Concise Report

Long-term NSAID use in primary care: changes over a decade and NICE risk factors for gastrointestinal adverse events

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Objectives. To examine prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) in general practice and to compare the results with a 1993 study. To assess numbers at risk of gastrointestinal adverse events using the National Institute for Clinical Excellence (NICE) guidance on the use of cyclo-oxygenase (Cox) II selective drugs.

Methods. Patients currently prescribed a NSAID for 2 months or more were identified from practice records. Demographic information, indications, previous gastrointestinal disease, serious co-morbidity and concomitant prescriptions were recorded. Data were compared with the 1993 survey and the NICE guidance.

Results. Seven thousand nine hundred and fifty-eight patients were registered with the practice in 2003. Two hundred and four patients were receiving repeat prescriptions for conventional NSAIDs and 63 for Cox II selective drugs. As in 1993 diclofenac (38%) and ibuprofen (24%) were the commonest individual agents and the main indication was regional pain. Seventy-three per cent of patients prescribed Cox II selective drugs and 64% of patients prescribed conventional NSAIDs had at least one NICE risk factor for gastrointestinal adverse events. Frequency of co-prescription of aspirin or antacids was similar for conventional NSAIDs and Cox II selective drugs, but prescription of antacids was higher with NICE risk factors.

Conclusion. The indications for NSAIDs have not changed since 1993. Cox II selective drug prescribing was within the NICE guidance but a substantial proportion of patients taking other NSAIDs had risk factors for gastrointestinal adverse events. Discussion with the GPs highlighted the difficulties of balancing perceived risk of gastrointestinal adverse events with cardioprotection and further guidance is urgently needed.

Key words: NSAIDs, Cox II selective drugs, NICE, Primary care.

Non-steroidal anti-inflammatory drugs (NSAIDs) exert their effect by blocking cyclo-oxygenase II (Cox II) while gastrointestinal adverse effects result from inhibition of Cox I. The Cox II selective drugs preferentially block Cox II with minimum effect on Cox I. Therefore, their gastrointestinal safety profile appears better than conventional NSAIDs although recent data have suggested that there is an increased risk of cardiovascular complications [1].

The National Institute for Clinical Excellence (NICE) published guidance in July 2001 for the use of Cox II selective drugs (celecoxib, rofecoxib, meloxicam and etodolac) for osteoarthritis and rheumatoid arthritis [2]. The guidance suggests that patients at high risk of developing gastrointestinal complications have one or more of the following risk factors and may be suitable for a Cox II selective drug: age over 65 yr; history of upper gastrointestinal perforation, ulcer or bleed; use of corticosteroids, aspirin and anticoagulants; serious co-morbidity; prolonged use of maximum dose.

In 1993 we undertook a survey examining long-term NSAID use in a semi-rural practice of 8000 patients in Dorset [3]. One hundred and sixty patients [mean (s.d.) age = 65 (13) yr, F:M = 1:1] prescribed NSAIDs for 2 months or more were identified. Thirty-four different NSAIDs had been prescribed with diclofenac (34%) and ibuprofen (24%) the most frequent. The commonest recorded indications were knee pain (41%), back pain (19%), shoulder pain (18%), hip pain (10%), neck pain (6%) and inflammatory arthritis (6%). The reported side-effects were those commonly associated with NSAID use. More side-effects were recorded for piroxicam and indomethacin than for other NSAIDs.

Following the introduction of Cox II selective drugs and publication of the NICE guidance we were interested in comparing drug use and indications in 2003 with those for 1993 in the same practice and assessing the use of NSAIDs and Cox II selective drugs in patients with NICE risk factors for gastrointestinal adverse events.

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Methods

Following Local Ethics Committee approval, all patients aged 18 yr and over currently prescribed NSAIDs or Cox II selective drugs for a minimum of 2 months were identified from GP computerized records (EMIS). Here ‘NSAIDs’ will refer to conventional, or non-selective drugs as opposed to Cox II selective drugs as defined by NICE. Demographic information, indications, side-effects, previous upper gastrointestinal history (perforation, ulcer or bleed), serious co-morbidity (cardiovascular disease, renal or hepatic impairment, diabetes or hypertension) and concomitant prescriptions of corticosteroids, anticoagulants, antacids (here defined as any gastric cytoprotective agent) or low-dose aspirin were recorded. The data were entered onto a Microsoft Access database and analysed using SPSS. We made an empirical comparison between the 1993 and 2003 surveys. The results were discussed with the GPs.

Results

In 2003, 7958 patients were registered with the practice [mean (s.d.) age 65 (12) yr, F:M 1:1] with 1445 patients (18%) aged over 65 yr (F:M = 1:2:1). Two hundred and four patients [mean (s.d.) age 61 (13) yr, F:M = 1:1] were prescribed NSAIDs for 2 months or more and 63 patients [mean (s.d.) age 61 (14) yr, F:M 1:9:1] were prescribed Cox II inhibitors. The proportion of women in the Cox II group was significantly greater than the NSAID group (P = 0.05, Mann–Whitney).

Diclofenac in various forms was the commonest prescribed drug (38%) with ibuprofen 24%, meloxicam 9%, etodolac 6%, rofecoxib 6%, naproxen 4%, piroxicam 2% and 12 others (11%). The four Cox II selective drugs accounted for 24% of prescriptions.

The recorded indications for prescriptions for NSAIDs and Cox II selective drugs are shown in Fig. 1. Significantly more patients with inflammatory conditions were prescribed Cox II selective drugs (P = 0.013, Mann–Whitney) while more patients with ‘other’ conditions (mostly non-rheumatological such as dysmenorrhea) were prescribed NSAIDs (P = 0.035). There were no other statistical differences.

Side-effects were recorded in only 4% of patients for currently prescribed NSAIDs and Cox II selective drugs. Sixty-eight per cent of patients prescribed NSAIDs and 73% of patients prescribed Cox II selective drugs had one or more NICE risk factors for gastrointestinal adverse events. There were no significant differences between the number of risk factors between the groups which were as follows: 33% NSAID, 21% Cox II = one risk factor; 15% NSAID, 21% Cox II = two risk factors; 11% NSAID, 17% Cox II = three risk factors; 4% NSAID, 5% Cox II = four risk factors; 5% NSAID, 9% Cox II = more than four risk factors.

The frequency of individual NICE risk factors identified in the NSAID and Cox II selective drug groups are shown in Fig. 2. Patients prescribed Cox II selective drugs had more previous gastrointestinal events (P = 0.001), diabetes (P = 0.031) and corticosteroid use (P = 0.02). There was a similar trend for cardiovascular morbidity, low-dose aspirin and antacid prescription that did not reach statistical significance. More patients prescribed NSAIDs with one or more NICE risk factors were co-prescribed antacids (24%) than those without NICE risk factors (6%).

Discussion

There were sufficient methodological differences between the 1993 and 2003 study to prevent direct statistical analysis. Nevertheless, there appears to be little change in the indications for prescribing NSAIDs or the popularity of diclofenac and ibuprofen.

The recorded indications were predominantly for regional pain rather than osteoarthritis or rheumatoid arthritis as recommended in the NICE guidance. At first sight this suggests inappropriate use of these drugs. However, other studies have shown a high incidence of arthritis in community-based patients with chronic pain [4]. In the context of this study we did not investigate this further so we are uncertain of the number of patients with non-arthritis regional pain.

The apparent increase in the numbers of patients prescribed NSAIDs and Cox II selective drugs between 1993 and 2003 may represent under-recording in the first survey, a national trend or increased prescribing of Cox II selective drugs for patients who would have previously been considered at too great a risk for a NSAID.

We found a no significant difference between the frequency of NICE risk factors for gastrointestinal adverse events in the NSAID and Cox II selective drug groups. While this means moderately high compliance with the guidance for

![Fig. 1. The written indications for prescribing NSAIDs or Cox II selective drugs.](image1.png)

![Fig. 2. The percentage of patients with a NICE guidance risk factor for gastrointestinal adverse reactions and those taking antacids for patients prescribed NSAIDs or Cox II selective drugs.](image2.png)
patients prescribed Cox II selective drugs (73% having at least one risk factor) it also means that a similar proportion of patients prescribed NSAIDs were at increased risk of gastrointestinal adverse events but were not prescribed a Cox II selective drug. This may be partly explained by the higher frequency of antacid prescription in patients with one or more NICE risk factors presumably reflecting attempts at gastric cytoprotection.

Discussions with the general practitioners suggested that they used the NICE guidance when starting a new patient on a NSAID or after an existing patient reported a side-effect with a NSAID and requested an alternative. Those patients already established on NSAIDs were, in general, left to continue with repeat prescriptions. The general practitioners were nervous about the prospect of reviewing all patients on long-term NSAIDs, mainly because of concerns about costs and the amount of work it would entail.

Although the overall frequency of NICE risk factors for gastrointestinal adverse events was similar between the NSAID and Cox II selective drug groups there were some differences in individual risk factors. The higher past history of gastrointestinal events, greater use of corticosteroids and use of antacids in the Cox II selective drug group perhaps suggests that general practitioners rank these risks more highly than high blood pressure and age over 65 yr.

It is of interest that aspirin was co-prescribed in 12% of patients taking NSAIDs and 14% of patients taking Cox II selective drugs despite the guidance suggesting an increased risk of gastrointestinal adverse reactions. Discussions with the GPs highlighted the difficulties of balancing perceived increased gastrointestinal adverse events against perceived cardiovascular protection in these patients.

Almost twice as many women than men were prescribed Cox II selective drugs compared with equal frequencies for NSAIDs. This can, at least in part, be explained by the greater frequency of inflammatory conditions as an indication for Cox II selective drug prescription in women (F:M 3:1) compared with NSAIDs (F:M 2:1).

We have identified a significant number of people repeatedly prescribed NSAIDs in general practice at increased risk of gastrointestinal adverse reactions. With the withdrawal of Vioxx and concern about the safety profile of the other Cox II selective drugs, the uncertainty about concomitant use of aspirin and the potential use of other gastric cytoprotective agents urgent advice is needed concerning the appropriate use of these drugs in primary care.

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**References**