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Patient awareness of the adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs)

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We set out to determine the extent to which two groups of patients reported having been informed about the adverse effects of NSAIDs. These consisted of 50 patients who had suffered an acute gastrointestinal bleed while taking a NSAID, and 100 age, sex and drug matched controls who had not. Eight (16%) of the index patients, and 41 (41%) of the control patients remembered having been informed of potential adverse effects, an odds ratio of 3.65 (95% CI 1.55–8.58, $P<0.002$). Two (4%) of the index patients recalled having been advised what to do should adverse symptoms develop, whereas 21 (21%) of the control patients did so, an odds ratio of 6.38 (95% CI 1.4–28.4, $P<0.01$). Eighteen (36%) of patients who bled had experienced gastrointestinal pain prior to the bleed, but of these only two (11%) admitted reduced compliance with NSAID therapy. In contrast, 10 (67%) of the 15 control patients who had suffered epigastric discomfort admitted reduced compliance, an odds ratio of 16.0 (95% CI 2.6–98.8, $P<0.001$). Our results suggest that patients who report not having been informed of adverse effects of NSAIDs are less likely to reduce intake in response to epigastric pain than patients who report having received such information. If the patients who bled had reduced their intake of NSAIDs to the same extent as apparently better informed control patients in response to epigastric pain, it is possible that some episodes of acute gastrointestinal bleeding would have been avoided.

Keywords NSAIDs GI bleeding adverse effects patient knowledge

Introduction

NSAIDs account for around 5% of all NHS prescriptions in Great Britain but in the 1980s were reported to be responsible for 25% of all yellow card reports to the Committee on Safety of Medicines [1]. As many as 15–25% of chronic users of NSAIDs develop gastric ulcers in the central and pre-pyloric regions of the stomach [2], with an estimated 6000 patients being admitted to hospital per year in the UK for ulcer bleeding or perforation [3].

Despite their widespread use, and extensive evidence of their adverse effects, patients' knowledge and awareness of potential side-effects of medicines including NSAIDs has been demonstrated to be poor [4]. Evidence suggests that increased information about NSAIDs and other drug therapy leads to greater patient satisfaction [5]. Whether this knowledge has any effect on the incidence of gastrointestinal bleeding is not known. We therefore studied the extent to which two groups of patients reported having been given information about the adverse effects of NSAIDs, and its influence upon compliance in a case-control design. Cases were patients who had suffered an acute gastrointestinal bleed while taking a NSAID, and controls were patients taking a NSAID who had not bled.

Methods

Fifty index patients were recruited as a consecutive series of patients presenting to three Newcastle hospitals with NSAID related acute gastrointestinal (GI) bleeding. All patients had been prescribed a NSAID for at least the previous week and had taken a NSAID within the previous 72 h. They were identified during their in-patient stay and then contacted by letter 1 month following discharge. They were invited to take part in the study by allowing a nurse to visit them to find out

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about their knowledge of their arthritis treatment. One hundred age (±5 years) and sex matched controls (two per index patient), taking the same NSAID at the same dosage for the same indication, were recruited using computerized prescribing records from 16 participating local general practices. Starting at the beginning of the alphabetical list, matched controls were selected from the same general practice as their index case, or from the nearest possible practice where necessary. Potential controls were invited to take part in the study by letter in a similar manner to the index cases. All subjects were asked for information in a structured interview by the same research nurse (A.L.), about their diagnosis and NSAID therapy, including knowledge of adverse effects of NSAIDs. The questions are shown in Table 1.

Differences between the replies of the patients with NSAID-related GI bleeding and their controls were assessed by calculating odd ratios and 95% confidence intervals. The significance of these differences was assessed by the Chi-square test and in length of treatment was assessed by the Mann–Whitney *U*-Test with $P < 0.05$ taken as indicating statistical significance.

Results

The median age of the index patients was 67 years (range 40–87) and of the controls 69 years (range 42–82). The median length of treatment for the index patients was 1 year (range 1 week–28 years) and for the control patients 2 years (range 1 month–25 years), $P < 0.0005$. Index patients were interviewed a median time of 4 months (range 1–7 months) after their acute gastrointestinal bleed. The main reasons for prescriptions in the patients were osteoarthritis (63%), rheumatoid arthritis (18%), spondylosis/back pain (15%) and gout (4%).

Table 1 Questions asked in the structured interviews

For what symptoms were/are you prescribed your arthritis tablet?
How long have you been taking this tablet?
Did you receive any information about possible side effects of this tablet?
If so, where did this information come from?
What were you advised to do if side effects occurred?
For index patients: Did you have any stomach problems, such as indigestion or pain before your stomach bleed?
For control patients: Have you had any stomach problems, such as indigestion or pain?
How much of the prescribed dose do you estimate you actually take?
— none
— up to a quarter
— a quarter to a half
— half to three-quarters
— three-quarters to almost all of it
— all of it
If not all, why do you take less than prescribed?

Significantly fewer index patients than control patients remembered having been informed of the potential adverse effects of the NSAID, or recalled advice about what to do should they develop an adverse effect (Table 2). For all patients who had been informed, this advice was to visit the general practitioner, two recalling that they should stop the tablet prior to this. Of the eight index patients reporting that information on side-effects had been given, their general practitioner was the source for five (63%), their hospital consultant for two (25%) and one (13%) had gained information by reading a leaflet provided with the prescribed medication. Of the 41 control patients, 32 (78%) had received this information from their general practitioner, five (12%) from their hospital consultant and four (10%) from a patient information leaflet. None of the patients interviewed reported having been given information about side-effects by the dispensing pharmacist.

Full compliance with NSAID medication was significantly greater by the index patients than by the controls (Table 2). Furthermore, 18 (36%) of the index patients had experienced epigastric pain before the bleed, all but two of whom had continued to take the NSAID, apparently unaware of a possible link. In contrast, only 15 (15%) of the control patients had suffered dyspeptic symptoms, of whom 10 (67%) had reduced their intake, an odds ratio of 16.0 (95% CI 2.6–98.8, $P < 0.001$).

Table 2 Details of knowledge of adverse effects and compliance with therapy in the patients with NSAID related acute gastrointestinal bleeding and controls

	Patients with acute gastrointestinal bleeding (n = 50)	*Control patients* (n = 100)	*Odds ratio 95% confidence interval*
Reported having been informed of adverse effects			
[Yes]	8 (16%)	41 (41%)	3.65
[No]	42 (84%)	59 (59%)	(1.55, 8.58)
			$P < 0.002$
Informed of what to do about NSAID therapy if adverse symptoms developed			
[Yes]	2 (4%)	21 (21%)	6.38
[No]	48 (96%)	79 (79%)	(1.4, 28.4)
			$P < 0.01$
Reported full compliance with therapy	48 (96%)	70 (70%)	10.3
	2 (4%)	30 (30%)	(2.3, 45.1)
			$P < 0.001$
Suffered epigastric pain	18 (36%)	15 (15%)	3.19
	32 (64%)	85 (85%)	(1.44, 7.07)
			$P < 0.002$
Consequent reduction in NSAID ingestion	2 (11%)	10 (67%)	16.0
	16 (89%)	5 (33%)	(2.6, 98.8)
			$P < 0.001$

Discussion

The observation that patients who bled had been taking treatment for a significantly shorter period than controls is consistent with epidemiological information which suggests that relative risk of presentation with haematemesis and melaena is greatest at the beginning of therapy. This rises to a maximum in patients who have received four prescriptions for a NSAID before falling to baseline in those who have received 10 prescriptions [6]. Mucosal adaptation may partly explain this [7]. Early bleeds may also result from NSAID exacerbation of pre-existing mucosal abnormalities.

Only 49 (33%) of all patients in this study remembered receiving information about potential side-effects of their NSAID medication. This is consistent with previous larger studies [8]. It has long been known that many patients feel that not enough information is given about medications and their side-effects by doctors or pharmacists [9]. Attempts at educating patients are often haphazard, uncoordinated and not successful in meeting their needs [10], with many prescribers thinking that information about side-effects might frighten patients. However, there is increasing awareness of the patient's basic right to know. The Health of the Nation document [11] emphasizes education as a key factor in ensuring that individuals have the necessary information to exercise choice. The Patient's Charter [12] confirms every citizen's right to be given a clear explanation of any treatment, appropriate to their circumstances. It is possible that patients had received adverse drug reaction information on initial prescribing which they had forgotten. It would be worthwhile to establish the merits of assessing knowledge and continued education of patients receiving medication chronically, largely through repeat prescription mechanisms.

The finding of this study, having controlled for likely confounding influences of age, sex, drug and indications, is that apparent lack of knowledge of NSAID adverse effects is associated with admission for acute gastrointestinal bleeding. Although this finding is plausible and potentially important, our data do not establish that this is a causal relationship. Bias, in particular recall bias, cannot be excluded as a contributor to the results, it is possible that patients who bled were equally informed but less likely to report that their doctor warned them that this might happen. Patients who bled had been prescribed NSAIDs for a shorter period than controls, and so had had a shorter period in which to forget any information given on initial prescribing, but conversely a shorter time to receive new information.

The study results indicate, albeit indirectly, that information about drug adverse effects might go some way to preventing such effects. Certainly, more than one third of the patients who presented with acute gastrointestinal bleeding had suffered epigastric pain, all but two of whom had continued to comply fully with NSAID therapy, apparently unaware of a possible link. By contrast, two-thirds of the control patients who had suffered epigastric symptoms were aware of adverse effects and had reduced their intake of drugs, thus possibly avoiding the complication of acute bleeding. This evidence is consistent with the results of Gibbs *et al.* [13], which demonstrated a reduction of NSAID compliance in patients informed of adverse effects. In the light of the differences in reported compliance by the two groups, and its possible contribution to the problem, we are investigating differences in compliance in more detail, including the use of general practitioner prescribing records, in patients with gastrointestinal haemorrhage and controls.

That 67% of the patients sampled were not informed of adverse effects is consistent with the work of McMahon *et al.* [14] which suggested that doctors and pharmacists do not provide enough information and that, when they do, patients very often forget or do not understand. Patients' understanding of medication can often be incorrect. Both verbal and written information are beneficial [15] and increased knowledge and satisfaction with therapy persists for at least 1 year after information leaflets are provided [16]. The small proportion (3%) of our study population who reported receiving information from package inserts reflects the situation in Britain where, at present, only 20% of medicines are given to the patient as they come from the manufacturer and most are repackaged. The programme to ensure that all patients receive their prescribed medicines in a complete manufacturer's pack, with NSAIDs being scheduled for March 1997, should rectify this situation.

As well as patients who bled being less likely to report having been informed of adverse effects, they were less informed about what to do if potentially related adverse symptoms developed than were control patients. Perhaps in consequence, possible warning symptoms were ignored, high compliance with therapy was maintained, and the potential for avoidance of serious morbidity was lost. A prospective study to determine effective methods of increasing patient knowledge of side-effects and the effect of this on the incidence of adverse effects would seem to be worthwhile.

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