

Are Antacids Necessary as Routine Prescriptives with Non-steroidal Anti-inflammatory Drugs?

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Abstract

In Singapore, there exists a local habit to routinely prescribe antacids with non-steroidal anti-inflammatory drugs (NSAIDs) perhaps in the belief that gastrointestinal (GI) symptoms and complications are common, and that antacids protect from them.

We prospectively studied 140 adults in an orthopaedic clinic who were prescribed a short course of NSAIDs (1 to 4 weeks) without antacids to determine the frequency and severity of GI symptoms. Symptomatic patients were then given antacids to determine their effect on the GI symptoms and followed up by telephone interview. These patients had mild inflammation, soft tissue rheumatism, injury or degenerative disease. All were otherwise well with no known peptic ulcer disease or major illness and were not on ulcerogenic drugs. Only 13 (9.3 %) had significant GI symptoms, of which 6 (4.2%) of the total took antacid and 5 (3.5%) had partial or total relief.

In this study, GI symptoms were not common with short course NSAIDs in otherwise well patients. Antacids may afford symptomatic relief for GI symptoms. However, because antacids may offer no significant protection against NSAID-induced peptic ulcer, may dangerously mask symptoms of GI irritation, may be troublesome to take and costly on a large scale, we should stop routine prescription of antacids in patients requiring only short-term NSAIDs and not at risk for peptic ulcer disease.

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Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for their analgesic or anti-inflammatory properties in musculoskeletal pain. However, they are not without adverse effects, such as abdominal pain, diarrhoea, nausea and fluid retention, which are reported to occur in 30% of people taking NSAIDs.¹ Allergy and ineffectiveness to a particular NSAID are other potential problems. Other side effects include renal and liver impairment and bleeding disorders.

The most prominent are the gastrointestinal (GI) side effects such as dyspepsia and NSAID gastropathy ranging from simple erythema to erosions, microbleeding and gastric ulcer crater disease with bleeding and perforation. However, NSAID-induced GI symptoms and complications may not occur in all users. The risk of a serious GI event increases with the dose of NSAID taken, is greater in the elderly²⁻⁴ and in people with a history of

peptic ulcer, GI bleeding from previous NSAID use, prednisolone use, history of heart disease, substantial disability, possibly smoking, alcohol consumption and *Helicobacter pylori* infection.^{2,3,5-7} Different NSAIDs also have different ulcerogenic potential.⁸⁻¹⁰

In Singapore, there exists a habit for antacids to be routinely prescribed with NSAIDs, even for NSAIDs prescribed for only a short course in otherwise well patients without risk factors for peptic ulcer disease. The reason could be the belief that GI symptoms and/or complications are likely in all users of NSAIDs and the belief that antacids substantially protect from them.

The aims of this study were to determine the frequency and severity of GI symptoms in patients prescribed a short course of NSAIDs without antacids, and to determine whether antacids help in their relief. We studied otherwise healthy adults without risk factors for peptic ulcer disease.

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Materials and Method

From 28 April 1995 to 29 September 1995, 166 patients seen in an orthopaedic clinic in Alexandra Hospital in Singapore for musculoskeletal pain who were prescribed NSAIDs were enrolled in the study. Patients with known chronic rheumatic disease, peptic ulcer disease, bleeding disorder, other serious medical conditions, allergy to NSAIDs, and those already on NSAIDs, warfarin, antiplatelet drugs or steroids were excluded from the study. Patients with pre-existing significant GI symptoms had endoscopy done first and only those with normal findings were enrolled in the trial. Most had rheumatological complaints due to trauma, sprains, soft tissue rheumatism or degenerative disease. For all, a short term prescription of 1 to 4 weeks of NSAIDs was prescribed with NSAIDs available from the hospital's pharmacy—indomethacin, mefenamic acid, ketoprofen (Oruvail®), or aspirin.

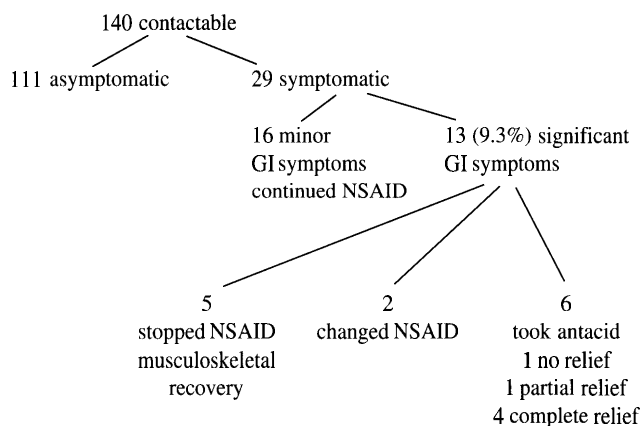
Patients were not given antacid but advised to take the NSAID with food, and to call the clinic if they had any GI symptoms. Patients were interviewed by telephone over the following 2 to 4 weeks to find out if they suffered pain, dyspepsia, hunger symptoms, nausea or vomiting. If present, a prescription for antacids was then given. We then noted if the antacid provided any symptomatic relief. If severe symptoms developed, patients were directed to go to the Accident and Emergency Department (A&E) for admission. Gastroscopy would be offered if necessary. If the original NSAID provided no relief, an alternative NSAID was chosen. Modifications to therapy were recorded. Data were entered on a standard entry form.

Results

One hundred and sixty-six adult patients were enrolled to take NSAID without antacid. One hundred and forty patients could be contacted for the outcome of treatment. The others were either foreigners or otherwise not contactable. They were between the ages of 18 and 71 years. The results are shown in Figure 1.

One hundred and eleven were asymptomatic and 29 were symptomatic. Of these, 16 had minor, transient GI discomfort only and continued the same NSAID.

Thirteen (9.3%) had significant GI symptoms of pain, dyspepsia, hunger, nausea or vomiting. Of these, 5 (3.6%) stopped NSAID, as their musculoskeletal pain had resolved, 2 (1.4%) saw a doctor who changed them to a different NSAID with relief and 6 (4.3%) took antacid. The antacid provided complete relief in 4 patients, partial relief in 1 patient and no relief in 1 patient. In this last patient, GI symptoms of pain, dyspepsia, nausea and vomiting only started on the third week of NSAID treatment (Oruvail 200 mg/day) for degenerative disorder. Once the musculoskeletal pain resolved,



NSAID: Non-steroidal anti-inflammatory drug
GI: gastrointestinal

Fig. 1. Outcome of 140 adults prescribed short course NSAID without antacid.

the NSAID was discontinued with relief of the GI symptoms. Endoscopy was not required.

Thus, antacids provided symptomatic relief from significant GI symptoms in only 5 out of 140 patients who were on a short course of NSAIDs (3.6%). In the remaining 96.4% of the patients, antacids were not required or were ineffective. In all of the patients, the NSAIDs could be discontinued after a short course due to recovery of the original musculoskeletal pain. One hundred and thirty (93%) of the patients were prescribed NSAID for 2 weeks or less, only 10 (7%) were prescribed NSAID for 2 to 4 weeks. In fact, many did not even complete the prescribed course because of resolution of the musculoskeletal pain (56/140 or 40%). None of the patients had persistent symptoms requiring endoscopy and none required treatment for complications such as peptic ulcer disease, severe abdominal pain or GI bleeding.

Discussion

None of the 140 patients given a short course of NSAIDs without antacids for musculoskeletal pain suffered significant GI symptoms needing endoscopy or admission. Only 29 had any GI symptoms out of which 13 had significant GI symptoms and 6 (4.3%) eventually took antacid for GI pain, dyspepsia, nausea or vomiting. The antacid offered relief in 5 of the 6 (total 3.7%), but all discontinued NSAID within 4 weeks with resolution of the musculoskeletal complaint. The 26 patients who could not be contacted may have affected the results e.g. by increasing the frequency of those with GI symptoms.

Thus few patients who are otherwise well and given a short course NSAIDs have GI symptoms. Only 3.7% of those on NSAIDs benefited from antacids. Thus, antacids may have a limited role in routine prescription with NSAIDs. Many patients seen at the Accident & Emer-

gency Department, the general practitioner's clinic or the orthopaedic clinic for musculoskeletal pain which is likely to be of short duration are only prescribed a short course of NSAIDs. If they are otherwise well with no previous history of peptic ulcer disease, chronic rheumatological disease, major medical illness, and are not on drugs such as steroids or warfarin which may contribute to a severe GI bleeding, a short course of NSAIDs is unlikely to cause significant GI symptoms. Thus it may not be necessary to routinely prescribe antacids for a short course of NSAIDs in a patient without risk factors for peptic ulcer disease.

Acute NSAID injury is due to direct irritation. Within minutes of the NSAIDs (most of which are weakly acidic) touching the gastric mucosa, local hyperaemia and subepithelial haemorrhages^{11,12} appear especially in the gastric antrum and fundus. Direct injury to the mucosa results in back diffusion of hydrogen ions with disruption of the capillary bed and microbleeding. With prolonged NSAID use over time (beyond 2 weeks), adaptation of the gut may develop with resolution of this gastropathy¹³ which may however not last with even more chronic use.¹⁴ Antacids, buffering, H₂ blockers, prodrugs (which are absorbed in an inactive state and are only activated after systemic absorption) and enteric coated drugs (which only get "uncoated" further down the GI tract) may help avoid these acute erosions. However, this form of gastropathy is not related to peptic ulcer disease.

Chronic NSAID use is associated with peptic ulcer disease. After systemic absorption, NSAIDs exert their anti-inflammatory action by reducing prostaglandin synthesis via inhibition of cyclo-oxygenase enzymes (COX enzymes).¹⁵ There exist 2 isoforms of COX enzymes in mammalian cells:^{16,17} COX-2; induced in cells exposed to pro-inflammatory agents and involved in production of inflammatory mediators, and COX-1; the "housekeeping enzyme" which is constitutively present under physiological conditions and involved in synthesis of prostaglandins protective to tissues such as the gastric mucosa, kidneys and platelets. The anti-inflammatory therapeutic effects of the NSAIDs are mainly due to their ability to inhibit COX-2 while the GI, renal and platelet adverse effects are largely the result of their ability to inhibit COX-1.

Prostaglandins protect the human GI system by reducing gastric acid secretion, increasing the production of mucus in the stomach and bicarbonate in the duodenum, and increasing submucosal blood flow, as well as by increasing the migration of basal cells towards the lumen to repair mucosal injury.¹⁸⁻²⁰ By inhibiting these defence mechanisms, NSAIDs tip the balance between GI protection and GI damage. Thus peptic ulcer disease related to chronic NSAIDs use is not due to acute contact with the gastric mucosa but rather to loss of

the cytoprotective effect of prostaglandin from COX-2 inhibition.

Antacids are alkaline but neutralise gastric pH to a small extent only in the standard doses taken²¹ such as 10 ml tds or 2 tablets tds pm as commonly prescribed. They are unlikely to protect the gastric mucosa from NSAID-induced peptic ulcer disease which is due to loss in mucosal cytoprotection. In 1990, there were several reports that demonstrated clinical efficacy using low dose antacids in treatment of peptic ulcer disease.²²⁻²⁶ It has been suggested that such antacids can be cytoprotective, suggesting a possible role in NSAID gastropathy.²⁷⁻³⁰ However more recently, most information on antacids pertain to their cost-effective role in relieving peptic symptoms mainly in duodenal ulcer. In 1991, a double-blind endoscopically verified, placebo-controlled crossover trial using naproxen as the NSAID and Maalox as antacid (1 tablet qid, acid neutralising capacity of 104 mEq/day) showed that patients on Maalox developed a significantly greater number of gastric erosions than those on placebo.³¹

Although NSAID use may result in an increased incidence of abdominal discomfort, the presence of dyspepsia is an unreliable marker for the presence of gastroduodenal mucosal injury.³² Peptic ulcer disease may be asymptomatic,³³⁻³⁵ possibly due to induction of local and systemic analgesia by NSAIDs.³⁶ Bleeding and perforation can occur without preceding warning symptoms.^{2,37} Antacids can thus unfortunately be harmful because by alleviating symptoms without adequately protecting the gut, they may further mask symptoms of GI peptic ulcer disease and allow progressive painless bleeding or ulceration.

Although antacids are relatively cheap drugs, cumulative prescription increases the health care cost burden unnecessarily and significantly. Unconsumed medication is wasted. Additional medication also makes it more inconvenient for the patient to consume, resulting in higher non-compliance to medication prescribed.

The suggestion that antacids need not be routinely prescribed with NSAIDs refers to a short course of NSAIDs for patients otherwise well and without risk factors for peptic ulcer disease. However, long-term NSAID use in patients with a history of peptic ulcer disease or other significant illness, or on other ulcerogenic drugs may be associated with a significant risk of peptic ulcer disease. In these patients, prostaglandin analogues or the newer selective COX-2 inhibitor NSAIDs may be appropriate, but they are expensive.

Conclusion

For patients who are prescribed a short course of NSAIDs and who are not at risk for peptic ulcer disease, it may not be necessary to routinely prescribe antacids. For example, many patients seen at the GP clinic, A & E

or orthopaedic clinic for sprains, osteoarthritis and minor trauma. Few patients who are given NSAIDs become symptomatic, and antacid may not offer significant protection from GI complications. Antacids may instead give a false sense of security and mask symptoms of adverse effects. Antacids as additional medication can be troublesome to take and costly to the patient and health care service. We should thus discontinue the routine prescription of antacids with NSAIDs.

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