Rheumatologists' Adherence to Guidelines for Misoprostol Use in Patients at High Risk for Nonsteroidal Antiinflammatory Drug Gastropathy

JOLANDA CIBERE, JOHN T. SIBLEY, and MAY HAGA

ABSTRACT. ***Objective.*** To determine the extent of evidence based practice among rheumatologists in the prevention of nonsteroidal antiinflammatory drug (NSAID) associated peptic ulcer disease and to seek ways to improve the management of high risk NSAID users.

Methods. In March 1996 all 7 rheumatologists from Saskatoon participated in a consensus conference to develop local guidelines for the prophylaxis of NSAID associated peptic ulcer disease. We performed a retrospective chart review for September/October 1995 (baseline) and for June/July 1996 (post-consensus guideline) of all patients from Saskatoon rheumatologists who were being treated with NSAID for either rheumatoid arthritis (RA) or undifferentiated inflammatory polyarthritis (IP). A prospective crossover intervention study was performed from January to April 1997 in which 2 subgroups of rheumatologists (university or private practice) had a reminder sheet of gastrointestinal (GI) bleeding risk assessment placed into the front of each patient's chart prior to each office visit. The GI bleeding risk for each patient at time of visit was later determined by chart review. The primary outcome was the proportion of adherence to guidelines for high risk NSAID users in the combined intervention group (reminder sheet) compared to the combined control group (no reminder sheet) in the prospective controlled crossover study.

Results. A total of 484 patients with RA or IP received NSAID during the 4 study periods. Of these, 82 patients (16.9%) were at high risk of GI bleed. In 1995, the proportion of high risk patients taking misoprostol was 29% for university and 33% for private practice rheumatologists. The establishment of local consensus guidelines in 1996 temporarily increased adherence to guidelines to 43%, but only for private practice rheumatologists. During the prospective study, adherence to guidelines was significantly greater in the intervention (reminder sheets) group compared to the control (no reminder sheets) group (53% vs 15%; p = 0.014).

Conclusion. The simple intervention of reminder sheets for GI bleeding risk assessment resulted in a significant increase in rheumatologists' adherence to guidelines, although a substantial number of patients remained untreated with misoprostol. This study illustrates the difficulty of incorporating new knowledge and recommendations into clinical practice. Additional strategies should be investigated to more effectively incorporate new knowledge in the practice of rheumatology. (J Rheumatol 2002;29:339–46)

Key Indexing Terms:
RHEUMATOID ARTHRITIS PEPTIC ULCER DISEASE MISOPROSTOL
GUIDELINE ADHERENCE REMINDER SYSTEM

Cyclooxygenase 2 (COX-2) selective nonsteroidal antiinflammatory drugs (NSAID) appear to be safe with respect to peptic ulcer disease (PUD)[1,2]. However, for those patients who remain dependent on conventional NSAID, NSAID associated gastropathy is a substantial health concern with significant morbidity and mortality[3-5]. In a risk assessment study for gastrointestinal (GI) bleed in rheumatoid arthritis (RA), Fries, *et al*[6] determined that the patient's age, history of NSAID GI side effects, concurrent corticosteroid use, and the presence of comorbid disease were associated with increased risk of NSAID induced GI bleed. In a subsequent study, these risk factors were incorporated into a simplified scoring system that allowed estimation of the risk of GI bleed in the next 12 months[7]. A risk of 2% or more per year was considered high.

The prevention of PUD in users of conventional NSAID has been the subject of many studies evaluating H2 receptor antagonists[8-12], sucralfate[13-15], misoprostol[14-20], and omeprazole[12,19,21,22]. Taha, *et al*[11] reported lower rates of duodenal and gastric ulcers in NSAID users treated with famotidine compared to placebo. However, most studies have shown H2

From the Arthritis Research Centre of Canada, Vancouver, British Columbia; and the Department of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

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J. Cibere, MD, FRCPC, Canadian Institutes of Health Research Clinician Scientist Fellow, Arthritis Research Centre of Canada; J.T. Sibley, MD, FRCPC, Assistant Professor, Department of Medicine; M. Haga, BA, Research Assistant, Rheumatic Diseases Unit, University of Saskatchewan.

Address reprint requests to Dr. J. Cibere, Arthritis Research Centre of Canada, 895 West 10th Avenue, Vancouver, BC, Canada V5Z 1L7. E-mail: jcibere@bc.arthritis.ca

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receptor antagonists to either confer no prophylactic benefit[8] or be protective for duodenal ulcers only[9-11]. Similarly, sucralfate has not been shown to prevent PUD in NSAID users[14,15]. In contrast, misoprostol reduces the risk of NSAID associated gastroduodenal ulcers in studies with endoscopic[14-19] as well as clinical endpoints[20]. Endoscopic studies have shown that omeprazole also prevents PUD in NSAID users[12,19,21,22]. However, at the time of this study, misoprostol was the recommended treatment of choice for the prevention of NSAID induced PUD. In addition, misoprostol is cost effective if used in elderly and high risk patients[23-25], whereas the cost effectiveness of omeprazole in the prophylaxis of PUD has not been established.

Because of the proven efficacy and the cost effectiveness of misoprostol in selective groups of patients, several authors[6,26-29], as well as the 1996 American College of Gastroenterology practice guidelines[30] have recommended the prophylactic use of misoprostol in high risk patients receiving conventional NSAID. In response to this issue, a consensus conference was held in March 1996 in Saskatoon with attendance by 5 of 7 Saskatoon rheumatologists and 2 local gastroenterologists. In 1996, there were 9 practicing rheumatologists in the province of Saskatchewan, 2 in Regina and 7 in Saskatoon. Therefore, the attending rheumatologists represented the majority of rheumatologists in the province of Saskatchewan. The Saskatoon conference led to the establishment of local practice guidelines that recommended misoprostol be used in, and only in, NSAID users who were at high risk of PUD[31]. In the Saskatoon consensus guidelines, the determination of PUD risk was based on a modified version of the Fries risk scoring system[7]. High risk was defined as a likelihood of PUD of 2% or more per year. All other patients were considered to be at low risk. The Saskatoon consensus guidelines were published[31] and mailed to all physicians in the province of Saskatchewan in 1996.

Although guidelines have been considered useful for ensuring evidence based treatment of patients, studies in many subspecialties have shown that adherence to recommended guidelines is poor[32-41]. Specific implementation strategies can enhance the adoption of guidelines into clinical practice[34,38,41]. Chart reminders are one strategy that has been shown to increase adherence to guidelines in many medical fields[42-48]. A recent metaanalysis reported that physician prompting resulted in a significant increase in the performance of all of 16 preventive care procedures[48]. However, in the rheumatology literature adherence to guidelines and interventions using chart reminders have received little attention.

We investigated the use of misoprostol in patients with RA or undifferentiated inflammatory polyarthritis (IP) taking conventional NSAID. The study was developed as a quality control project in October 1996. It was designed to evaluate retrospectively the effect of the published literature and the establishment of local consensus guidelines on the practice patterns of Saskatoon rheumatologists. In a prospective controlled crossover study, we then evaluated whether adherence to guidelines could be improved by placing a reminder sheet for GI bleed risk assessment into patients' charts prior to their office visit with the rheumatologist.

MATERIALS AND METHODS

Study population. All adult rheumatologists in the city of Saskatoon (n = 7) were invited and agreed to participate in the study. Three rheumatologists were fulltime university based and 4 were in private practice. Patients were included if they met each of the following criteria: (1) International Classification of Diseases (ICD) billing codes for RA (714.0) or IP (716.5); (2) receiving treatment with conventional NSAID; and (3) seen by one of the participating rheumatologists during one of the following time periods: September–October 1995 (n = 109), June–July 1996 (n = 116), January–February 1997 (n = 125), and March–April 1997 (n = 134). The time periods were selected such that the effect on rheumatology practice of the published literature (1995), of the establishment of local guidelines (1996), and of our study intervention (1997) could be evaluated. A patient was not included in more than one study period, and if seen more than once during a particular study period, only the latest visit would be used. Patients with RA or IP were chosen for study because they generally receive chronic NSAID therapy. Treatment with NSAID was defined as the use of any conventional (nonselective) NSAID at any dose other than cardiovascular prophylactic use of low dose aspirin. The use of billing codes allowed for identification of potential study patients through computer based records of billings. The record of billings was searched by the rheumatologists' staff for patients with ICD codes 714.0 and 716.5. A list of identified patients who were seen in the periods September–October 1995 and June–July 1996 was provided to the study investigators for chart review.

Study design. The prospective controlled crossover study was initiated in January 1997. The reminder sheet for GI bleed risk assessment form is shown in Figure 1. The reminder sheet was identical to a table in the Saskatoon consensus guidelines[31] assessing the one year risk of GI bleed. The list of patients with ICD codes 714.0 and 716.5 served for the identification of potential study subjects. When a clinic visit of a potential study patient was identified during the appropriate study period, the secretary included a reminder sheet in the front of the chart. For all patients with no prior clinic visit, a reminder sheet was also included into the chart. Reminder sheets were kept in the chart until chart review, such that we were able to verify the institution of the intervention. Study rheumatologists were invited to use the reminder sheets at their discretion. Reminder sheets were placed in the charts of the 3 university rheumatologists in January–February 1997 (prospective phase 1) and in the charts of the 4 private rheumatologists in March–April 1997 (prospective phase 2). Study rheumatologists were informed of the nature of the study, but not of the exact dates for the prospective study periods or of the crossover study design.

Charts of all patients that met the inclusion criteria were reviewed by one investigator (JC), who was not blinded to the study intervention. Extracted data included age, sex, year of disease onset, history of prior PUD, comorbid conditions, extent of disability, type and dose of NSAID, and use of prednisone, misoprostol, omeprazole, sucralfate, H2 receptor antagonists and disease modifying antirheumatic drugs (DMARD). DMARD included chloroquine, hydroxychloroquine, injectable gold, methotrexate, sulfasalazine, azathioprine, cyclophosphamide, and cyclosporine. Prior misoprostol use, side effects, and any reason for non-use of misoprostol were also recorded.

GI bleeding risk was calculated according to the Fries risk scoring system as adapted by the local consensus guidelines[31] (Figure 1): (1) 0.3 points for each 5 years above age 50, (2) 1.4 points for a prior history of PUD, (3) 1.2 points for current prednisone use, (4) 0.5 points for disability or comorbid condition. The total "points" is a measure of the risk (%) of GI bleed over the next 12 months[7]. Current prednisone use included oral corticosteroid at any dose or parenteral corticosteroids given monthly or more frequently, but excluded topical and intraarticular corticosteroids. Disability was defined as RA functional class III or IV according to the American College of

Is my patient at risk of gastrointestinal bleeding from NSAIDs?
The Fries Risk Formula
Adopted from Fries JM. NSAID gastropathy: Epidemiology. J Musculoskeletal Med 8(2):21-8, 1991.

Risk factor	Adds what risk per year?	Example	Example Risk
Age	0.3% for each 5 years over 50	75 year old man	1.5%
Past History of Ulcers	1.4% if the answer is Yes	Yes, upper gastrointestinal bleed in 1980	1.4%
Steroid Use (any dose)	1.2% if the answer is Yes	Yes, on prednisone for rheumatoid arthritis	1.2%
Disability	0.5% if some other body system is abnormal	Yes, cardiovascular disease	0.5%
TOTAL RISK IN THE NEXT 12 MONTHS			**4.6%**

Risk <1% = low risk Risk 1-2% = moderate risk Risk >2% = high risk
According to the Saskatchewan consensus guidelines, when a high risk patient is identified and NSAIDs cannot be avoided cytoprotection is appropriate.

Figure 1. Reminder sheet for the risk assessment of peptic ulcer disease complications based on the Saskatoon consensus conference[31].

Rheumatology criteria[49]. Comorbid conditions included coronary artery disease, congestive heart failure, creatinine level ≥ 200 μmol/l, concurrent use of warfarin or heparin, or any other illness felt to be clinically significant. In accordance with our local consensus guidelines, high risk for GI bleed was defined as a risk of 2% or more per year[31].

For patients at high risk of GI bleed, adherence to guidelines was present if the NSAID was stopped or the patient was already taking misoprostol or misoprostol was recommended or any reason for the non-use of misoprostol was indicated, such as pregnancy or prior side effects. This information was sought in the entire rheumatologists' chart, not just in the 2 month study period. For patients at low risk for GI bleed (< 2% per year) adherence to guidelines was present if the patient was not taking misoprostol or if cessation of misoprostol was recommended.

Outcome measures. The proportion of adherence to guidelines was calculated for each group of rheumatologists (university and private) for each of the 4 time periods. The primary outcome was the proportion of high risk NSAID users for which adherence to guidelines was present in the combined intervention group (reminder sheets) compared to the combined control group (no reminder sheets) in the prospective crossover trial. Secondary outcomes included (1) a comparison of adherence to guidelines for each time period to baseline (1995) in each group of rheumatologists; (2) the proportion of adherence to guidelines for high risk patients using alternative GI bleed risk score cutoffs of 1.0%, 1.5%, 2.5%, and 3.0%; (3) the proportion of adherence to guidelines for low risk patients; and (4) a comparison of misoprostol users with nonusers to determine which factors were associated with misoprostol use.

Statistical analysis. The proportion of adherence to guidelines in the combined intervention group (reminder sheets) was compared with that of the combined control group (no reminder sheets) using the chi-square test. Fisher's exact test or chi-square test (as appropriate) was used to compare adherence to guidelines for each time period with baseline (1995) for each group of rheumatologists both for high and low risk patients. Misoprostol users and nonusers were compared by univariate analysis using Student's t test for continuous variables and chi-square test for dichotomous variables. Because no variable approached statistical significance in the univariate analysis, multivariate analysis was not performed.

RESULTS

A total of 885 patients with RA or IP were reviewed during the 4 time periods (Figure 2). Of these, 401 patients were not taking NSAID and thus were excluded. Of the remaining 484 patients who met the inclusion criteria, 82 patients (16.9%) were at high risk of GI bleed. Overall, 29% (24/82) of high risk NSAID users received GI prophylactic treatment with misoprostol, indicating that in 71% of patients (58/82) either NSAID were not discontinued or misoprostol was neither initiated nor recommended (Figure 2). Clinical characteristics of high and low risk patients are shown in Table 1. As expected, high risk patients were significantly older ($p < 0.001$), and had more frequent prednisone use, history of PUD, and disability compared to low risk patients ($p < 0.0001$ for all), while sex was not different in the 2 groups ($p = 0.2$). The proportion of patients taking DMARD was significantly greater in the low risk group ($p = 0.02$). Use of misoprostol, sucralfate, or omeprazole was similar in the 2 groups, whereas the use of H2 receptor antagonists was significantly greater in the high risk group (22% versus 8%; $p = 0.0003$).

For the prospective crossover study, adherence to guidelines for high risk patients was 53% (9/17) for the intervention group and 15% (3/20) for the control group. This difference was statistically significant ($p = 0.014$). The proportion of adherence for high risk patients for private and university rheumatologists in each time period is shown in Figure 3. For private rheumatologists, the use of misoprostol or its recommendation in high risk patients was seen in 33% (3/9), 43% (3/7), 15% (2/13), and 60% (6/10) of patients in 1995, 1996, prospective phase 1 (no reminder sheet), and prospective phase 2 (reminder sheet), respectively. Among university rheumatologists, misoprostol use or its recommendation was found in 29% (4/14), 13% (2/15), 43% (3/7), and 14% (1/7) of patients in 1995, 1996, prospective phase 1 (reminder sheet), and prospective phase 2 (no reminder sheet), respectively. Differences in adherence to guidelines were not statistically significant for any time period compared to baseline for either group of rheumatologists. This is likely due to small patient numbers.

Underutilization of misoprostol was not related to differences in definition of what constitutes high risk for PUD. Virtually identical adherence rates were seen whether high

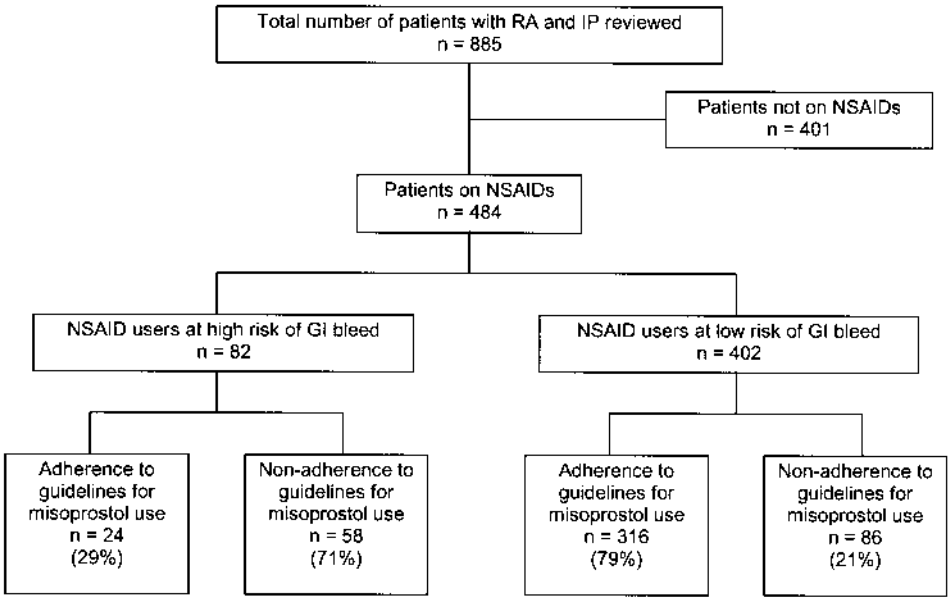

Figure 2. Procedure for inclusion of patients with RA and undifferentiated inflammatory polyarthritis (IP), their gastrointestinal (GI) bleeding risk status, and adherence to guidelines for misoprostol use in high and low risk patients.

risk was defined as greater than 1.0%, 1.5%, 2.0%, 2.5%, or 3.0% (results not shown). Similarly the use of omeprazole did not account for the underutilization of misoprostol. Two of 82 high risk patients (2.4%) were treated with omeprazole. Reanalysis of our data allowing misoprostol or omeprazole as appropriate ulcer prophylaxis did not alter our findings (results not shown). Overall adherence to guidelines for low risk NSAID users was 79% (316/402), indicating that 21% (86/402) were treated with misoprostol despite low risk of GI bleed (Figure 2). In the prospective study, overall adherence to guidelines for low risk patients was similar in the intervention and control groups (77% versus 73%; p = 0.44). For the individual time periods, the rate of adherence to guidelines for low risk patients was 87% (39/45), 75% (48/64), 68% (51/75), and 73% (59/81) for private rheumatologists in 1995, 1996, prospective phase 1 (no reminder sheets), and prospective phase 2 (reminder sheets), respectively; while for university rheumatologists adherence to guidelines ranged from 83% to 90% (Figure 4). These differences were not statistically significant, except for private rheumatologists prospective phase 1 compared to 1995 (68% versus 87%; p = 0.022).

In the univariate analysis comparing misoprostol users with nonusers, no significant differences were found between the 2 groups with respect to any of the variables assessed (Table 2). Patients at high risk for GI bleed accounted for 20.6% (22/107) of the misoprostol users and 15.9% (60/377) of misoprostol nonusers (p = 0.33). The mean GI bleed risk in the misoprostol users and nonusers was also similar at 1.08% and 0.98%, respectively (p = 0.4), as were sex, mean age, use of DMARD, and use of GI drugs other than misoprostol. Thus we were unable to identify any patient characteristics, not even GI bleeding risk, that were associated with the use of misoprostol.

DISCUSSION

Difficulties with the implementation of proven therapeutic interventions or guidelines into practice have been documented in many medical specialties[32-43]. In 2 reviews, it was concluded that the influence of guidelines depends on the strategies used for their development, dissemination, and implementation[34,38]. Internally derived guidelines and patient-specific reminders are considered superior to national guidelines and general reminders[34]. With the use of more direct interventions, such as the incorporation of specific guidelines or checklists into patients' charts or specific physician reminders, significant improvements in patient care have been reported[32,42-48].

In rheumatology practice, 2 studies on osteoporosis prophylaxis revealed that calcium supplementation was pre-

Table 1. Characteristics of patients at high and low risk for gastrointestinal bleed.

	High Risk, n = 82	Low Risk, n = 402	p
Female, %	69.5	76.4	0.2
Mean age, yrs (range)	70.8 (36.8–88.3)	52 (18.2–88.3)	< 0.001
Prednisone use, %	70.3	15.7	< 0.0001
History of PUD, %	32.9	3.0	< 0.0001
Disability, %	69.1	19.5	< 0.0001
Mean risk score (range)	2.77 (2.0–5.2)	0.64 (0.0–1.9)	< 0.001
H2 receptor antagonist use, %	22.0	8.0	0.0003
Sucralfate use, %	4.9	2.7	0.5
Omeprazole use, %	2.4	1.0	0.6
Misoprostol use, %	26.8	21.0	0.3
DMARD use, %	59.8	73.4	0.02

PUD: peptic ulcer disease, DMARD: disease modifying antirheumatic drug.

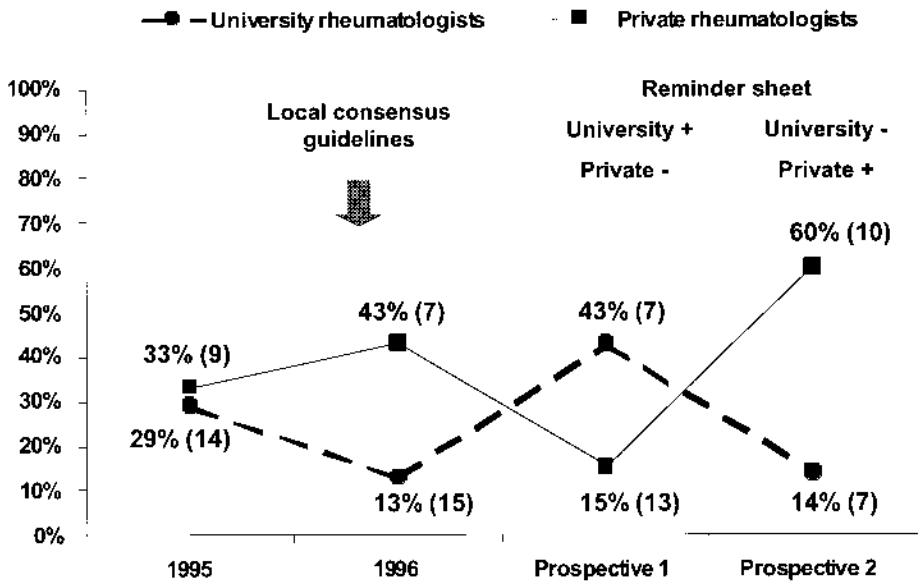

Figure 3. Adherence to guidelines for misoprostol use in high risk NSAID users by time period and type of rheumatology practice. Numbers in brackets indicate the total number of high risk patients with RA or undifferentiated IP seen during that time period.

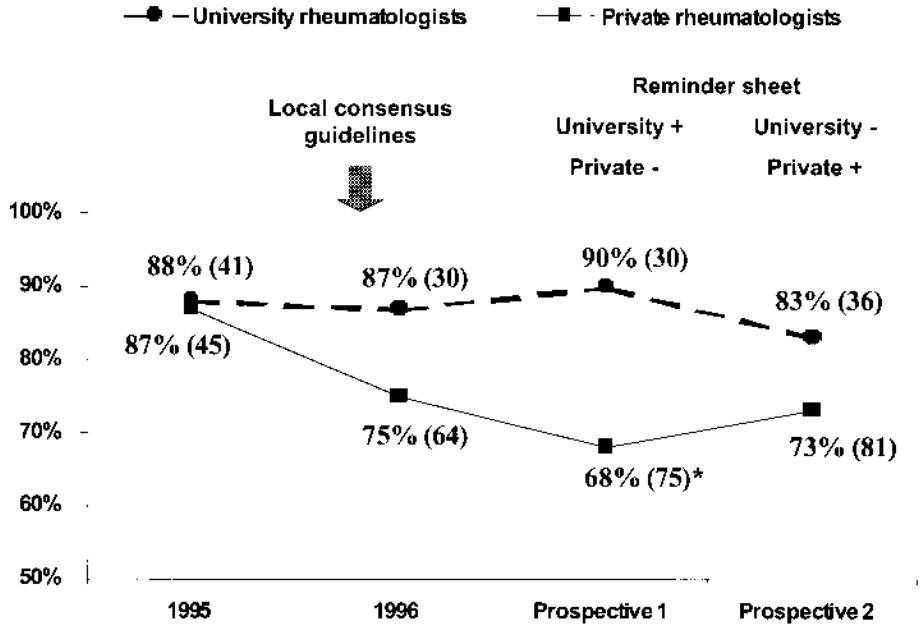

Figure 4. Adherence to guidelines for misoprostol use in low risk NSAID users by time period and type of rheumatology practice. Numbers in brackets indicate the total number of low risk patients with RA or undifferentiated IP seen during that time period. *p = 0.022 (comparison with 1995).

scribed in only 27% and 40% of patients undergoing chronic glucocorticoid therapy[39,40]. Similarly, the use of prophylactic misoprostol was found to be low in 3 recent studies[50-52]. Bakowsky, *et al*[50] reported that among patients admitted to hospital with GI complications associated with NSAID, misoprostol was used in only 8% of patients with one GI risk factor, and in 2% of those with 2 or more risk factors. In addition, they found no increase in the frequency of misoprostol use between 1990-91 and 1995-96. Studies by Hogan, *et al*[51] and Peloso, *et al*[52] have reported similarly low rates of misoprostol coprescriptions in NSAID users (3.5% and 11%, respectively).

In our study, the rate of adherence to guidelines for misoprostol use by rheumatologists was low in 1995, at a time

Table 2. Comparison of misoprostol users with nonusers.

	Misoprostol, n = 107	No Misoprostol, n = 377	p
Mean age, yrs (range)	55.9 (19.8–86.3)	55.0 (18.2–88.3)	0.60
Female, %	77.6	74.5	0.61
Current prednisone use, %	26.2	24.7	0.85
History of PUD, %	9.4	7.7	0.72
Current disability, %	29.9	27.2	0.67
High risk patient (risk score ≥ 2.0),%	20.6	15.9	0.33
Mean risk score (range)	1.08 (0–5.2)	0.98 (0–4.9)	0.40
H2 receptor antagonist use, %	9.4	10.6	0.84
Sucralfate use, %	2.8	3.2	0.91
Omeprazole use, %	1.9	1.1	0.86
Current DMARD use, %	71.0	71.1	0.91

PUD: peptic ulcer disease, DMARD: disease modifying antirheumatic drug.

when misoprostol was established in the literature as an effective preventive treatment for NSAID induced PUD[16-18,20]. Although low, the proportion of high risk NSAID users who were treated with misoprostol (29%) was higher than reported by previous studies[50-52]. This may stem from our definition of adherence to guidelines, which included not only the actual use of misoprostol, but also the mere recommendation to either start misoprostol or stop NSAID, whether the patient ultimately complied or not. The discrepancy in the rates of misoprostol use between previous studies and this study suggests that factors such as patient compliance or side effects play a role in the low rates of misoprostol use, as reported in the literature. However, because these factors were taken into account in this study, one can conclude that adherence to guidelines was present in only 29% of high risk patients, and therefore 71% of patients appeared to remain untreated.

A previous report indicated that locally developed guidelines are more effective than simple dissemination of information by journal publication[34]. In our study, we found that the development of local consensus guidelines in 1996 was followed by an improvement in the management of high risk patients by private but not university rheumatologists, although the influence was limited, in that 57% of high risk patients remained untreated and the increased adherence to guidelines was not maintained longterm.

As expected, in the 1997 prospective study, the patient-specific reminders had a more pronounced effect on both university and private rheumatologists, with statistically significant improvements in adherence to guidelines for the reminder phase. However, even with the reminder sheets present, the rate of adherence to the PUD prophylaxis guidelines was only 53% for university and private rheumatologists combined, leaving almost half the high risk patients untreated. In addition, despite the expectation of a carryover effect from the study intervention, the improvement in practice pattern did not appear to be sustained beyond the intervention period. These results may not be surprising, considering that our intervention was simple and not instituted repeatedly. Future studies will need to focus on more specific intervention strategies and determine which implementation techniques can effect permanent change in physicians' practices.

Two potential reasons for the underutilization of misoprostol in high risk NSAID users in this study are the use of other GI drugs and misclassification of patients, but neither of these factors appears to have played a significant role in our findings. Omeprazole was used infrequently in our study population (2.4%) and reanalysis of our data allowing misoprostol or omeprazole as appropriate ulcer prophylaxis did not alter our findings. H2 receptor antagonists, while useful for the treatment of GI symptoms, do not prevent NSAID associated PUD. Indeed, with the exception of famotidine, they are associated with an increased incidence of PUD complications, likely due to their ability to mask dyspepsia and other GI symptoms[7,53]. We found that H2 receptor antagonists were used more frequently in high risk compared to low risk patients (22% versus 8%; p = 0.0003), and thus their use may have detracted from the utilization of misoprostol. However, the increased use of H2 receptor antagonists in high risk patients accounted for only a small proportion of those high risk patients in whom misoprostol was not recommended. Similarly, the slightly greater use of sucralfate in high risk patients is insufficient to explain the low utilization of misoprostol in these patients.

Misclassification of patients could occur if misoprostol had been recommended but not recorded in the patient's chart. Due to the complex nature of medical management and decision making, it is possible that for some high risk patients information on the reasons for non-use of misoprostol may not have been transparent or accessible by chart review. However, our chart review did include the entire rheumatology patient chart, looking for any evidence of contraindications to misoprostol, previous side effects, or any indication that misoprostol had been recommended in the past. If any such documentation was found, the patient was then considered appropriately treated. Thus, although misclassification of some patients is possible, it seems unlikely that a large number of patients

were misclassified due to poor chart documentation. More likely, the apparent underuse of misoprostol is true and reflects the difficulty of incorporating new knowledge into practice.

In addition to underutilization of misoprostol in high risk patients, there was overuse in low risk patients. The latter may relate to patients' request for cytoprotection and as such is not a concern, other than the potential for side effects and the poor cost effectiveness associated with treatment of low risk patients[23-25]. However, overtreatment of low risk patients coincided with increased awareness for misoprostol use in high risk patients, at least for private rheumatologists. Therefore, increased awareness of misoprostol appears to have led to its increased use in a nondiscriminatory fashion. This finding was further supported by our comparison of misoprostol users with nonusers, which showed that misoprostol use did not correlate with any patient-specific factors, not even GI bleeding risk.

There are several weaknesses of this study. In a retrospective chart review, it is likely that not all medical information can be completely ascertained and hence there may have been some misclassification of patients. In addition, the investigator performing the chart review was not blinded to the intervention. However, the main data searched for in the chart review were evidence for misoprostol use and risk status for PUD, both of which were based on objective criteria defined a priori, thereby minimizing potential bias. A further weakness was the small number of patients in the individual time periods. No conclusive statements can therefore be made on whether changes in adherence to guidelines occurred compared to baseline. Contamination of intervention and control periods is a possibility. Rheumatologists became aware of the study in January 1997, which may have resulted in a change in practice. However, such a change in practice would have biased the results against finding a difference between the intervention and control groups. Therefore, this further supports the effectiveness of our simple intervention on adherence to guidelines.

In this study of misoprostol for the prophylaxis of NSAID associated PUD, we found both undertreatment of high risk and overtreatment of low risk patients. Further, we were unable to identify any patient-specific factors, including GI bleeding risk, that correlated with misoprostol use. However, we were able to demonstrate that adherence to guidelines for misoprostol use could be improved significantly by our specific intervention of incorporating a reminder sheet for GI bleeding risk into the patient's chart. Despite these improvements, the underutilization of misoprostol in this study highlights the difficulties of incorporating new knowledge into practice. If, as the literature would suggest, this problem of inadequate incorporation of recommendations into clinical practice is not just a local phenomenon, then rheumatologists are exposing many patients to misoprostol unnecessarily and yet are failing to treat many patients at high risk of NSAID associated gastropathy. The extent of this problem and possible solutions need to be evaluated further.

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