pylori?

CJ Hawkey DM FRCP

Helicobacter pylori and nonsteroidal anti-inflammatory drugs (NSAIDs) have been described as uncomfortable bedfellows (1). This, in part, reflects a view that patients affected by the two factors, known on their own to cause ulcers, seem likely to be at double risk. However, a better description of the relationship may be “a strange affair”!

PATHOGENESIS
Although both NSAIDs and H pylori cause peptic ulceration, they do so by different mechanisms. In the case of H pylori, inflammatory changes and cytotoxin are probably important (2,3). NSAIDs have a variety of actions, but one commonly thought to be central to their ulcerogenic activity is inhibition of prostaglandin synthesis leading to abrogation of prostaglandin-dependent defence mechanisms (4). Thus, ulcers caused by NSAIDs and by H pylori are superficially similar end results of fundamentally different pathological processes.

EFFECTS OF H PYLORI ON NSAID-ASSOCIATED DISEASE
The effect of H pylori on NSAID-associated mucosal injury, ulceration and symptoms has been investigated.

Acute mucosal injury: Most studies have shown no enhancement of acute mucosal injury caused by NSAIDs in subjects who are H pylori-positive compared with that in those who are negative (5-9). Where a difference has been shown, it may be attributable to differences in the amount of mucosal injury at baseline, which is higher in H pylori-infected individuals.

Ulcers: About as many studies have shown more NSAID-associated ulcers in H pylori-infected individuals than in noninfected individuals (10-15) as have shown no difference (16-19). Many of these studies concerned patients presenting for endoscopy. In view of the fact that H pylori enhances NSAID-associated dyspepsia (13,20-22), increases in ulcers may have been found spuriously as a result of bias due to increased presentation of H pylori individuals.

Dyspepsia: Although evidence regarding the effects of H pylori on NSAID-associated dyspepsia is not uniform, a majority of studies have shown that more patients who are H pylori-positive get dyspepsia when taking NSAIDs than those who are H pylori-negative (13,20-22).

Ulcer complications: There is only one full paper on the effects of H pylori on NSAID-associated ulcer complications (23). The study indicates no difference in the rate of presen-
tation with ulcer bleeding by \textit{H pylori} status in NSAID users. Other studies of perforation have similarly failed to show any significant interaction (24,25). One study, published in abstract form only, has suggested that there may be an enhancement of ulcer bleeding risk but that the magnification factor is less than two (26). If \textit{H pylori} does enhance NSAID-associated bleeding, the effects are relatively small.

**\textbf{H PYLORI ERADICATION IN NSAID USERS}**

Three studies have investigated directly the effect of \textit{H pylori} eradication in infected individuals who need to take NSAIDs (27-29). Patients enrolled in the first study had had no past history of dyspepsia or ulceration, were not currently taking NSAIDs and had had no more than one-month lifetime exposure to NSAID (27). In this study, use of a bismuth-containing regimen to eradicate \textit{H pylori} was associated with a reduction in the development of gastric ulcers at two months. Notable features of this study were a very high rate of gastric ulceration in the control group and use of bismuth in the eradication regimen, which has potentially cytoprotective actions. It should also be noted that this study did not investigate patients with a past history of ulcers or those already taking NSAIDs. Another study that specifically investigated such patients showed no effect of \textit{H pylori} eradication with a proton pump inhibitor-based regimen when assessed at six months (28). In fact, among patients with ulcers initially, those who received eradication treatment had a reduction in the rate of gastric ulcer healing. A third study compared \textit{H pylori} eradication and prophylaxis with omeprazole as maintenance treatment in patients who had already presented with a bleeding peptic ulcer (29). During the next six months, those receiving omeprazole had 2% recurrence compared with 20% recurrence in those receiving \textit{H pylori} eradication.

From these data, it can be concluded that outcome may vary according to the patient group studied. It is possible that, in patients with a 'virgin' mucosa, \textit{H pylori} eradication may protect against ulceration, but whether it does so for longer than two months requires further study. Among patients with previous or current ulcer disease, \textit{H pylori} eradication by itself does nothing beneficial and appears to impair the effects of ulcer healing drugs.

**EFFECT OF \textbf{H PYLORI STATUS ON THE EFFECTIVENESS OF ACID-SUPPRESSING TREATMENT}**

Concepts regarding the effect of \textit{H pylori} status on the effectiveness of acid-suppressing treatment are supported by large studies of patients treated with omeprazole, ranitidine or misoprostol for healing and maintenance of NSAID-associated ulcers (30,31). In these studies, patients consistently had faster ulcer healing and reduced tendency to relapse while taking acid-suppressing drugs if they were \textit{H pylori}-positive compared with if they were negative. Among those treated with misoprostol, the differences were not significant, and, if anything, the trends were in the opposite direction.

**MECHANISMS**

It is well known that a higher pH is achieved in patients treated with omeprazole or ranitidine if they are \textit{H pylori}-positive rather than -negative (32,33). This may well explain the better outcome in such individuals. Another factor that may operated to enhance the effectiveness of acid-suppressing drugs and partially protect patients not taking acid-suppressing drugs relates to the ability of \textit{H pylori} to enhance prostaglandin synthesis in NSAID users (13).

**CONCLUSIONS**

The idea that \textit{H pylori} protects against the effects of NSAIDs is not as counterintuitive as it may at first seem. In practical terms, fracture of the favourable relationship between \textit{H pylori} and NSAIDs in patients requiring acid-suppressive treatment for protection might be regarded as a crime of passion!


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