Which patients are prescribed COX-2 inhibitors rather than nonspecific anti-inflammatory drugs?

Katie Paddon, BPharm (Hons), is pre-registration pharmacist, Pharmacy Department, Royal Brisbane Hospital, Queensland.

Bruce Green, BPharm (Hons), MSc, DClinPharm, is Lecturer, School of Pharmacy, University of Queensland.

Nonsteroidal anti-inflammatory drugs (NSAIDs) including cyclooxygenase-2 (COX-2) specific inhibitors are commonly prescribed by general practitioners. One of their principal side effects is gastrointestinal (GI) ulceration. Early data suggested COX-2 inhibitors had fewer GI side effects compared to NSAIDs,[1–4] and were therefore recommended for patients at risk of adverse GI events.[5] However, industry sponsorship of guidelines, together with only short term evaluation of side effects, overestimated COX-2 inhibitor superiority.[6–8]

The COX-2 inhibitors celecoxib and rofecoxib have had a significant impact on health costs since their introduction onto the Pharmaceutical Benefits Scheme, costing $90 and $81 million respectively for the year ending March 2003.[9] This has created interest in prescribing patterns,[10–12] which we explored to try to predict the probability of COX-2 inhibitor prescribing.

Methods

The study was prospective, with potential subjects identified by one of the authors (KP) examining the medical notes and prescription charts of all patients admitted to the Royal Brisbane Hospital (Queensland). Physician approval was sought before approaching patients, from whom consent was obtained. Eligible subjects were those prescribed either a COX-2 inhibitor or nonspecific NSAID initiated by their GP (determined during the patient interview). Several patient demographic and disease state data were obtained from the patient, the hospital medical notes and the patient's GP. Dose was represented as a fraction of the defined daily dose (FDDD), ie. the ratio of dose over the defined daily dose, (the assumed average maintenance dose per day for a drug used for its main indication in adults).[13] The study was approved by the Royal Brisbane Hospital Human Research Ethics Committee, and conducted from January to March 2003. Data were analysed using descriptive statistical tests and a logistic regression model.

Results

One hundred and six patients were included, with age, FDDD, indication for treatment, location of participant residency, and presence of hypertension the only statistically significant differences identified (*Table 1*). We found a trend for more patients to have heart failure treated with a COX-2 inhibitor than NSAIDs, significantly more with hypertension, and living in the city ($p<0.01$) (*Table 1*). The best logistic regression model to predict COX-2 inhibitor prescribing included the following factors: age, presence of osteo- or rheumatoid arthritis, and FDDD (*Figure 1*).

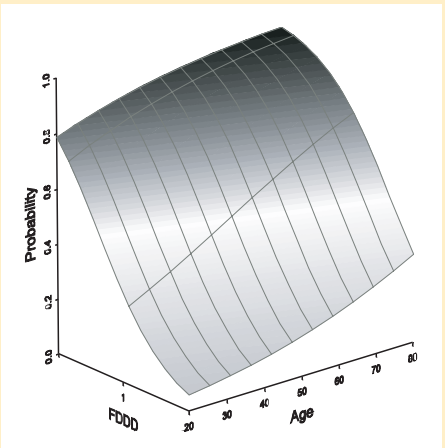

Figure 1. Probability of a COX-2 being prescribed rather than a nonspecific NSAID dependent upon age and FDDD for a patient with arthritis. At FDDD equal to 1 (shown as - on the probability surface), it can be seen that a patient 20 years of age has a 33% probability of being prescribed a COX-2 rather than a NSAID, rising to 73% at 70 years of age

Discussion

This study is not without limitations: the sample size was small, it was conducted in a hospital setting (where subjects are unlikely to represent the wider population), there was a disproportionately large number of women, (perhaps in part because of the greater prevalence of arthritis in females), and we had to infer prescribing intent (as GPs were not personally interviewed). We found arthritis and increasing age were predictors for COX-2 inhibitor prescribing. Drug dose (FDDD) was also a significant factor, although this should be viewed with caution as the smallest available dose unit for COX-2 inhibitors is equal to the DDD, while NSAIDs are available in smaller dose units. Similarly, the fewer dose choices available for COX-2 inhibitors result in FDDD reaching a maximum more frequently for COX-2 inhibitors than NSAIDs. Nevertheless these observations suggest that more research is necessary if we are to understand why GPs use COX-2 inhibitors rather than nonspecific NSAIDs.

Table 1. Subject characteristics

Variable	COX-2 n=70	NSAID n=36	p value
Fraction of defined daily dose	1.49 ± 0.568	0.820 ± 0.603	<0.0001*
Indication			
Osteoarthritis/rheumatoid arthritis	59 (84.3)	17 (47.2)	<0.001†
Other	11 (15.7)	19 (52.8)	
Location			
Brisbane	58 (82.9)	21 (58.3)	<0.01†
Not Brisbane	12 (17.1)	15 (41.7)	
Age (years)	66.2 ± 13.8	59.1 ± 16.9	<0.05*
Weight (kg)	78.3 ± 18.8	79.7 ± 19.5	NS*
Serum creatinine (mmol/L/minute)	0.0810 ± 0.0290	0.0830 ± 0.0420	NS*
Estimated glomerular filtration rate (mL/minute)	89.6 ± 43.5	102 ± 49.3	NS*
Sex			
Male	9 (12.9)	5 (13.9)	NS†
Female	61 (87.1)	31 (86.1)	
Concomitant medications			
Anticoagulants	31 (44.3)	11 (30.6)	NS†
Paracetamol	41 (58.6)	14 (38.9)	NS†
Gastroprotective agents	26 (37.1)	11 (30.6)	NS†
Oral corticosteroids	5 (7.1)	4 (11.1)	NS††
Concomitant disease states			
Hypertension before admission	40 (57.1)	13 (36.1)	<0.05†
Previous GI ulcer/bleed	12 (17.1)	8 (22.2)	NS†
Congestive cardiac failure	6 (8.6)	0 (0)	NS††
Previous Helicobacter pylori infection	3 (4.3)	1 (2.8)	NS††

Data expressed as mean ± standard if continuous and number (%) if categorical
* = two-tailed student's t-test, † = chi-squared test, †† = Fisher's exact test
NS = not statistically significant
Anticoagulants include aspirin 325 mg per day, warfarin, clopidogrel and dipyridamole
Gastroprotective agents include proton pump inhibitors and H2 antagonists
GRF = estimated glomerular filtration rate, GORD = gastro-oesophageal reflux disease

Implications of this study for general practice

- COX-2 inhibitors are more commonly prescribed than nonspecific NSAIDs.
- COX-2 inhibitors are more commonly prescribed for older patients with arthritis.
- They may not offer any benefits over nonspecific NSAIDs for patients with hypertension or heart failure.

Conflict of interest: none declared.

References

1. McCarthy D. Comparative toxicity of nonsteroidal anti-inflammatory drugs. Am J Med 1999;107:37S-48S.
2. Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis. The CLASS study: A randomised controlled trial. JAMA 2000;284:1247-1255.
3. Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. N Engl J Med 2000;343:1520-1528.
4. Geba G, Weaver A, Polis A, Dixon M, Schnitzer T. Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee. JAMA 2002;287:64-71.
5. Laine L. Approaches to nonsteroidal anti-inflammatory drug use in the high risk patient. Gastroenterology 2001;120:594-606.
6. Considerations for the safe prescribing and use of COX-2 specific inhibitors. Med J Aust 2002;176:328-331.
7. Agnes I, Hurley V, Hurley E. The road to consensus: considerations for the safe use and prescribing of COX-2-specific inhibitors. Med J Aust 2002;177:572-573.
8. US Food and Drug Administration. Celebrex capsules (celecoxib). NDA 20-998/S-009. Medical officer review. Available at: http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_03_med.pdf. Accessed 18 September, 2003.
9. Highest government cost PBS drugs by generic name, year end: June 2003. http://www.health.gov.au/pbs/general/pubs/pbbexp/pbjun03/pdf/book27.pdf. Accessed 22 September, 2003.
10. Graudins L, Gazarian M. Celecoxib use and overuse: too much 'celebration'? J Pharm Prac Res 2002;32:104-107.
11. Cutts C, LaCaze A, Tett S. A clinical audit of the prescribing of celecoxib and rofecoxib in Australian rural general practice. Br J Clin Pharmacol 2002;54:522-527.
12. Kerr SJ, Mant A, Horn FE, et al. Lessons from early large scale adoption of celecoxib and rofecoxib by Australian general practitioners. Med J Aust 2003;179:403-407.
13. The DDD: definition and principles. Available at: http://www.whocc.no/atcddd/. Accessed 22 September, 2003.

AFP

Correspondence
Email: brucegreen@verizon.net