Editorial

How safe is low dose aspirin in clinical practice?

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(Key words: NSAIDs - Non Steroidal Anti inflammatory Drugs; PUD - Peptic Ulcer Disease; GU - Gastric Ulcer; DU - Duodenal Ulcer)

Abstract

Objective: To study the safety of low dose aspirin on the upper gastrointestinal tract.

Design and Setting: Endoscopy findings of 993 patients who had gastroscopies done for any reason in the Department of Medicine - Withybush District General Hospital in Pembrokeshire from 14-08-92 to 01-08-94 were re-examined. The notes of any patient who had clinical evidence of upper gastrointestinal damage and had been on low dose aspirin, were reviewed.

Results: Total number on low dose aspirin - 41. Age range 40 - 90 yrs. Majority: 50 - 70 age group. Male: Female = 30 : 11. Profile of clinical presentations: Malaena (15), Dyspepsia (12), Haemetemesis (10), Vomiting (5). Endoscopy Finding: GU in 17, DU in 8, erosions alone in 7, Oesophagitis in 3, overlaps in 8. Types of aspirin used: Soluble aspirin in 25; dose range: 75 mg in 6, 150 rng in 10, 300 mg in 9; Enteric coated aspirin in 16; dose range: 75mg in 9, 150 rng in 7. Duration of aspirin therapy: > 2 yrs - 10, 2 yrs to 1 yr - 13, 6 m - 9, < 6m - 9. Indications: Cardiovascular events -15, Cerebrovascular events - 20, Prophylactic - 6. The clinical implications are discussed in the text.

Conclusions: 1. Low dose aspirin too causes considerable gastrointestinal morbidity. 2. There seems to be no great safety with enteric-coated types, as well. 3. Risk – Benefit evaluation is essential, prior to prescription of low dose aspirin with adequate preventive measures.

Introduction

The number of reported beneficial effects of low dose aspirin (≤ 325 mg daily) continue to increase. Used as secondary prevention, low dose aspirin reduces the incidence of myocardial infarction, strokes and vascular deaths by about 25%[1]. Evidence is also accumulating that regular aspirin use reduces the risk of developing colo-rectal cancer, the commonest cause of nonsmoking cancer related deaths[2]. The studies are also in progress with regard to effect of low dose aspirin on vascular dementias. With all these 'positive' results, it seems that the general public is of the opinion that, 'as aspirin a day keeps doctor away'. With this background, it is not surprising that many young adults and elderly will be inclined to use low dose aspirin indiscriminately as a primary prophylactic agent against the above disease. Kelly et al[3] reported that in the USA 9% of healthy control subjects with a median age of 60 years were taking low dose aspirin regularly, at least every other day. A similar UK based case control study found that 8% of the hospital and 6% community controls were consuming ≤ 300 mg aspirin at least 5 days per week[4].

With this background a retrospective study was designed to evaluate the safety of low dose aspirin on the upper GI tract including the enteric coated varieties.

Objective

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Design and Setting

Endoscopy findings of 993 patients who had gastroscopies done for any reason in the Department of Medicine – Withybush District General Hospital in Prembrokeshire from 14-08-92 to 01-08-94 were re-examined. The notes of patients who had evidence of Upper GI damage and had been on low dose aspirin, were reviewed.

Duration of aspirin therapy:

> 2 yrs	10
2 yrs ~ 1 yr	13
1 yr ~ 06 months	09
< 06 months	09

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Indications for aspirin therapy:

Cerebrovascular events	20
Cardiovascular events	15
Prophylactic	06

Discussion

It has been proved beyond doubt that NSAIDs are a potent cause of upper GI morbidity and mortality[5-7]. Aspirin too is a NSAID which is now a days used in small doses in secondary prevention of cardiovascular and cerebrovascular disease. Its major indication to be used in larger doses is rheumatic arthritis, which is relatively a disease of the developing countries in the modern era.

Several hypothetical mechanisms by which aspirin could bring about Upper GI bleeding have been proposed[8-9]. The back diffusion of acid into the gastric mucosa could occur due to local irritation thus damaging the mucosal cells and submucosal capillaries with an end result of necrosis and bleeding. Cyclooxygenase which catalises the synthesis of gastric prostoglandins PG12 and PGE2 are inhibited by aspirin. These prostoglandins inhibit acid secretion and enhance synthesis of cyto-protective mucus. Impairment of platelet aggregation may increase the tendency to bleed. An aspirin tablet coated with a combination of silicon, cellulose or other inactive ingredients has resistance to disintegrate in the stomach. This feature allows the drug to dissolve in the neutral to alkaline medium in the duodenurn[10]. The safety of this type of product has been confirmed by several endoscopic studies comparing plain aspirin with enteric coated preparations on[11-13] healthy volunteers. Less gastric erosion and micro bleeding were noted with enteric coated preparations. Buffering agents lowered hydrogen ion concentration in the microenvironment of aspirin particles, thus resulting in a reduce contact time between aspirin particles and gastric mucosa and enhance the gastrointestinal solubility of aspirin[8,9,12]. However the belief that buffering would reduce the gastric damage has been largely unsupported by endoscopic studies[11-12]. Recently Kelly et al reported that the use of low dose of enteric coated or buffered aspirin carries a three fold increase in the risk of major upper GI bleeding[3]. Therefore the assumption that those formulations are less harmful than plain aspirin may be mistaken.

Results

Total number of patients on low dose asprin: 41

Age range:	**Yrs.**		**No.**
	40~50	-	05
	51~60	-	12
	61~70	-	17
	71~80	-	06
	81~90	-	01

Sex distribution:

Male: Female: 30: 11

Profile of clinical presentations:		
	Malena	- 15
	Dyspepsia	- 12
	Haematemesis	- 10
	Vomiting	- 05

Endoscopy findings:		
	GU	- 17
	DU	- 08
	Erosions alone	- 07
	Oesophagitis	- 03
	Overlaps	- 08

Types of aspirin used:

Soluble asprin	- 25
Enteric coated	- 16

Dose range:		
	75 mg	- 06
	150 mg	- 07
	300 mg	- 09

dose range in enteric coated type:

75 mg	- 09
150 mg	- 07

In the study 16 were on enteric coated aspirin with a dose range of 75-150 mg daily. There were no patients on buffered aspirin. Doses as minimum as 75mg has caused upper GI bleeding. Studies show that doses of aspirin even as low as 75mg a day are harmful, though to a lesser extent than 300 mg daily[14]. The risks and benefits of aspirin therapy need to be assessed for each patient. For example, the attribut-

able risk of haematemesis is 0.2 to 1.0 per 1000 person-years of exposure[4], whereas in a patient with a history of myocardial infarction the absolute reduction in vascular events is 40 per 1000 patients treated[1]. It is also worth exploring the protective effect of misoprostol and stroke or H2 antagonists in patients at high risk of GI bleeding, who needs aspirin prophylaxis. In rheumatoid disease, co-prescription of misoprostol with NSAIDs reduces the frequency of upper GI ulceration, perforation and obstruction by 04% to 50%[15], but not the frequency of haematamesis. One should also discourage the indiscriminate use of aspirin, as it has no proven value in primary prevention of cerebrovascular and cardiovascular events[1]. In the study 06 patients were on prophylactic aspirin. It is also equally important to use the minimum effective dose. Several studies have shown that the desired benefit could be achieved with doses of 75mg daily or less.

In conclusion, the physicians who recommend aspirin whether enteric coated or buffered, should not assume that these forms are less harmful to the GI tract and individuals who use these preparations in the belief that they are safer than plain aspirin, still subject themselves to a significant risk of major upper gastrointestinal bleed.

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