

PRACTICE OBSERVED

Practice Research

Repeat prescribing of non-steroidal anti-inflammatory drugs excluding aspirin: how careful are we?

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Abstract

About 5% of all National Health Service prescriptions in Britain and a quarter of reports of suspected adverse reactions are accounted for by non-steroidal anti-inflammatory drugs. Their prescription was investigated in two computerised group practices serving 11850 patients. Altogether 198 patients receiving repeat prescriptions of non-steroidal anti-inflammatory drugs were identified and relevant clinical details extracted from their notes. Of these patients, 119 were over 65 years old; 172 were receiving one of six different non-steroidal anti-inflammatory drugs; and 76 were taking drugs that can interact with non-steroidal anti-inflammatory drugs. Ninety one patients had one or more medical conditions that may be aggravated by non-steroidal anti-inflammatory drugs, and 36 had experienced side effects important enough for their treatment to be changed.

A questionnaire to assess opinions and knowledge of non-steroidal anti-inflammatory drugs was given to 42 general practitioners and 26 rheumatologists. Although the two groups showed a comparable knowledge of the properties and costs of non-steroidal anti-inflammatory drugs, they differed significantly in their views on the circumstances under which these drugs

should be used. Clear guidelines on the prescription of these drugs would indicate when careful monitoring is essential for patients to benefit from them safely.

Introduction

Non-steroidal anti-inflammatory drugs currently account for more than 20 million prescriptions a year in Britain (about 5% of all National Health Service prescriptions).¹ Recent reports from the Committee on Safety of Medicines indicate that such drugs are responsible for a quarter of yellow card reports of suspected adverse reactions, the most common being gastrointestinal reactions.¹

Nausea, dyspepsia, and gastrointestinal irritation are common side effects with non-steroidal anti-inflammatory drugs,² but gastrointestinal haemorrhage may also occur. Patients aged 60 and over are two to four times more likely to suffer bleeding from a peptic ulcer than the rest of the population, and, although they receive only half of all prescriptions for non-steroidal anti-inflammatory drugs, two thirds of all ulcer bleeding occurs in this group.³ Although the exact relation between intestinal bleeding and non-steroidal anti-inflammatory drugs remains unclear,⁴ the fact that some degree of gastrointestinal microbleeding occurs with aspirin, and to a lesser extent with other non-steroidal anti-inflammatory drugs, is not disputed. Non-steroidal anti-inflammatory drugs sometimes cause fluid retention⁵ or hypertension,⁶ and some reports suggest that they may interfere with the effects of certain antihypertensive drugs.⁷⁻¹⁰ Several workers have suggested that they may cause acute or chronic renal failure, or both.¹¹⁻¹³ Other potential adverse effects include rashes¹⁴ and dizziness and drowsiness,¹⁵ and many of the older drugs in this group interact with oral anticoagulants and sulphonylureas.¹⁶

Despite these potential problems there is little published information on the side effects and interactions of non-steroidal anti-inflammatory drugs and their prescription in general practice.

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The main aim of this study was to identify all patients currently receiving repeat prescriptions for non-steroidal anti-inflammatory drugs (excluding aspirin) from a practice population of about 12 000 patients and to record all relevant prescribing information from their medical notes. Additionally, we assessed the attitudes of general practitioners and consultant rheumatologists to prescribing non-steroidal anti-inflammatory drugs with a simple, one page questionnaire.

Patients and methods

The study population consisted of two group practices with just under 12 000 patients. One practice consisted of three principals holding joint contracts with Queen's University and the Eastern Area Health and Social Services Board (Northern Ireland) and one practitioner on a half time service contract; the other comprised four full time principals and one principal holding a similar joint contract.

Both practices' records were stored on a Stride 400 multiaccess computer, which provided lists identifying morbidity, full recording of all consultations, and a facility for repeat prescriptions. We used this computer to identify patients who had collected a repeat prescription for a non-steroidal anti-inflammatory drug (excluding aspirin) in the three months before the study. We excluded aspirin as we had found that patients receiving repeat prescriptions of aspirin were taking the drug as an antithrombotic. Repeat prescriptions were defined as those in which the general practitioner had indicated that a specified number of further identical prescriptions were to be issued to the patient via the computerised system.

The following information was recorded from the medical records: age, sex, current and previous treatment with non-steroidal anti-inflammatory drugs and the main reason for their prescription, other relevant diagnoses, and concurrent drug treatments. Side effects were recorded if they could be attributed to treatment with non-steroidal anti-inflammatory drugs. Only side effects important enough for treatment to be altered were recorded as we considered that it would otherwise be difficult to determine if particular symptoms were attributable to the non-steroidal anti-inflammatory drugs. We also noted whether the patient had received simple analgesics before the non-steroidal anti-inflammatory drugs and whether treatment with non-steroidal anti-inflammatory drugs had been initiated in the general practice or in hospital.

We established diagnostic criteria before assessing the patients' records. Osteoarthritis was recorded as a primary diagnosis only if the notes contained x ray evidence. Rheumatoid arthritis had to have been confirmed by a consultant rheumatologist and gout by a record of a raised serum uric acid concentration in the notes. Conditions such as low back pain (with no evidence of osteoarthritis) and frozen shoulder were categorised as soft tissue rheumatism. Patients were considered to have hypertension if they were currently being treated with antihypertensive drugs or if hypertension was expressly mentioned in the clinical notes. Heart failure was recorded only if there was documentary evidence of it in the notes; similarly, renal failure was recorded only if the diagnosis had been confirmed by hospital referral.

Patients were classified into one of five groups according to the degree of gastrointestinal ulceration: (a) those presenting currently with symptoms suggestive of ulceration or those having treatment for ulcers, or both, but with no ulcer proved previously; (b) those with no current symptoms but with an ulcer proved more than six weeks previously; (c) those presenting currently with symptoms suggestive of ulceration or those having treatment for ulcers, or both, and with an ulcer proved more than six weeks previously; (d) those with an ulcer proved endoscopically less than six weeks previously; and (e) those with no relevant history of peptic ulceration.

A questionnaire on the prescription of non-steroidal anti-inflammatory drugs was given to 42 general practitioners and 26 consultant rheumatologists at postgraduate meetings.

Results

Table I shows the age and sex distribution of the 198 patients studied compared with the practice population of 11 850. Female patients and men and women over 65 were significantly more likely to be receiving repeat prescriptions for non-steroidal anti-inflammatory drugs ($p < 0.001$ in each case, χ^2 test).

Table II shows the indications for non-steroidal anti-inflammatory drugs. Ninety one patients had one or more medical conditions that could be aggravated by non-steroidal anti-inflammatory drugs. Of these, 52 were classed as being hypertensive. Altogether 172 patients were taking one of just six non-steroidal anti-inflammatory drugs: ibuprofen (Brufen), 48 patients; diclofenac (Voltarol), 39; piroxicam (Feldene), 28; naproxen

(Naprosyn), 26; mefenamic acid (Ponstan), 16; and indomethacin (Indocin), 15. Table III gives details of concurrent drug treatment. No patients were receiving both an oral anticoagulant and a non-steroidal anti-inflammatory drug.

TABLE I—Age and sex distributions of patients. (Values in parentheses are percentages)

	Patients in study (n=198)	Patients in practices (n=11850)
Age (years):		
≤65	79 (40)	10018 (85)
>65	119 (60)	1832 (16)
Sex:		
Male	52 (26)	5259 (44)
Female	146 (74)	6591 (56)

TABLE II—Diagnoses for patients studied

Diagnosis	No of patients
<i>Primary</i>	
Osteoarthritis	137
Rheumatoid arthritis	16
Soft tissue rheumatism	19
Other*	19
More than one	7
<i>Other†</i>	
Hypertension	52
Heart failure	11
Renal impairment	1
Upper gastrointestinal ulceration:	40
Symptoms or treatment, or both; ulcer not proved	10
Inactive but proved >6 weeks previously	19
Symptoms or treatment, or both; ulcer proved >6 weeks previously	9
Proved <6 weeks previously	2
None of above	106

*Includes calcium pyrophosphate deposition disease, ankylosing spondylitis, dysmenorrhoea, and spina bifida.

†12 Patients had more than one other diagnosis.

TABLE III—Concurrent drug treatment. (Many patients were taking more than one drug)

	No of patients
Simple non-aspirin analgesics	74
Antihypertensives (excluding diuretics)*	25
Diuretics*	58
Combined antihypertensive and diuretic	2
Oral hypoglycaemics	7
None of relevance	79

*15 Patients were taking both an antihypertensive and a diuretic.

Twenty four patients had started their current treatment with a non-steroidal anti-inflammatory drug in hospital, and eight of these had rheumatoid arthritis. Most patients (170) had had their treatment started by their general practitioner, but for four patients we were unable to find out where it had been started. Although 48 patients had had no previous treatment with non-steroidal anti-inflammatory drugs, eight patients had been prescribed six others; six patients five others; 12 four others; 34 three others; 35 two others; and 55 one other. Thirty six patients had experienced side effects bad enough for treatment to have been changed. Of these, 20 experienced dyspepsia; one oedema; six rashes; and 15 other effects, including nausea, headache, dizziness, and drowsiness.

Questionnaires were completed by all the recipients. All but one doctor (a general practitioner) knew that Brufen was available in generic form; far fewer knew that Feldene was available generically, probably because its generic equivalent (piroxicam) had become available only recently. We found no significant difference between rheumatologists and general practitioners in their ability to rank selected non-steroidal anti-inflammatory drugs according to cost. Both groups of doctors showed a high level of awareness of the variation in the cost of treatment with different non-steroidal anti-inflammatory drugs.

Rheumatologists were significantly more likely to prescribe non-steroidal anti-inflammatory drugs for patients who had had a duodenal ulcer confirmed by gastroscopy less than six weeks previously ($p < 0.01$) or who had chronic renal failure ($p < 0.001$). Significantly more general practitioners thought that non-steroidal anti-inflammatory drugs should be prescribed to elderly patients only after simple analgesics had been tried ($p < 0.01$).

Discussion

In our study population female patients and men and women over 65 were significantly more likely to be receiving repeat prescriptions for non-steroidal anti-inflammatory drugs; Walt *et al* also found a high rate of prescribing of non-steroidal anti-inflammatory drugs to patients over 60.¹⁷ The high proportion of elderly women (69%) taking these drugs may have been due to the increased prevalence of osteoarthritis in this group. Only 10% of patients were receiving long term treatment with non-steroidal anti-inflammatory drugs for non-specific complaints; most had a diagnosed arthropathy. Many patients may be prescribed a non-steroidal anti-inflammatory drug on a single occasion for trauma or minor aches and pains, but these patients were not included in the present study as we looked only at repeat prescribing.

Hypertension, heart failure, renal impairment, and upper gastrointestinal irritation can all be aggravated by non-steroidal anti-inflammatory drugs. Altogether 91 patients showed evidence in their records of one or more of these problems and would therefore require careful monitoring. More than a quarter of the patients in the study were hypertensive. As non-steroidal anti-inflammatory drugs may themselves cause hypertension we may be using an antihypertensive drug to treat iatrogenic disease.

Somerville *et al* showed that elderly patients admitted with upper gastrointestinal bleeding were twice as likely to have taken non-steroidal anti-inflammatory drugs than those in a control group,¹⁸ and the Committee on Safety of Medicines recommended that these drugs should not be prescribed to patients with an active peptic ulcer.¹ Patients shown to have an ulcer by endoscopy in the six weeks before the study was started were regarded as having active disease. Most of the 40 patients in the study with gastrointestinal symptoms suggestive of ulceration fell into the category of suspected rather than active upper gastrointestinal ulceration, on the basis of symptoms, treatment, or past diagnostic evidence. Only two patients had active upper gastrointestinal ulceration. One had been given the non-steroidal anti-inflammatory drug in the form of a suppository at the time of endoscopy and was continuing treatment under the supervision of a consultant; in the other case the general practitioner had changed the route of administration of the drug from oral to rectal. Patients with symptoms or a history of upper gastrointestinal ulceration should be prescribed non-steroidal anti-inflammatory drugs only when simple analgesics have failed.

Although 14 different non-steroidal anti-inflammatory drugs, excluding aspirin, were being prescribed, most patients (87%) were taking one of only six different drugs. This agrees with the findings of Freeborn *et al*, who surveyed all the general practitioners in their area and found that 71% of the prescriptions for non-steroidal anti-inflammatory drugs were for only four drugs.¹⁹ The most frequently prescribed drug was ibuprofen, probably for several reasons including its low cost and established share of the market. This is encouraging as it was the one non-steroidal anti-inflammatory drug that the Committee on Safety of Medicines thought showed a slightly reduced rate of upper gastrointestinal bleeding.

Altogether 38% of the patients were being prescribed one or more of the following groups of drugs: antihypertensives, diuretics, and oral hypoglycaemics. All these drugs can interact with non-steroidal anti-inflammatory drugs. We suggest that all patients should have their current treatment carefully assessed before a non-steroidal anti-inflammatory drug is started.

Although eight patients had been prescribed six different non-steroidal anti-inflammatory drugs, 103 patients (52%) had not been prescribed more than two different types which might imply that the patients were satisfied with their treatment. We know,

however, that 37% of the patients studied were taking a simple non-aspirin analgesic as well as their non-steroidal anti-inflammatory drug. This may well be an underestimate as some patients may have been buying analgesics direct from a chemist, which suggests that over a third of the patients studied required combined treatment to achieve adequate pain relief.

Altogether 36 patients (18%) experienced one or more side effects bad enough for their treatment with non-steroidal anti-inflammatory drugs to be altered. This is a high figure, especially as it does not include those patients who experienced adverse reactions but continued with the same treatment. This finding suggests that patients being treated with non-steroidal anti-inflammatory drugs need to be monitored closely. We did not study patients who developed side effects early in their treatment, who consequently never received repeat prescriptions.

We found that rheumatologists were more likely to prescribe non-steroidal anti-inflammatory drugs for patients who had a duodenal ulcer or renal failure. This is probably because rheumatologists are dealing generally with more severely affected patients and are prepared to treat with one of these drugs even in the presence of accepted contraindications. General practitioners confronted by similar dilemmas would probably refer the patient to a consultant for his or her opinion.

No strict guidelines exist for prescribing non-steroidal anti-inflammatory drugs: each case has to be assessed on its merits. Our results show, however, that most prescribing is for elderly patients, a considerable proportion of whom need to be closely monitored because of either a pre-existing condition or the possibility of interactions with existing medicines. Non-steroidal anti-inflammatory drugs as a group are undoubtedly important in improving the quality of life for many patients but sometimes with a considerable cost in terms of morbidity and mortality. Perhaps clear guidelines for prescribing non-steroidal anti-inflammatory drugs would help to highlight specific instances in which careful monitoring of patients is essential if they are to benefit safely from this powerful groups of drugs.

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