CONCISE REPORT

Helicobacter pylori does not play a part in the dyspeptic complaints of rheumatology patients receiving long term treatment with non-steroidal anti-inflammatory drugs

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Ann Rheum Dis 2002;61:641–643

Background: The presence of dyspeptic symptoms is a common finding in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs). Some studies seem to support the involvement of *Helicobacter pylori* infection in the dyspeptic symptoms reported by these patients, and suggest that eradication may be useful.

Objective: To determine the variables related to dyspepsia in rheumatology patients requiring NSAID treatment, assessing in particular the role of *Helicobacter pylori* infection.

Methods: One hundred and eighty six consecutive patients with a rheumatological disorder requiring NSAID treatment (68 male, 118 female; mean (SD) age 55 (15) years) were included in a cross sectional study; dyspeptic symptoms were measured by a previously validated scale. *Helicobacter pylori* infection was determined by serology. Variables related to the severity of symptoms and the need for antisecretory drugs were determined by multivariate analysis.

Results: No relation was found between *Helicobacter pylori* infection and dyspepsia or any of its surrogate markers (antisecretory drug use or NSAID intolerance). Female sex and treatment with antisecretory drugs were found to be independent predictors for the appearance and severity of dyspeptic symptoms. The only independent predictive variables of the requirement for antisecretory drugs were age, previous ulcer disease, taking NSAIDs with a medium or high anti-inflammatory potential, and the symptoms score.

Conclusion: *Helicobacter pylori* infection does not seem to play any part in the gastric symptoms of patients treated long term with NSAIDs.

The presence of dyspeptic symptoms is a common finding in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs). Ascertaining whether or not *Helicobacter pylori* plays a part in dyspeptic complaints of chronic NSAID users has therapeutic implications, as a positive relationship would support the case for *Helicobacter pylori* eradication in these patients.

Although some authors suggest that there is a relationship between *Helicobacter pylori* infection and dyspeptic symptoms in subjects receiving NSAIDs, the published evidence remains controversial.^{1–3} Moreover, most studies have focused only on current symptoms and do not evaluate surrogate markers for dyspepsia such as intolerance to NSAIDs or antisecretory drug requirements.

Against this background, this study aimed at evaluating the factors related to gastric complaints and antisecretory drug requirements in rheumatology patients receiving long term

NSAID treatment. We placed particular emphasis on the role of *Helicobacter pylori* infection.

PATIENTS AND METHODS

One hundred and eighty six consecutive patients who attended our outpatient rheumatology clinic were included in a cross sectional study. All of them had a clinical indication for NSAID treatment. Sixty eight were male and 118 female with a mean (SD) age of 54.9 (15) years; 77 (41%) patients had rheumatoid arthritis, 66 (35%) spondyloarthropathies, 24 (13%) connective tissue diseases, and the remaining 19 (10%) other chronic rheumatic diseases.

Dyspeptic symptoms were measured by a previously validated scale⁴ designed using earlier Likert-type scales.⁵ The scale grades symptoms and scores from 0 to 11, and evaluates five dyspeptic symptoms: abdominal pain, abdominal bloating, heartburn, nausea, and vomiting. These scales have been used in previous studies to ascertain dyspeptic symptoms in NSAID users.¹

Helicobacter pylori infection was determined with a commercial enzyme linked immunosorbent assay (ELISA) kit (*H pylori* IgG, Wampole laboratories, Cranbury, NJ).

The anti-inflammatory potential of NSAID treatment was assessed as high, medium, or low according to the family and the dose of the NSAID by one of the authors (JG) who was unaware of the symptoms score or the concomitant treatment of the patients.

Statistical methods

Univariate analysis was performed in two ways. Firstly, mean values of heartburn, nausea, vomiting, bloating, and total symptoms score were compared using Student's *t* test with the patients split into two groups according to sex, *Helicobacter pylori* status, concomitant use of steroids or immunosuppressive drugs, and the additional variables evaluated. Comparison of more than two means was performed by analysis of variance. Finally, a stepwise linear regression analysis was performed using the total score of symptoms as a dependent variable to determine which variables were related to the appearance and severity of dyspeptic symptoms.

The variables related to the use of antisecretory drugs were also determined in a univariate analysis using the χ^2 test and Student's *t* test. Multivariate analysis was performed by stepwise logistic regression analysis for variables predicting the use of antisecretory drugs. Values are given as mean (SD). The Hosmer-Lemeshow test was used to evaluate the goodness of fit of the logistic regression analysis. Conventional software (SPSS 10.0 for Windows) was used for the analysis.

RESULTS

Use of NSAIDs, gastroprotective drugs, steroids, and immunosuppressive drugs

Twenty patients were currently not receiving NSAIDs, in most cases owing to digestive intolerance. These patients were

Figure 1 Percentage of patients with dyspeptic symptoms, according to *Helicobacter pylori* (Hp) status.

Figure 2 Mean scores of patients reporting dyspeptic symptoms according to *Helicobacter pylori* (Hp) status.

excluded from further analysis; the age and sex distribution, *Helicobacter pylori* seroprevalence, use of steroids, gastroprotective or immunosuppressive drugs, or the type of underlying rheumatological disease of these patients did not differ from those of the main group.

Of the remaining 166 patients, 64 (39%) were taking an NSAID that was considered highly powerful, 45 (27%) were taking medium power combinations, and 57 (34%) were receiving a low risk NSAID. No patients were taking selective Cox-2 inhibitors. Nineteen patients (11%) were taking aspirin in addition to the NSAID. Concomitant steroid treatment was given in 74 (45%) patients, and second line drugs treatment in 32 (19%).

Eighty five patients (51%) were taking gastroprotective agents—16 (10%) proton pump inhibitors, 52 (31%) H_2 blockers, and 17 (10%) misoprostol. Additionally, 47 (28%) used antacids, seven (4%) of them every day.

***Helicobacter pylori* seropositivity**

Of 166 patients, 124 (75%) had a positive *Helicobacter pylori* serology. No patients had received eradication treatment before the beginning of the study.

Type and severity of dyspeptic symptoms

Eighty three patients (50%) reported some degree of dyspeptic symptoms. Figure 1 shows the prevalence of different symptoms and fig 2 the mean scores of symptomatic patients.

Factors predicting symptoms appearance

Univariate analysis showed that nausea, vomiting, heartburn, bloating, abdominal pain, and the combination of the mean scores of all symptoms were higher in women than in men, and higher in patients taking antisecretory drugs than in those not receiving those drugs. No differences in symptoms scores were found between *Helicobacter pylori* positive and negative patients (mean symptoms score 2.8 (5.2) v 3.3 (4.9), $p=0.47$), between patients requiring additional steroids, immunosuppressive drugs or aspirin and those who did not, between those with or without a history of peptic ulcer, or between those receiving low v medium or high risk NSAID treatment. Nor were any differences found in relation to the baseline disease or to age. The linear regression analysis was performed using the total symptoms score as a dependent variable and included age, sex, *Helicobacter pylori* status, and

Table 1 Results of linear regression analysis: independent factors predicting high total dyspepsia symptoms score

Variables	OR	95% Confidence interval	p Value
(Constant)	-0.215	-2.698 to 2.267	0.864
Use of antisecretory drugs	1.723	0.316 to 3.130	0.017
Female sex	1.441	0.015 to 2.867	0.048

need for antisecretory drugs. Only female sex and current treatment with antisecretory drugs were selected as independent predictive variables (table 1).

Factors predicting the need for antisecretory treatment

In the univariate analysis many factors were significantly related to the requirements for antisecretory treatment: the use of concomitant steroid or immunosuppressive treatment, history of previous ulcer, the presence of dyspeptic symptoms, administration of medium or high risk NSAID treatment, and age. *Helicobacter pylori* status was not a predictor of the need for antisecretory drugs in the univariate analysis. Forty one per cent of *Helicobacter pylori* positive patients received antisecretory treatment compared with 38% of *Helicobacter pylori* negative patients ($p=0.71$). All the significant variables together with the *Helicobacter pylori* status were introduced in a stepwise logistic regression analysis to determine independent predictors of the need for antisecretory treatment. Age, use of medium or high risk NSAID treatment, overall symptoms score, and history of previous ulcer were selected as independent predictors of the need for antisecretory drugs.

DISCUSSION

The relation between dyspeptic symptoms and *Helicobacter pylori* in chronic NSAID users remains controversial. Early studies suggested an association,^{1-6,8} although later reports found no such relationship.⁹⁻¹³ Dealing with dyspeptic symptoms in NSAID users is a difficult task; indeed, in a population of chronically ill patients with multiple organic complaints who receive multiple treatments and carry the psychological burden of chronic disease, it is virtually impossible to ascertain which dyspeptic symptoms are NSAID related. Additional difficulties arise from the use of antisecretory drugs. Antisecretory drugs may be prescribed for dyspepsia and therefore be a surrogate marker for dyspeptic symptoms. In contrast, their use as ulcer prophylaxis could mask such symptoms. In addition, patients who do not tolerate NSAIDs because of severe dyspepsia are usually not included in studies because they are not receiving NSAIDs at the moment of the recruitment.

We found no differences between patients who did not tolerate NSAIDs and the others. In particular, no role was found for *Helicobacter pylori* in NSAID intolerance, as the prevalence of infection was equal in the two groups. However, as the number of patients in this group is small, the power to rule out an association is limited.

The analysis of factors related to dyspeptic symptoms showed that dyspepsia in NSAID users was more common in women, as is the case in the general population. The finding that receiving antisecretory drugs is an independent predictor for dyspeptic symptoms is especially interesting. It means that a substantial proportion of patients with dyspepsia remain highly symptomatic despite the antisecretory treatment. This suggests that a significant percentage of dyspeptic symptoms in NSAID users are not acid related because symptoms remain despite the use of H_2 blockers or proton pump inhibitors. In addition, the study fails to demonstrate any role for *Helicobacter pylori* infection. All these facts suggests that the

behaviour of dyspepsia may be similar in NSAID users and in the general population.

Helicobacter pylori status does not seem to play any part in the prescription of antisecretory drugs. In this case the majority of the predicting factors—age, history of previous ulcer, and power of the NSAID schedule—seem related to the use of antisecretory drugs for peptic ulcer prophylaxis, more than to its use for the treatment of dyspepsia.

The results of this paper strongly suggest that patients with *Helicobacter pylori* infection do not have a greater incidence of non-ulcer NSAID related dyspeptic symptoms than uninfected patients.¹⁴ Whether *Helicobacter pylori* should be eradicated to prevent ulcers and ulcer complications in chronic NSAID users remains controversial.^{2,3} However, what seems clear from the results of this paper is that *Helicobacter pylori* eradication should not be indicated for treating dyspepsia in NSAID users.

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Accepted 18 December 2001

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