Non-steroidal anti-inflammatory and cytoprotective drug co-prescription in general practice

A general practitioner-based survey in France

Abstract Background and aim: Non-steroidal anti-inflammatory drugs (NSAIDs) represent one of the most frequently prescribed drugs. Gastrointestinal damage, the most common side effect of NSAIDs, can be limited by the prescription of cytoprotective agents. In order to assess determinants of NSAID-associated cytoprotective agent prescriptions in primary care practice, we performed a general practitioner (GP)-based study.

Methods: After a 2-month intensive information campaign, the participation of all GPs of the Côte d'Or (France) administrative area was requested. During a 2-month period, GPs had to return a mailed questionnaire on NSAID prescription for up to ten consecutive patients aged over 18 years who required NSAIDs. This 30-item questionnaire included questions about the patient, the type of NSAID and the GP.

Results: GP participation rate was 24%, and 791 prescriptions were provided. GPs who participated in the study were representative of GPs of the area in terms of sex, time elapsed since graduation and GP practice area.

Around 80% of the patients included in the study were under the age of 65 years. The proportion of prescriptions combining NSAIDs and gastroprotective agents was 29.5%. Omeprazole accounted for 58% of the co-prescriptions and misoprostol for 29%. Independent determinants associated with the co-prescription of a cytoprotective agent were age [odds ratio (OR) 4.1; confidence interval (CI) 95% 2.3–7.4], previous history of poor NSAID tolerance (OR 10.4; CI 95% 5.8–18.6), previous history of moderate to severe digestive disorders (OR 13.4; CI 95% 5.1–35.4) and indication for chronic illness (OR 1.8, CI 95% 1.1–3.1). Prescriptions of cytoprotective drugs were in conformity with official guidelines for 78.3% of the patients. Although around 60% of the patients with risk factors for poor tolerance received a gastroprotective drug, 50% of the patients over 65 years did not receive it. Conversely, nearly 12% of the patients with no risk factors were prescribed cytoprotective agents. Patient history was the main reason put forward by GPs for prescribing cytoprotective drugs.

Conclusion: Although a large majority of GP prescriptions were in accordance with official recommendations, inadequate NSAID prescription practices remain relatively frequent especially with regard to the elderly.

Keywords Anti-inflammatory agents · Gastroprotective agents · Drug utilisation

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently prescribed drugs in developed countries. Ingestion of NSAIDs increases the risk of gastrointestinal complications, which range from dyspepsia to gastrointestinal bleeding and perforation [1]. Gastrointestinal bleeding rate in NSAID users is
around 0.5–0.6% [2]. In a 60-million inhabitant country such as the UK or France, NSAID-induced gastrointestinal bleedings may be responsible for about 500–2000 deaths [2, 3]. Patients with a history of ulcer injury, concomitant use of anticoagulants or corticosteroid treatment, use of high dose or multiple NSAIDs and advanced age have the highest risk of developing NSAID-associated gastrointestinal complications [4].

Histamine H₂ antagonists, Proton pump inhibitors (PPIs) and prostaglandin analogues (PAs) have been shown to reduce gastrointestinal injury related to NSAIDs [4, 5, 6, 7], but histamine H₂ antagonists are less effective than omeprazole in healing NSAID-related ulcers [8]. In 1998, the French Ministry of Health defined official guidelines for the use of NSAIDs, especially regarding the duration of treatment, parenteral administration and co-administration of other drugs including the use of cytoprotective agents in agreement with the available international scientific evidences: NSAID prescriptions have to be as short as possible, parenteral administration is only recommended for the first days of the treatment, and concomitant use of anticoagulants, corticosteroids or multiple NSAIDs has to be avoided. In France, only omeprazole and misoprostol have to be used as cytoprotective agents in patients with identified risk factors (age over 65 years and previous gastrointestinal history related or unrelated to NSAID use).

Despite the high frequency of NSAID prescriptions and the potential severity of their adverse effects, relatively few studies examining NSAID prescription patterns in primary care practice have been carried out [9, 10, 11, 12, 13, 14]. The aim of the present analysis was to examine potential determinants of NSAID-associated cytoprotective drug prescription in a general practitioner (GP)-based study performed in a well-defined French administrative area.

Methods

Study design

This study was performed in the French administrative area of Côte d’Or (around 500,000 inhabitants). In January and February 1999, general information about the study was given to the GPs during several post-graduate training sessions devoted to other topics. One month later, the participation of all GPs (n = 513) of the area was requested by means of a postal campaign, which contained further information about the objective and design of the study.

The study was conducted between April and June 1999. All GPs who did not respond to the postal campaign were contacted by telephone in order to encourage them to participate and, in case of definite refusal, to identify the reasons why they were not willing to participate. During a 3-month period, the participating GPs had to include up to ten consecutive patients aged over 18 years whose health status required NSAID prescription (excluding isolated prescription of NSAIDs for transdermal administration).

Amongst the 513 GPs practising in the Côte d’Or area, 65 reported to be non-prescribers of NSAIDs because of their medical practice (homeopathy, allergy, acupuncture, dietetic, sophrology). Among the potential prescribers, 111 (24.8%) actively participated. Participating GPs provided 791 NSAID prescriptions that fulfilled the inclusion criteria. Eighteen prescriptions were excluded because they corresponded either to patients included twice (n = 4) or to patients under 18 years (n = 14). Participant GPs did not differ from non-participants with regard to sex, time elapsed since graduation and GP practice area. Of participant GPs, 62% returned ten questionnaires, 25% provided between six and nine questionnaires and 13% returned fewer than five questionnaires. There were no differences in the main characteristics of the patients (age, sex, digestive history, NSAID indication) according to the number of questionnaires returned by the GP.

Data collection

A standardised 30-item questionnaire was used to collect information on patient characteristics and on NSAID prescription (drug name, pharmaceutical form and strength, doses, duration of the prescription performed at the time of the visit, indication), associated drugs (especially gastroprotective drugs), NSAID use in the past 6 months and past medical history. GPs were asked to give the full name of the drug they prescribed to avoid NSAID-related side effects and to report the reasons why they prescribed it (with suggested items such as patient request, age of patient, treatment duration, NSAIDs known for their side effects).

Statistical analysis

All analyses were performed using the Stata package (Stata Corp. 1999, College Station, Tex.). A univariate analysis was performed using Chi² tests in order to identify factors associated with the co-prescription of gastroprotective drugs. Factors with P values lower than 0.15 were introduced in a logistic regression model. As several patients could be recruited by the same GP, prescriptions within such a cluster cannot be regarded as independent. A slight degree of within-dependence was measured using a kappa statistic of intra-class correlation. For the gastroprotective co-prescription rate, the intraclass correlation was 0.114. This means that prescribing a gastroprotective drug was more related to the patient than to prescriber habits. Nevertheless, this cluster randomisation effect was taken into account in the logistic model. GP practice area was coded as rural/urban according to the definition of the Institut National de la Statistique et des Etudes Economiques. Indications for NSAID prescriptions were categorised into three groups: acute disorders re-grouping tendonitis, periarthritics, microcrystalline arthritis, fever, articular or periartricular injuries, renal colic, menstral pain and any kind of acute pain such as that affecting the mouth and the sinuses; subacute disorders mainly represented by illnesses affecting the vertebral column, i.e. neck pain, lumbago or sciatica; and chronic disorders including osteoarthritis and chronic rheumatism. Previous history of digestive disorders was separated into four groups: no history; minor disorders, i.e. gastro-oesophageal reflux disease, or minor pain from unknown origin; moderate disorders, i.e. gastritis or bulbitis; and severe disorders, i.e. oesophagitis, gastric or duodenal ulcers and upper digestive haemorrhage.

Results

General data

The main characteristics of the patients are given in Table 1. The majority of patients were under 65 years (78.6%). Most of the 791 prescriptions collected (57.4%) were given for an acute disease. This proportion was higher in women (64.2%) than in men (48.2%). Only 6.4% of the patients received NSAIDs for more than 28 days. The distribution of NSAID prescriptions shown in Fig. 1 did not reveal any significant sex differences. In both sexes, three molecules (piroxicam,