Observational survey of NSAID-related upper gastro-intestinal adverse events in Belgium

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Abstract

Objectives : **To evaluate the impact of NSAID use on current routine upper GI endoscopy (UGIE) and to compare the lesions found in NSAID users and non-users.**

Methods : **Participating gastroenterologists consecutively documented outpatients with and without suspicion of bleeding, referred for upper gastrointestinal endoscopy. Patient characteristics, presence of risk factors, NSAID use and endoscopic findings were reported on standard data collection forms.**

Main results : **A total of 2685 non-bleeding and 159 bleeding patients were enrolled within a time period of 2 months. NSAID therapy was present in 20% of the non-bleeding patients and at least 9% of referrals for endoscopy were directly related to suspected NSAID adverse events. Nearly half of acute bleeding patients (42%) were NSAID users, including aspirin for cardioprevention. Warning digestive symptoms prior to acute bleeding were frequently absent (56%). Oesophagitis was the main endoscopic diagnosis (51% of patients). Gastroduodenal (GD) ulcer was significantly more frequent in NSAID users, whereas oesophagitis and bleeding oesophageal varices were more frequent among non-users. Analysis of odds ratio's demonstrated NSAID use to significantly increase the risk for gastric ulcer in the whole patient group (OR = 2.73 ; 95% confidence interval (CI) : 1.98-3.77 ; p < 0.001) and, in addition, for duodenal ulcer in the elderly (>65y) subgroup (OR = 2.91 ; 95% CI : 1.52-5.59 ; p < 0.05).**

Conclusions : **This survey confirms the high incidence of GD ulcers in NSAID users and the risk for serious gastrointestinal complications, often occurring without warning symptoms. It underlines the impact of NSAID use on the routine endoscopy load, the necessity of careful selection of patients for NSAID prescriptions and the need for gastropreventive measures, particularly in elderly patients and patients associating multiple risk factors.**
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Key words : anti-inflammatory agents, non-steroidal / adverse effects, endoscopy, gastrointestinal, risk factors, gastrointestinal diseases / chemically induced, peptic ulcer / chemically induced, gastrointestinal hemorrhage / chemically induced, health survey.

Introduction

NSAID are key agents in the management of arthritic and inflammatory diseases. They are currently among the most frequently prescribed medications. A large number of patients are therefore exposed to the potential side effects related to these drugs.

Most common NSAID-induced problems are upper gastrointestinal (GI) disorders, which range from minor digestive complaints as dyspepsia and nausea to severe, life-threatening complications. These serious complications, mainly GI haemorrhage and perforation, are relatively rare (1-2% of NSAID users) but important in absolute numbers, considering the high prescription frequency of NSAID (1-4). Therefore NSAID adverse events are an important health problem that needs serious attention.

In addition, it is generally accepted that minor digestive symptoms are poor predictors of major GI events (5). Therefore, many efforts have been directed at identifying subcategories of "high-risk" NSAID users. Several risk factors (e.g. advanced age, history of ulcer, presence of associated morbidity) have been shown to increase patient risk for NSAID-induced upper GI complications, but their precise contribution remains open to debate (4,6).

The current survey aimed to evaluate the impact of NSAID use on Belgian UGIE practice and to document the risk profile for NSAID-induced lesions in patients referred for UGIE. The incidence and type of different GI lesions in NSAID users and non-users were compared.

Methods

The survey of routine UGIE in outpatients consisted of two parallel sections. The first section is further referred to as the "Endoscopy survey", the latter as the "Bleeding survey".

Investigators participating in the Endoscopy survey, prospectively recorded, within a time frame of 10 consecutive working days, each non-bleeding outpatient referred for UGIE.

The Bleeding survey documented, within a period of 20 consecutive working days, all patients referred for UGIE because of clinically diagnosed bleeding or with bleeding diagnosed during UGIE.

Information on patient demographics and risk profile were retrieved by means of a standard data collection form that has been submitted with the paper for the reviewers. We hereby define a series of terms that used in the questionnaire and presented in the results. Naïve patients are patients without previous history of upper gastro-intestinal tract disease. Health status was classified on a 5-point scale from bad to very good and left to

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the appreciation of the clinician. Cardio-vascular disorders include previous history of myocardial infarction, vascular neurologic disorders and hypertension. Anticoagulant use corresponds to any anticoagulant drug including antivitamin K and heparin derivatives. Comorbidity corresponds to any condition considered as clinically significant by the clinician and was classified as cardiovascular, metabolic, respiratory, rheumatologic, hepatic disease, cancer or other. The endoscopic lesions were defined by usual criteria except for gastritis and bulbitis that were left to the appreciation of the endoscopist without providing clear criteria. Attention was given to the presence of associated morbidity, mainly to hepatic, pulmonary, cardiovascular and renal diseases. Results of UGIE, Helicobacter *pylori (*Hp) status and therapeutic approach following UGIE were reported. In bleeding patients, clinical symptoms at referral and degree of bleeding were recorded in addition ; out of the endoscopically diagnosed lesions, the main source of bleeding was identified. A lesion was considered as the source of bleeding if there was an active bleeding or a clear proof of recent bleeding (visible vessel or clot).

NSAID use was documented by the type of drug, the time relation between NSAID therapy and occurrence of digestive symptoms and the presence of acid-disease-related co-medication.

Statistical analysis

Differences in NSAID user and non-user population were evaluated using the Chi-square test. Fisher's exact test was applied for samples of limited size (< 30 subjects). Odds ratio (OR) analysis was performed to compare the risk for developing different lesions in subpopulations with different risk profiles. OR superior to 1 means a higher chance for finding the evaluated lesion in the NSAID user group compared to the non-user group. Confidence intervals for the OR were calculated by first calculating the confidence interval for the *logarithm* of the odds ratio and then exponentiating those limits. In addition logistic regression was used to distinguish the important risk factors associated with NSAID complications (gastroduodenal ulcer, bleeding). Variables entered into the model were age, gender, history of ulcer, presence of comorbidity, concomitant anticoagulant or corticosteroid use. All tests were interpreted at the 5% a-level.

Results

Endoscopy survey

Referral

Between May and July 2000, 2685 non-bleeding patients were enrolled by 115 Belgian gastroenterologists from 59 different centres, including hospitals (58% of centres), private practices (27%) and clinics (15%). The average inclusion period was 25.6 days (± 24.8 SD) per centre and 15.5 days (± 18 SD) per specialist. Patients were referred for UGIE mainly by general practitioners (73% of patients), GI-specialists (7%), surgeons (3%) and emergency staff (3%). Most UGIE were performed on naïve patients (58% of endoscopies). Follow-up UGIE was primarily indicated for history of oesophagitis (49% of follow-up endoscopies) or GD ulcer (18% of follow-up endoscopies).

Patient profile

Patients were predominantly female (ratio male/female = 0.87). The general health status was rated "good to very good" in 68% of patients, "intermediate" in 26% and "poor to very poor" in 7%. Within the total patient group 880 subjects were aged over 65 years (33%). As expected, the percentage of patients in good condition and the proportion of male patients gradually declined with aging.

History of GD ulcer was present in 27% of patients (Table I). Information about the aetiology of the previous ulcer was available in 62% (n = 441) of these cases and indicated that ulcers were mainly related to NSAID use (37% ; n = 165) or Hp infection (40% ; n = 176). Of the total patient group, 38% (n = 1016) suffered from associated morbidity. The highest incidence was found for cardiovascular disease (27% of patients with associated diseases ; n = 276), followed by metabolic disorders (13% ; n = 134) ; 6% of co-morbid patients (n = 59) had severe psychiatric disease. Co-morbidity, concomitant corticosteroid (4% of patients) and anticoagulant therapy (3% of patients) were equally distributed over both genders. In contrast, history of ulcer was predominantly found in male patients (29% of males (n = 363) and 24% of females (n = 349) ; $p < 0.001$).

Results of endoscopy, Hp test and therapeutic approach

The results of UGIE showed normal findings in 24% of patients. Oesophagitis was the most frequently detected lesion (51% of patients). Gastric and duodenal ulcers were found respectively in 8% and 6% of patients, malignancy in 1% of patients. Out of the patients presenting with GD ulcers, 86% were checked for Hp (Table II) and 75% of the test results were available at the moment of data collection. Mostly (78% of cases) only 1 test modality was applied to diagnose Hp infection (80% histology, 11% urea breath test, 6% rapid urease test and 1% culture), while 2 or 3 different Hp tests were used in 17% and 5% of cases respectively.

Following UGIE, 5% of patients were admitted to hospital (n = 137). Medical treatment was initiated in 74% of patients (n = 1989), including 79% proton-pump inhibitors, 6% prokinetics and 3% H_2-receptor antagonists.

NSAID use

NSAID were used by 543 patients (20% of the whole patient group), including 36% of aspirin users (n = 193). NSAID were mainly indicated for articular diseases

Table I. — **Patient risk profile**

	Total patients	NSAID users	NSAID non-users	NSAID users vs. non-users
Endoscopy survey	n = 2685	n = 543	n = 2142	
Male/female ratio	0.87	0.70	0.92	p < 0.005
Number of patients (%)				
age > 65y	880 (33%)	229 (42%)	651 (30%)	p < 0.001
history of ulcer	712 (27%)	161 (30%)	551 (26%)	p = 0.06
co-morbidity	1016 (38%)	281 (52%)	735 (34%)	p < 0.001
corticosteroid use	100 (4%)	32 (6%)	68 (3%)	p < 0.01
anticoagulant use	76 (3%)	18 (3%)	58 (3%)	
Bleeding survey	n = 159	n = 66	n = 93	
Male/female ratio	1.5	0.82	2.13	p < 0.01
Number of patients (%)				
age > 65y	83 (52%)	43 (65%)	40 (43%)	p < 0.05
history of ulcer	33 (21%)	9 (14%)	24 (26%)	
co-morbidity	95 (60%)	40 (61%)	55 (59%)	
corticosteroid use	9 (6%)	4 (6%)	5 (5%)	
anticoagulant use	17 (11%)	13 (20%)	4 (4%)	p < 0.05

Table II. — **Diagnosis of Hp infection in patients with GD ulcers from Endoscopy survey**

	Number of patients	Hp check performed	Hp-positive	Hp-negative	Hp status unknown
GU	185	151 (82%)	41 (36%)	73	37
DU	137	125 (91%)	63 (69%)	28	34
GU+DU	26	22 (85%)	11 (58%)	8	3
Total	348	298 (86%)	115 (51%)	109	74

(41% of patients) or cardiovascular prevention (21%). The NSAID intake was daily in 64% of users. It was noted that the digestive symptoms, which led to UGIE, appeared during NSAID treatment in 44% of users and were the reason for NSAID discontinuation in 8% of users. Only a minority of NSAID users (25%) were taking acid-disease-related therapy. This included proton-pump-inhibitors (57% of co-prescriptions), H_2-receptor antagonists (12% of co-prescriptions), prokinetics and antacids as well.

Profile of NSAID users

Compared to the non-users, NSAID users were significantly older ($p < 0.001$) and held more female patients ($p < 0.005$) (Table I). Co-morbidity and co-prescription of oral corticosteroids were also significantly more frequent in NSAID users ($p < 0.001$ and $p < 0.01$ respectively). History of ulcer tended to be more frequent in NSAID users compared to non-users ($p = 0.06$).

Relative risk for developing upper GI lesions in NSAID users versus non-users

Results of UGIE showed an increased frequency of abnormal findings in the NSAID user group compared to the non-users ($p < 0.001$), particularly duodenal ulcers, erosive gastritis and gastric ulcer (Fig. 1).

Odds ratio analysis demonstrated that NSAID users were more at risk for developing gastric ulcer, compared to non-users (Fig. 2). The difference was highly significant (OR = 2.73 ; 95% CI : 1.98-3.77 ; $p < 0.001$).

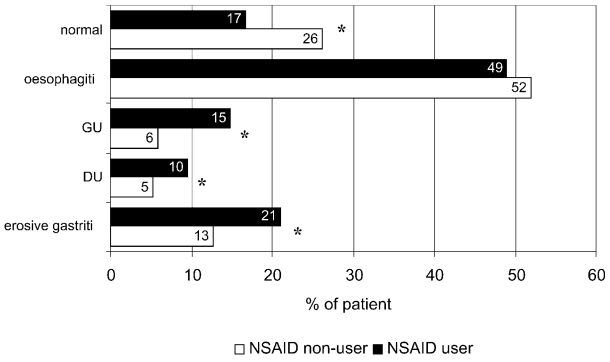

Fig. 1. — Lesions detected at UGIE in patients from Endoscopy survey - NSAID users compared to non-users (*$p < 0.001$).

Gastritis and bulbitis, alone (OR = 1.61 ; 95% CI : 1.24-2.09) or combined with oesophagitis (OR = 1.49 ; 95% CI : 1.22-1.82), were also more frequent in the NSAID user group, although less significantly ($p < 0.01$). Inversely, oesophagitis was predominantly found in non-users (OR = 0.66 ; 95% CI : 0.49-0.90 ; $p < 0.001$).

The increased risk for gastric ulcer in NSAID users compared to non-users was even more pronounced in the subpopulation with associated morbidity (OR = 3.74 ; 95% CI : 2.31-6.05 ; $p < 0.001$). The risk for combining gastritis and oesophagitis was also higher in co-morbid NSAID users (OR = 1.79 ; 95% CI : 1.18-2.72 ; $p < 0.01$). Non-users with associated morbidity were more

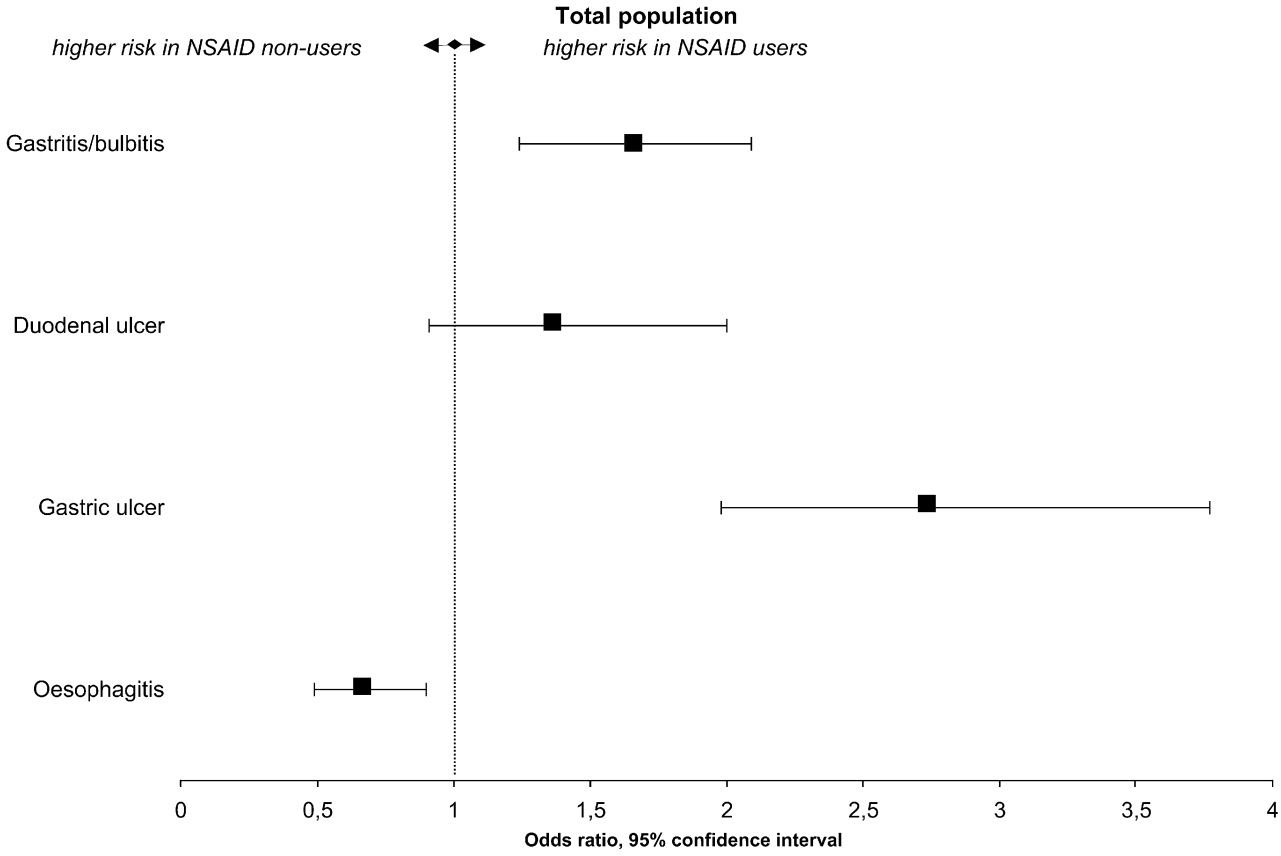
Total population
higher risk in NSAID non-users
higher risk in NSAID users
Gastritis/bulbitis
Duodenal ulcer
Gastric ulcer
Oesophagitis
0
0,5
1
1,5
2
2,5
3
3,5
4
Odds ratio, 95% confidence interval

Fig. 2.a

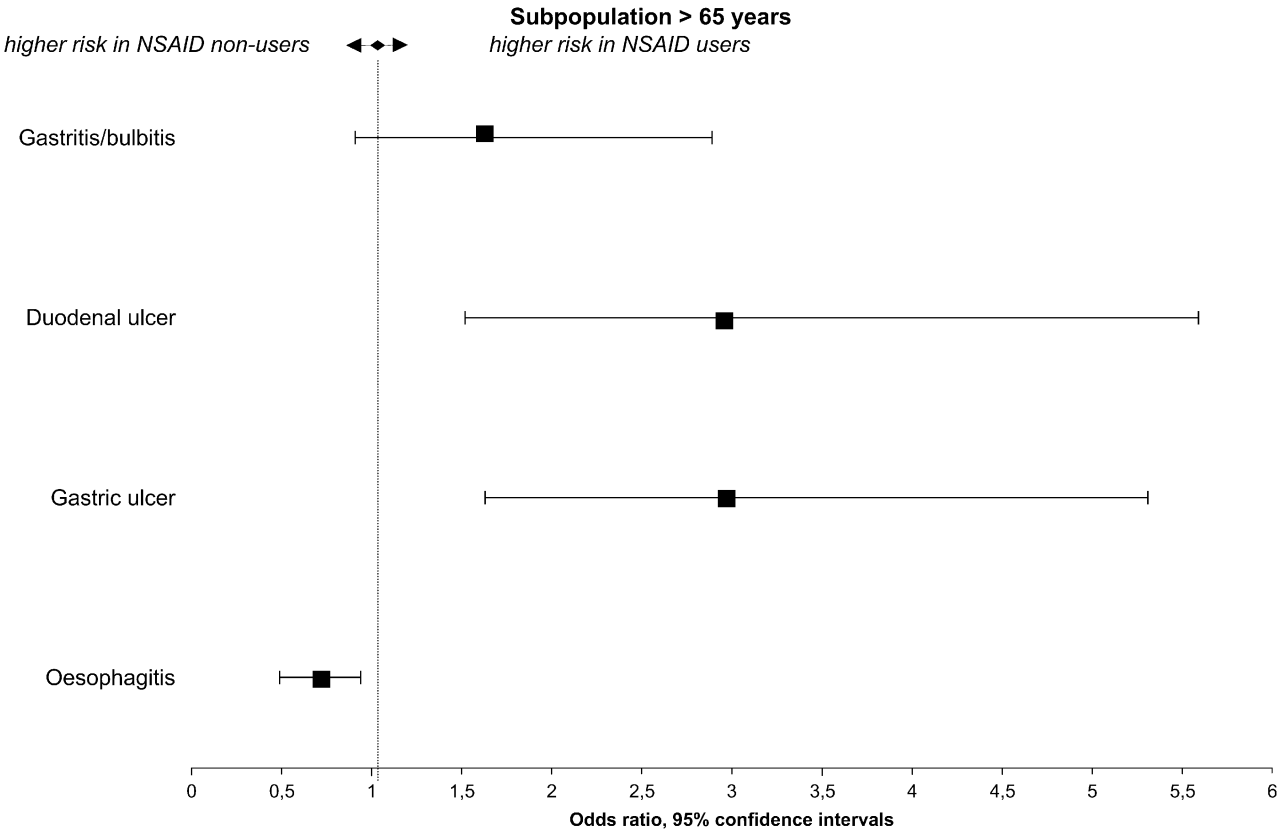
Subpopulation > 65 years
higher risk in NSAID non-users
higher risk in NSAID users
Gastritis/bulbitis
Duodenal ulcer
Gastric ulcer
Oesophagitis
0
0,5
1
1,5
2
2,5
3
3,5
4
4,5
5
5,5
6
Odds ratio, 95% confidence intervals

Fig. 2.b

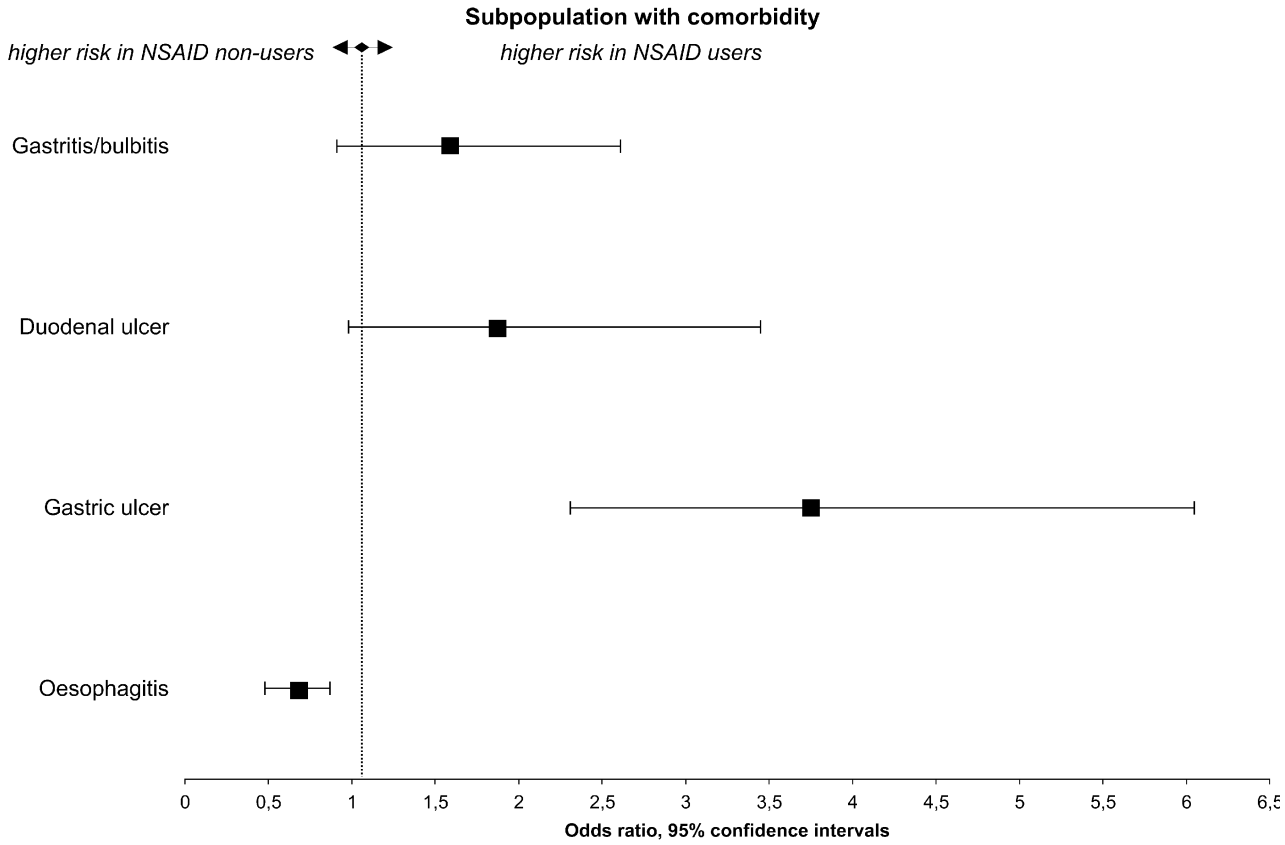

Fig. 2c

Fig. 2. — Relative risk for the development of upper GI lesions in patients from the Endoscopy survey – NSAID users compared to non-users – different subgroups.

prone to oesophagitis (OR = 0.65 ; 95% CI : 0.48-0.87 ; $p < 0.01$).

Similarly, elderly NSAID users, aged over 65 years, were at higher risk for gastric ulcer compared to elderly non-users (OR = 2.94 ; $p < 0.01$: 95% CI : 1.63-5.31) while non-users were more at risk for oesophagitis (OR = 0.68 ; 95% CI : 0.49-0.94 ; $p < 0.05$). In addition and in contrast to the total population, the risk for duodenal ulcer significantly increased in the elderly NSAID users subpopulation compared to elderly non-users (OR = 2.91 ; 95% CI : 1.52-5.59 ; $p < 0.05$).

The logistic regression analyses showed that a history of ulcer significantly increased the risk for developing NSAID-related gastroduodenal ulcer ($p < 0.01$). Other possible risk factors, including age, gender, presence of associated morbidity and the concomitant use of anticoagulants or corticosteroids had no statistically significant impact on the development of gastroduodenal ulcer in the current study sample.

Bleeding survey

Referral

Within a time frame of 2 months (May to July 2000), 159 bleeding patients were included in the survey by 47 gastroenterologists from 40 recruiting centres. The average inclusion period was 9.7 days (± 11.6 SD) per investigator and 12.8 (± 14.3 days SD) per centre. Patients were mainly referred for UGIE by the emergency unit (54% of patients) or by general practitioners (35%).

Patient profile

Patients were predominantly male (male/female ratio = 1.5) and more than half of them were older than 65 years. Women with acute bleeding were on average significantly older than men (average age men 58.5 yr versus women 68.6 yr ; $p < 0.01$). A total of 60% of patients suffered from associated morbidity, mainly cardiovascular (19% of all patients) and hepatic disease (10% of all patients). Pulmonary, renal and other comorbidity were reported in respectively 9%, 2% and 19% of patients. History of GD ulcer was present in 21% of patients. Anticoagulant drugs and oral corticosteroids were used by 11% and 6% of patients respectively (Table I).

Clinical symptoms and results of endoscopy

Melena was the main clinical symptom of bleeding in 53% of patients. Hematemesis or a combination of melena and hematemesis were found both in 20% of cases. The lowest haemoglobin level measured, used as an indicator for severity of bleeding, was below 8 or between 8 and 10 g haemoglobin/dl in 40% (n = 62) and 30% (n = 47) of documented patients (n = 156) respectively.

The main source of bleeding, identified at endoscopy, was duodenal ulcer in 55 patients (35%), gastric ulcer in 43 patients (27%), gastric erosions in 17 (11%), varices in 15 (9%), oesophagitis in 10 (6%), Mallory-Weiss in 10 (6%) and other lesions in 9 patients (5%).

NSAID use

A total of 66 patients were NSAID users (42% of the total bleeding population).These included 31 patients using non-salicylated NSAIDs as monotherapy. Mainly diclofenac (n = 9), piroxicam (n = 9), ibuprofen (n = 4) and naproxen (n = 3) were used by these patients ; 1 patient was treated with nimesulide ; no COX-2 selective inhibitors were reported. A further 25 patients used only low dose of aspirin (≤ 160 mg/day) and 6 patients combined non-salicylated NSAIDs with low dose aspirin or used a higher dose of aspirin. NSAID were mainly prescribed for articular diseases (45%) ; 29% of patients received aspirin for cardiovascular prevention. Aspirin users were mostly over 65 years of age (83% of aspirin users ; n = 24), receiving aspirin for cardiovascular prevention (79% of elderly NSAID users ; n = 19). NSAID intake was daily in 80% of patients. Digestive symptoms at referral for UGIE were reported by 33% of NSAID users (n = 22). These symptoms, mainly epigastric pain (86%), appeared during NSAID therapy in 94% of cases. The absence of symptoms prior to bleeding was explicitly mentioned in 56% of NSAID users (n = 37). Only 8% of NSAID users were taking acid-disease-related co-medication.

Profile of NSAID users

NSAID users were significantly older than non-users ($p < 0.05$) and held slightly more female than male patients ; the non-users were predominantly male ($p < 0.01$) (Table I). Co-morbidity was present in both subgroups to the same extent. However, significant variation existed regarding the type of disease. Cardiovascular disease was the main associated disease in NSAID users (30% versus 12% of patients in NSAID user and non-user group respectively ; $p < 0.05$). Hepatic disease was present in 17% of co-morbid non-users while NSAID were not prescribed in patients with hepatic disease. History of ulcer was more frequent in the non-user group but the difference was not statistically significant. Anticoagulant therapy was significantly more frequent in NSAID users compared to non-users (20% versus 4% of patients respectively ; $p < 0.05$). Corticosteroids were used by 6% and 5% of NSAID users and non-users respectively.

Relative risk for developing upper GI lesions in NSAID users compared to non-users

GD ulcers were the primary source of bleeding, in NSAID users as well as in non-users, explaining 75% and 53% of bleeding respectively (Fig. 3). The incidence of all bleeding lesions was comparable between NSAID users and non-users, except for oesophageal varices,

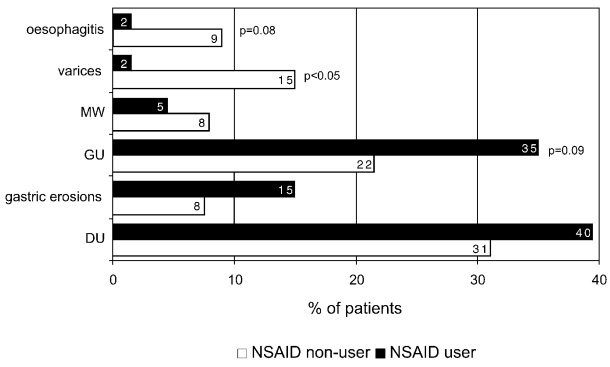

Fig. 3. — Cause of bleeding detected at UGIE in patients from the Bleeding survey – NSAID users compared to non-users.

which were found more often in the non-user compared to the NSAID user group (2% vs. 15% of NSAID users and non-users respectively ; $p < 0.05$) and for bleeding gastric ulcers which were more frequent in the non-salicylated NSAID user group (49% vs. 22% of non-salicylated NSAID users and non-users respectively ; $p = 0.002$; data not shown). Non-users tended to be more prone to bleeding oesopaghitis (2% vs. 9% in NSAID users and non-users respectively ; $p = 0.08$).

Odds ratio analysis revealed no significant differences between the NSAID user and non-user group as a whole. However, the group of non-salicylated NSAID users as well as the total group of NSAID users with a prior history of ulcer were more prone to develop gastric ulcer compared to the group of non-users (respectively OR = 3.40 ; 95% CI : 1.33-8.69 ; $p < 0.01$ and OR = 5.60 ; 95% CI : 0.90-34.67 ; $p = 0.059$). In the subpopulation aged over 65 years with at least 1 other risk factor, non-salicylated NSAID users were also at significantly higher risk for developing gastric ulcer than a comparable group of non-users (OR = 4.10 ; 95% CI : 1.31-12.88 ; $p = 0.01$).

The logistic regression analyses identified an age over 65 years, the presence of associated morbidity and the use of anticoagulants as independently associated with a risk of bleeding complications ($p <= 0.01$), while female gender was identified as a negative risk factor for bleeding ($p < 0.01$).

Discussion

This is the first large observational survey of UGIE in Belgium. It provides a snapshot of the current routine practice for non-bleeding and bleeding outpatients and evaluates the impact of NSAID use on the finding of upper GI complications. The endoscoped patients were treated with all different types of routinely used NSAIDs ; only a limited number of patients using COX-2 selective inhibitors participated in this survey (7 patients in the endoscopy survey and 0 patients in the bleeding survey). Perhaps this is explained by a relatively low prescription rate of these NSAIDs at the moment

the survey was running ; the design of the present survey did not allow to evaluate theoretical differences in gastrotoxicity between NSAIDs .

Endoscopy survey

Endoscopic routine and Hp testing

Within an average period of 15.5 calendar days, 115 gastroenterologist performed and documented 2685 UGIE in non-bleeding patients. The planned inclusion period of 10 consecutive working days was well respected. This supports the validity of the data. According to data from INAMI-RIZIV, the calculated number of UGIE performed in outpatients in Belgium over this period of time was 12.971 (total number of UGIE in the year 2000 is 305.351). Our sample therefore represents about 20% of UGIE performed over the country.

UGIE were mainly prescribed by primary care physicians (approx. 75%), while referral by GI specialists was rather limited (7%). The endoscoped population was predominantly female, whereas previous history of gastroduodenal ulcer was more frequently present in males.

Oesophagitis was the most common diagnosis (51% of patients) and also the most frequent reason for follow-up UGIE. GD ulcer was demonstrated in 13% of referred patients. Hp checking was performed in 86% of these ulcer patients, but definitive results were not always available at the moment of data collection. The present survey found a relatively low rate of Hp positive results (51%). This might partly be explained by the unavailability of test results at the moment of completion of the data collection form, but might also reflect a declining incidence of Hp-associated GD ulcers or a low sensitivity of the routinely applied diagnostic modalities. Indeed, only one diagnostic test was used in 3 patients out 4 and histology was the only diagnostic method used in more than 80% of the cases, although the 1998 Belgian Consensus recommended to use at least 2 different diagnostic tests (e.g. biopsy urease test and histology) (7).

NSAID use

NSAID therapy was present in 20% of routinely endoscoped patients and 9% of prescribed endoscopies were directly linked to NSAID adverse events. This percentage is to be interpreted taking into account the total number of NSAID prescriptions in Belgium : 430.729 patient years in the year 2000 (data from IMS). From these data, it is concluded that NSAID use increases the Belgian out patient upper GI endoscopy load with at least 10%. Nevertheless, only 1 patient out of 4 was under acid-related co-medication, which, in addition, was probably not prescribed for preventive purposes but mainly triggered by co-existing oesophagitis. Furthermore, it is known from a parallel survey with general practitioners (unpublished data) that general practitioners consider a wide range of drugs, including antacids, prokinetics and low dose of H_2-receptor antagonists, capable of protecting their NSAID using patients. Medical literature however, recently reviewed by Rostom *et al*.. has clearly shown that only proton-pump inhibitors, misoprostol and double dose of H_2-receptor antagonists are effective at preventing NSAID-related endoscopic GD ulcers (8). Therefore it is concluded that there is an obvious need for information and direction on primary prevention of NSAID-related upper GI complications in general practice.

Comparison of endoscopic lesions in NSAID users and non-users

GD ulcer and to a lesser extent also erosive gastritis, were the main lesions in NSAID users. In line with other reports, these lesions were significantly more frequently diagnosed in the NSAID user group compared to the non-users (see Fig. 1) (9-11). Oesophagitis, in contrast, was predominantly found in non-users.

Various risk factors are generally recognized to predispose to the development of NSAID-related GI problems, including history of previous gastrointestinal events, concomitant corticosteroid use, associated morbidity and the use of high-dose or multiple NSAID (12-14). Advanced age and the presence of multiple risk factors increase the risk (4,15-17). The results of the present survey (see Table I) showed that within the patient population referred for endoscopy, several of these risk factors, particularly advanced age, corticosteroid use and co-morbidity, were significantly more common among NSAID users compared to non-users. History of ulcer tended to be more frequent in NSAID users.

Odds ratio analysis (see Fig. 2) confirmed that in this population of patients undergoing routine endoscopy, NSAID use significantly increased the risk for gastric ulcer (OR = 2.73 ; 95% CI : 1.98-3.77 ; $p < 0.001$) and, to a lesser extent, for erosive gastritis (OR = 1.61 ; 95% CI : 1.24-2.09 ; $p < 0.01$). The risk for developing gastric ulcer was more pronounced in NSAID users in a subpopulation with associated morbidity or advanced age. NSAID users over 65 years of age were in addition at increased risk for developing duodenal ulcer compared to the elderly non-users (OR = 2.91 ; 95% CI : 1.52-5.59 ; $p < 0.05$).

As discussed in the introduction, however, identification of a particular group of high-risk patients that will most benefit from gastroprotective co-medication remains a problem.

Bleeding survey

GI complications and the role of NSAID

This prospective observational survey also provided information on 159 bleeding patients referred for endoscopy. In line with the previously performed case-control study by Holvoet *et al*. (18) and other corresponding reports (16,17,19), the data demonstrated that a large percentage of acute upper GI bleeding was associated with the use of NSAIDs (42%), including aspirin,

and that the presence of peptic ulcer disease played a major role. Laine's recent warning to avoid underestimation of the risk associated to even low dose of cardiopreventive aspirin should be kept in mind (4).

In more than half of bleeding patients (56%) no digestive symptoms were reported prior to bleeding. These findings are in line with Singh, who reported that even 4/5 of NSAID users with serious GI complications had no prior warning symptoms (20). The frequent absence of antecedent GI complaints, which could be related to the decreased pain perception in NSAID users, underlines the need for identifying subgroups of patients that are at particular risk for developing upper GI complications.

Profile of bleeding patients

Bleeding patients were predominantly male and generally older than the non-bleeding patients referred for endoscopy. Associated diseases, anticoagulant therapy and corticosteroid use were also more frequent in bleeding patients.

Bleeding NSAID users were significantly older than bleeding non-users and more patients were female. Anticoagulant use was also significantly higher among NSAID users, compared to non-users (20% versus 4% ; $p < 0.05$).

Comparison of endoscopic lesions in NSAID users and non-users

UGIE identified GD ulcer as the main source of bleeding and non-salicylated NSAID users were statistically significantly more prone to gastric ulcer than non-users ($p < 0.005$). NSAID non-users differed significantly from users by the higher frequency of oesophageal varices ($p < 0.05$).

Particularly in non-salicylated NSAID users with a previous history of ulcer, advanced age and in patients associating different risk factors the relative risk for gastric ulcer was increased compared to non-users. Prevention of NSAID related hemorrhagic lesions might therefore be cost-effective in these patients.

Conclusion

This survey confirms the high incidence of GD ulcers in NSAID users. Serious gastrointestinal complications in NSAID users are relatively rare but often occur without prior warning symptoms. Consequently it seems advisable to carefully evaluate the need for NSAID prescription to patients with increased risk for GI complications and to consider gastropreventive measures, particularly in elderly patients and patients with multiple risk factors.

The identification of the relative contribution of different risk factors remains a difficult issue and should be further investigated. In order to evaluate the impact of different gastroprotective strategies on the incidence of serious upper GI complications, outcome research would provide further insights.

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FICHE PATIENT n°..... OBSERVATOIRE AINS	Cachet Docteur :

Rappel : doit être inclus dans cet observatoire, tout patient ambulatoire chez qui vous soupçonnez une lésion du tractus digestif supérieur et chez qui vous pratiquez une endoscopie.

❑ Hôpital ❑ Privé ❑ Polyclinique **Date de l'endoscopie :␣␣ /␣␣ / 2000**

1. Données personnelles du patient

- Initiales : ␣␣␣␣
- Sexe : ❑ Masculin ❑ Féminin
- Age : ❑ <20 ❑ 21-25 ❑ 26-30 ❑ 31-35 ❑ 36-40 ❑ 41-45 ❑ 46-50 ❑ 51-55 ❑ 56-60 ❑ 61-65 ❑ 66-70 ❑ 71-75 ❑ 76-80 ❑ 81-85 ❑ >85 ans
- Etat de santé actuel : ❑ très mauvais ❑ mauvais ❑ moyen ❑ bon ❑ très bon

2. Profil du patient

- Antécédents d'ulcère: ❑ oui ❑ non Année: ␣␣␣␣ Etiologie: ❑ Hp ❑ AINS ❑ Autre
- Utilisation actuelle de corticoïde p.o./IV ❑ oui ❑ non Dose : .....mg/j Nbre de mois/dernière année : .....
- Utilisation actuelle d'anticoagulant ❑ oui ❑ non Dose : .....mg/j Nbre de mois/dernière année : .....
- Alcool (1 unité : 1 bière=1 verre de vin=1 whisky) ❑ oui ❑ non Nombre d'unités / semaine : .....
- Tabac ❑ oui ❑ non Nombre de cigarettes / jour : .....
- Co-morbidité ❑ oui ❑ non Laquelle .....

3. Raison de l'endoscopie

- Adressé par: ❑ GP ❑ Rhumato ❑ Ortho/Physio ❑ Chirurgien ❑ Urgence ❑ Autre .....
- Origine : ❑ Nouveau patient ❑ Contrôle : ❑ Oesophagite ❑ Ulcère ❑ Autre .....
- Symptômes : ❑ douleurs épigastriques ❑ pyrosis ❑ vomissement ❑ nausée ❑ ballonnement ❑ dysphagie ❑ douleur thoracique ❑ satiété précoce ❑ autre .....

4. Résultats de l'endoscopie

				Autres
• Oesophage:	❑ Normal	❑ Oesophagite →	❑ G1 ❑ G2 ❑ G3 ❑ G4	❑ Biopsie
• Estomac :	❑ Normal	❑ Ulcère	❑ Gastrite érosive	❑ Biopsie
• Bulbe :	❑ Normal	❑ Ulcère	❑ Bulbite	❑ Biopsie

- Recherche Status Hp : ❑ oui ❑ non
  Si oui : Status Hp : ❑ négatif ❑ positif Méthode : ❑ culture ❑ UBT ❑ Histo. ❑ autre

5. Attitude

- Traitement proposé pour les lésions digestives ❑ IPP ❑ AH2 ❑ Prokinétique ❑ Autre .....
- Hospitalisation subséquente : ❑ Oui ❑ Non
- Autres examens effectués .....

UTILISATEUR AINS ❑ OUI ❑ NON SI OUI , TOURNEZ LA PAGE! →

FICHE PATIENT n°..... OBSERVATOIRE AINS	Cachet Docteur :

6. Utilisateur AINS

- **Traitement :** ❑ Airtal® ❑ Apranax® ❑ Aspirine® ❑ Biofenac® ❑ Brexine®
  ❑ Brufen® ❑ Feldene® ❑ Indocid® ❑ Mesulid® ❑ Mobic®
  ❑ Naprosyne® ❑ Nurofen® ❑ Rofenid® ❑ Tilcotil® ❑ Voltaren®
  ❑ Autre .....

Dose: ..... mg/j

Prise quotidienne : ❑ oui ❑ non Délai dernière prise: ❑ <1 jour ❑ 1-3 jours ❑ 3-7 jours ❑ >7 jours

Protection gastrique ❑ IPP ❑ AH2 ❑ Misoprostol ❑ Autres .....

- **Indication AINS :** ❑ arthrose ❑ arthrite (rhumatoïde) ❑ pathologie abarticulaire
  ❑ prévention vasculaire ❑ autre .....
- **Plaintes digestives:** ❑ oui ❑ non

Si oui → ❑ présentes avant AINS Nbre de mois/dernière année ❑ 1-3 ❑ 4-6 ❑ 6-12
❑ apparues pendant la prise d'AINS Délai : ❑ < 48h ❑ > 48h
❑ provoquant l'arrêt récent d'AINS Délai : ❑ < 48h ❑ > 48h

Spécifiez : ❑ douleurs épigastriques ❑ pyrosis ❑ vomissement ❑ nausée
❑ ballonnement ❑ dysphagie ❑ douleur thoracique ❑ satiété précoce
❑ autre .....

Intensité des plaintes : ❑ légère ❑ modérée ❑ sévère

- **Antécédents** d'effets secondaires GI liés aux AINS : ❑ oui ❑ non

7. Attitude au niveau AINS

- ❑ Arrêter l' AINS
- ❑ Remplacer l' AINS par un analgésique
- ❑ Continuer l' AINS ❑ même dose
  ❑ dose adaptée :.....mg/jr
- ❑ Autre AINS Nom : ..... Dose : ..... mg/jr
- ❑ Association ❑ anti-acides ❑ Anti-H2 ❑ IPP ❑ Misoprostol
  ❑ Autres .....

FICHE PATIENT n°..... **OBSERVATOIRE AINS** **PARTIE HEMORRAGIE**	Cachet Docteur :

Rappel : doit être inclus dans cet observatoire hémorragie, **tout** patient qui présente une hémorragie digestive aiguë, endoscopé dans les 24h.

❑ **Hôpital** ❑ **Privé** ❑ **Polyclinique** **Date de l'endoscopie : ␣␣ / ␣␣ / 2000**

1. Données personnelles du patient

- Initiales : ␣␣␣␣
- Sexe : ❑ Masculin ❑ Féminin
- Age : ❑ <20 ❑ 21-25 ❑ 26-30 ❑ 31-35 ❑ 36-40 ❑ 41-45 ❑ 46-50 ❑ 51-55
  ❑ 56-60 ❑ 61-65 ❑ 66-70 ❑ 71-75 ❑ 76-80 ❑ 81-85 ❑ >85 ans
- Etat de santé actuel : ❑ très mauvais ❑ mauvais ❑ moyen ❑ bon ❑ très bon

2. Profil du patient

- Antécédents d'ulcère: ❑ oui ❑ non Année: ␣␣␣␣ Etiologie: ❑ Hp ❑ AINS ❑ Autre
- Utilisation actuelle de corticoïde p.o./IV ❑ oui ❑ non Dose : ..... mg/j Nbre de mois/dernière année : .....
- Utilisation actuelle d'anticoagulant ❑ oui ❑ non Dose : ..... mg/j Nbre de mois/dernière année : .....
- Alcool (Une unité : 1 bière=1 verre de vin=1 whisky) ❑ oui ❑ non Nombre d'unités / semaine : .....
- Tabac ❑ oui ❑ non Nombre de cigarettes / jour : .....
- Co-morbidité ❑ oui ❑ non Laquelle .....

3. Raison de l'endoscopie

- Adressé par: ❑ GP ❑ Rhumato ❑ Ortho/Physio ❑ Chirurgien ❑ Urgence ❑ Autre .....
- Hémorragie (haute) : ❑ cliniquement diagnostiquée
  ➥ ❑ méléna ❑ hématémèse ❑ Autre .....
  ❑ diagnostiquée en cours d'endoscopie, ex: caillot(s) (sans signe préalable d'hémorragie)

4. Résultats de l'endoscopie

					Autres
• Oesophage:	❑ Normal	❑ Oesophagite ➔	❑ G1 ❑ G2 ❑ G3 ❑ G4	.....	❑ Biopsie
		❑ Varice	❑ Mallory Weiss		
• Estomac :	❑ Normal	❑ Ulcère	❑ Gastrite érosive	.....	❑ Biopsie
• Bulbe :	❑ Normal	❑ Ulcère	❑ Bulbite	.....	❑ Biopsie
• Recherche Status Hp :		❑ oui	❑ non		
Si oui : Status Hp :		❑ négatif	❑ positif	Méthode : ❑ culture ❑ UBT ❑ Histo. ❑ autre	

- Forrest classification : ❑ Type IA: spurtin vessel ❑ Type IIA: visible vessel ❑ Type III: clean base
  ❑ Type IB: oozing bleeding ❑ Type II B : adherent clot
  ❑ Type II C : flat black base

FICHE PATIENT n°..... **OBSERVATOIRE AINS** **PARTIE HEMORRAGIE**	Cachet Docteur :

5. Score de gravité de l'hémorragie

- Instabilité hémodynamique ❑ oui ❑ non
- Taux d' hémoglobine le plus bas ❑ >12 grammes ❑ 10-12 grammes ❑ 8-10 grammes ❑ < 8 grammes
- Transfusion Nombre d'unités transfusées : .....
- Admission USI ❑ oui ❑ non

6. Traitement

- Traitement hémorragie Préciser
  - ❑ Endoscopie .....
  - ❑ Chirurgie .....
  - ❑ Médicamenteux .....
  - ❑ Embolisation .....
  - ❑ Autres .....
- Traitement proposé pour les lésions digestives

❑ IPP	Dose : ..... /jour	Forme :	❑ orale	❑ IV
❑ AH2	Dose : ..... jour	Forme :	❑ orale	❑ IV
❑ Prokinétique	Dose : ..... /jour	Forme :	❑ orale	❑ IV
❑ Misoprostol	Dose : ..... /jour	Forme :	❑ orale	❑ IV
❑ Autre				
	Dose : ..... /jour	Forme :	❑ orale	❑ IV

- Récidive hémorragique (≤ 7 jours) : ❑ oui ❑ non

  Si oui, traitement proposé : .....

  Dose : ..... /jour Forme : ❑ orale ❑ IV

UTILISATEUR AINS ❑ OUI ❑ NON SI OUI , TOURNEZ LA PAGE! ⟶

FICHE PATIENT n°..... OBSERVATOIRE AINS PARTIE HEMORRAGIE	Cachet Docteur :

7. Utilisateur AINS

- **Traitement :** ❑ Airtal® ❑ Apranax® ❑ Aspirine® ❑ Biofenac® ❑ Brexine®
  ❑ Brufen® ❑ Feldene® ❑ Indocid® ❑ Mesulid® ❑ Mobic®
  ❑ Naprosyne® ❑ Nurofen® ❑ Rofenid® ❑ Tilcotil® ❑ Voltaren®
  ❑ Autre .....

  Dose: ..... mg/j

  Prise quotidienne : ❑ oui ❑ non Délai dernière prise: ❑ <1 jour ❑ 1-3 jours ❑ 3-7 jours ❑ >7 jours

  Protection gastrique ❑ IPP ❑ AH2 ❑ Misoprostol ❑ Autres .....

- **Indication AINS :** ❑ arthrose ❑ arthrite (rhumatoïde) ❑ pathologie abarticulaire
  ❑ prévention vasculaire ❑ autre .....

- **Plaintes digestives:** ❑ oui ❑ non

  Si oui → ❑ présentes avant AINS Nbre de mois/dernière année ❑ 1-3 ❑ 4-6 ❑ 6-12
  ❑ apparues pendant la prise d'AINS Délai : ❑ < 48h ❑ > 48h
  ❑ provoquant l'arrêt récent d'AINS Délai : ❑ < 48h ❑ > 48h

  Spécifiez : ❑ douleurs épigastriques ❑ pyrosis ❑ vomissement ❑ nausée
  ❑ ballonnement ❑ dysphagie ❑ douleur thoracique ❑ satiété précoce
  ❑ autre .....

  Intensité des plaintes : ❑ légère ❑ modérée ❑ sévère

- **Antécédents** d'effets secondaires GI liés aux AINS : ❑ oui ❑ non

8. Attitude au niveau AINS

- ❑ Arrêter l' AINS
- ❑ Remplacer l' AINS par un analgésique
- ❑ Continuer l' AINS ❑ même dose
  ❑ dose adaptée :.....mg/jr
- ❑ Autre AINS Nom : ..... Dose : ..... mg/jr
- ❑ Association ❑ anti-acides ❑ Anti-H2 ❑ IPP ❑ Misoprostol
  ❑ Autres .....