## SCIENTIFIC PAPERS

# Psychological profiles of patients with upper gastrointestinal symptomatology induced by non-steroidal anti-inflammatory drugs

Angela Juby, Paul Davis

#### Abstract

Eighty three patients with classical or definite rheumatoid arthritis taking non-steroidal antiinflammatory drugs (NSAIDs) were studied in an attempt to determine whether a patient's personality and psychological profile might contribute to the development of NSAID induced gastrointestinal symptomatology. It was found that the personality profile of the group of 45 asymptomatic patients was similar to that of a previously reported control group. In contrast, the 37 patients with gastrointestinal symptoms attributed to NSAIDs had a significantly higher mean score for free floating anxiety, depression, and somatisation than controls, suggesting that a patient's personality may influence the development of NSAID induced gastric symptoms.

Upper gastrointestinal symptomatology induced by non-steroidal anti-inflammatory drugs (NSAIDs) is a common clinical problem, though its exact prevalence and cause are unknown. Clinical trials and post-marketing surveillance have reported the prevalence of gastrointestinal adverse symptoms to be between 8 and 34%. In addition, endoscopic studies have shown a prevalence of between 8 and 18% for gastric ulcers and 0 to 16% for duodenal ulcers in patients ingesting NSAIDs.<sup>2</sup> Any explanation for the apparent discrepancy between the prevalence of patients' symptoms and endoscopic findings must also take into account the observation that many patients with gastrointestinal symptoms have no demonstrable gastrointestinal abnormality and, conversely, those patients presenting with gastrointestinal ulcers or haemorrhage attributed to NSAIDs may be asymptomatic.<sup>3-5</sup>

The pathogenesis of NSAID induced gastric symptomatology is likely to be multifactorial as supported by the determination of a number of risk factors in a large group of patients with rheumatic diseases. In patients who are not taking NSAIDs both non-ulcer dyspepsia and that due to chronic peptic ulcer have been associated with specific patient personality and psychological profiles. In these and other studies patients have been found consistently to show significantly greater anxiety, depression, and neuroticism than control populations. Our study was undertaken to determine whether

these same psychological profiles might be yet another relevant factor in NSAID induced gastrointestinal symptomatology.

#### Patients and methods

Eighty three unselected patients (58 female, 25 male), with a mean age of 51 years (range 16-78), attending the rheumatic disease unit of the department of medicine at the University of Alberta were invited to participate in this study by completing two questionnaires. All patients had classical or definite rheumatoid arthritis of at least one year's duration. All patients were receiving a stable therapeutic dose of at least one NSAID. Each patient completed the two questionnaires anonymously.

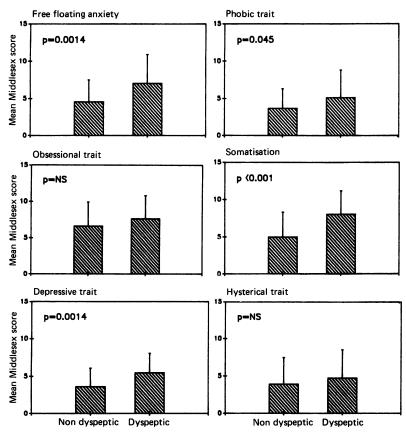
Questionnaire 1 consisted of nine questions about the frequency and severity of gastrointestinal symptoms attributed to either current or previous exposure to NSAIDs. Anwsers were given a score from 0 to 3, where 0=no symptoms; 1=mild symptoms, do not interfere with daily activities or sleep; 2=moderate symptoms, may interfere with daily activities or sleep; 3=severe symptoms, daily routine not possible or sleep interrupted regularly. A response of 2 or greater to any two of the nine questions was used to separate the patients into two groups consisting of 38 patients with dyspeptic symptoms attributable to NSAIDs and 45 patients without significant dyspeptic symptoms. Patients in the dyspeptic group did not differ significantly from the non-dyspeptic group in age (49 v 53 years), duration of disease  $(4.3 \ v \ 5.2 \ years)$ , or severity as assessed by the need for treatment (68% v 65%) and erythrocyte sedimentation rate (29 v 36 mm/h). The proportions of patients in anatomical stages II and III were the same in each group.

Questionnaire 2, the Middlesex Hospital questionnaire,  $^9$  consisted of 48 random questions to test six groups of symptoms and traits: free floating anxiety, phobic anxiety, obsessive compulsive traits and symptoms, somatic symptoms, depressive symptoms, and hysteria: Individual answers were scored on a 0 to 2 scale and a score calculated for each subset of questions (maximum score 16). The mean score for each subset of questions for the patients in the NSAID/dyspeptic group was compared with the mean score for the non-dyspeptic group, and statistically analysed by an unpaired Student's t test.

Department of Rheumatology, University of Alberta, Edmonton, Alberta A Juby P Davis

Correspondence to: Dr P Davis, 562 Heritage Medical Research Centre, University of Alberta, Edmonton, Alberta T6G 2S2, Canada.

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Comparison of mean personality trait scores in dyspeptic and asymptomatic patients receiving non-steroidal anti-inflammatory drugs.

#### Results

Thirty eight patients with dyspeptic symptoms attributed to NSAIDs formed one group on the basis of their response to the gastrointestinal questionnaire. The ratio of women:men in the dyspeptic group was higher than in the non-dyspeptic group (3:1 v 1·9:1). The mean age was similar in the two groups (49 v 53 years), however, as was the age range. The proportion of elderly women (age >60 years) in the two groups was also similar (about 17%).

The mean score in the dyspeptic group for the six groups of questions was compared with that of the other 45 patients (figure). No significant difference between the two groups was noted in their response to the questions relating to obsessive-compulsive traits and symptoms and hysteria. Responses to questions relating to phobic anxiety showed a small significant difference between the two groups (p=0.045). In contrast, patients with dyspeptic symptoms attributed to their NSAID ingestion had significantly higher mean scores for free floating anxiety (p=0.0014), somatis-(p<0.001), and depressive symptoms (p=0.0014) than the non-dyspeptic patients. The mean scores for the six personality profiles in the non-dyspeptic patients were similar to results in normal controls, as previously published.

### **Discussion**

One of the most controversial aspects in rheumatology is the relation between NSAID ingestion and upper gastrointestinal tract symp-

tomatology. 10 Despite the fact that up to 30% of patients ingesting NSAIDs develop gastrointestinal symptoms, most have only minor gastrointestinal lesions or none at all on endoscopy. Up to 5% of patients without symptoms, however, will have endoscopically proved gastric or duodenal ulcers with a significant risk of gastrointestinal haemorrhage or perforation. Many risk factors have been identified as potential variables in the pathogenesis of NSAID related gastrointestinal symptomatology. In rheumatic diseases these may include age, sex, previous history of peptic ulcer disease, steroid use, and previous side effects attributed to NSAIDs, in addition to environmental factors such as smoking and excessive alcohol ingestion.6

This study was undertaken to determine whether a patient's personality and psychological profile might be yet another factor which contributed to the development of NSAID induced gastric symptomatology. We showed that the personality profile of a group a 45 asymptomatic patients was not significantly different from that previously reported in a control group using the Middlesex Hospital questionnaire. In contrast, 37 patients with gastric symptomatology attributed to NSAID ingestion showed a statistically significant higher mean score for free floating anxiety, depression, and somatisation than the nondyspeptic group. These results suggest that a patient's personality profile may influence the development of NSAID induced 'gastric symptoms'. This has not previously been noted in this clinical setting, though similar results have shown that certain personality characteristics may influence the development of symptoms in non-ulcer dyspepsia and in patients with chronic peptic ulcer disease.<sup>7 8</sup> The patients with dyspeptic symptoms were similar to the non-dyspeptic group in age, duration and severity of disease, and drugs taken, suggesting that these factors were not relevant to the difference in personality profiles noted. There were, however, a higher proportion of women in the dyspeptic group, though the number of elderly women was similar, a subset previously identified as being at particular risk of NSAID induced gastrointestinal haemorrhage.

Our observations may in part explain the relatively high prevalence of gastric symptomatology in placebo treated patients enrolled in clinical trials of NSAIDs and the previously noted discrepancy between patients' symptoms and endoscopic gastrointestinal lesions.

As this study was retrospective we cannot entirely rule out the possibility that differences between patient groups represent differences in state of mind as a result of dyspepsia rather than different personality traits. Clearly the observations of this pilot study require further clarification with prospective study of patients before NSAID treatment and with endoscopic evaluation. This study however, does emphasise further the need for careful clinical evaluation of patients for potential risk factors, including personality and psychological profile, when assessing NSAID related gastrointestinal

symptomatology. It also supports the use of conservative management before resorting to extensive investigative procedures, including endoscopy.10

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