Increased Prevalence of Sicca Complex and Fibromyalgia in Patients With Irritable Bowel Syndrome

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OBJECTIVE: As many as 70% of patients with fibromyalgia complain of the symptoms of irritable bowel syndrome (IBS), but there is a clinical impression that IBS patients do not suffer from fibromyalgia as frequently. The sicca complex (dry eyes and mouth) is also commonly observed in fibromyalgia, but its prevalence in IBS has not been evaluated. Our objective was to assess the frequency of fibromyalgia and sicca complex in secondary care patients with IBS.

METHODS: Forty-six secondary care patients with IBS and 46 healthy controls were assessed by a rheumatologist for the presence of fibromyalgia and objective evidence of sicca complex (Schirmer and Rose-Bengal tests). Psychological status was also assessed (HAD questionnaire).

RESULTS: Thirteen (28%) IBS patients suffered from fibromyalgia, compared with five (11%) controls, a difference of 17% (95% confidence intervals [CI], 2–33%). Fifteen (33%) IBS patients *versus* three (6%) controls had sicca complex, a difference of 27% (95% CI, 11–45%).

CONCLUSIONS: These results suggest that the prevalence of fibromyalgia in IBS is approximately half that of IBS in fibromyalgia. Furthermore, sicca complex seems to be another complaint that should be added to the list of extracolonic manifestations of IBS. Study of the overlap between functional disorders presenting to different specialties may give new insights into the pathophysiology of these puzzling conditions. (Am J Gastroenterol 1999;94:1898–1901. © 1999 by Am. Coll. of Gastroenterology)

INTRODUCTION

Many different medical specialties see patients with syndromes that are often referred to as functional in nature and for which an immediate cause is not apparent. These conditions are often more common in women, associated with multiple symptoms, and sometimes have an increased prevalence of psychopathology such as anxiety and depression. The overlap between these conditions is often not well studied because of the current trends towards specialization in medicine. Fibromyalgia (FM), irritable bowel syndrome (IBS), and some forms of Sjogren's syndrome are examples of these conditions.

Fibromyalgia is a syndrome of chronic widespread, unexplained musculoskeletal pain associated with multiple tender spots (1). Estimates of prevalence vary between 2% in the general population and 20% of hospital patients (2), although a more realistic estimate is that of Wolfe *et al.*, suggesting that 5.8% of women aged 40–80 yr in the general population are affected (3). Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by recurrent abdominal pain or discomfort associated with altered stool frequency or form, altered stool passage, passage of mucus, and abdominal distension (4). Estimates of prevalence in the general population vary widely according to the population studied (5). However, in the U.K. it is probably in the order of 22%, although only one-third of sufferers seek medical advice (6). Sjogren's syndrome is a triad of dry eyes (keratoconjunctivitis sicca), dry mouth (xerostomia), and a connective tissue disease, usually rheumatoid arthritis (7, 8). The presence of the first two symptoms, in the absence of aberrant immune function, is often referred to as the sicca complex (SC) and appears to behave somewhat differently from classic Sjogren's syndrome (9). There have been two recent evaluations of the prevalence of SC in the general population, with one reporting a figure of 6% (10) and another, confined to elderly women, giving a value of 2% (11).

It is well recognized in rheumatological circles that the symptoms of IBS are commonly seen in FM patients, with a number of studies suggesting a figure of between 50–70% (12–14) However, the converse, *i.e.*, the prevalence of FM in IBS, has not been as well studied, although a figure of 65% has been suggested by Veale *et al.* (14). It should be noted that Veale's paper did use rather small numbers and older classification systems.

Sicca symptoms are well recognized in patients with FM (13) but, to our knowledge, an association of SC with IBS has not been previously investigated. The aim of the current study was to compare the prevalence of FM and SC in IBS

Table 1. Comparison of Prevalence of Fibromyalgia Sicca Complex (SC), and Other Symptoms in Patients With Irritable Bowel Syndrome (IBS) and Controls

	IBS (n = 46)	Controls (n = 46)	χ^2 (1 Degree of Freedom)	p Value
Fibromyalgia				
CWP and ≥11/18 tender points	13 (28%)	5 (11%)	3.384	0.06
SC				
Xerophthalmia	25 (54%)	4 (9%)	20.142	<0.001*
Xerostomia	25 (54%)	4 (9%)	20.142	<0.001*
Abnormal Schirmer test	15 (33%)	3 (7%)	8.357	0.004*
Abnormal Rose-Bengal staining	15 (33%)	3 (7%)	8.357	0.004*
Other symptoms				
Poor sleep	16 (35%)	14 (30%)	0.049	0.82
Easy fatiguability	42 (91%)	11 (24%)	40.058	<0.001*
Morning stiffness	31 (67%)	5 (11%)	28.522	<0.001*
Paraesthesiae	30 (65%)	5 (11%)	26.562	<0.001*
Headaches	29 (63%)	14 (30%)	8.558	0.003*

CWP = chronic widespread pain.

patients with those of a control group using the latest classification criteria.

MATERIALS AND METHODS

Patients

Forty-six secondary care patients (general practitioner referrals) with IBS (38 women; average age, 44 yr; range, 20–70 yr) attending a specialist gastrointestinal clinic were recruited. Tertiary care patients were specifically excluded, as these subjects are often poorly representative of the IBS population as a whole. Consecutive new and follow-up patients were studied after the exclusion of those taking medications with anticholinergic activity. All patients had symptomatic IBS and satisfied the Rome criteria (4). Forty-six age- and gender-matched controls, with no prior history of gastrointestinal or rheumatological complaints, were recruited from a random selection of all categories of hospital staff. For the diagnosis of FM, the American College of Rheumatology (ACR) classification criteria (1) were used, and for the diagnosis of SC, positive reporting of ocular and oral symptoms associated with objective evidence of reduced tear production was used.

A questionnaire was administered to patients with IBS and to the control group to compare a variety of symptoms associated with both SC and FM. Hospital anxiety and depression (HAD) questionnaires were also administered to all patients (15).

The study was approved by the South Manchester University Hospitals Ethics Committee.

Examination

All patients underwent a detailed clinical examination by an experienced rheumatologist blinded to whether the person had IBS or not. Formal tender point scoring was also performed. Schirmer test for tear production and Rose-Bengal testing for keratoconjunctivitis sicca was performed in all patients, as these are considered the most reliable tests for eye involvement in Sjogren's syndrome (16–18). In addition, blood was taken for antibody to extractable nuclear antigen, specifically to Ro and La, as these are most commonly present in primary Sjogren's syndrome patients (8, 16, 17, 19).

Statistics

Patients and controls were compared using a χ^2 test with 1 degree of freedom. Yates' continuity correction was used and a p value of <0.05 was regarded as significant. Ninety-five percent confidence intervals (CI) were calculated using a Confidence Interval Analysis package.

RESULTS

Fibromyalgia

Thirteen of the 46 patients (28%) with IBS and five of 46 control subjects (11%) had chronic widespread pain (CWP, defined as pain affecting contralateral body segments for >3 months) associated with a tender point score of ≥11/18 (Table 1) (p = 0.06). These patients satisfied ACR criteria for FM (1). The IBS patients were more likely to have features of fibromyalgia syndrome, with a prevalence of 17% higher than the controls (95% CI, 2–33%). The CI quoted would lead to a p value of 0.036 (because they were calculated using a normal approximation). However, for these data, it is more appropriate to use a Yates' continuity correction, which results in a more conservative p value of 0.06.

Hospital anxiety and depression scores were higher in IBS patients with FM than in IBS patients without FM and control patients. Combined anxiety and depression scores of >18 were found in 85% of IBS patients with FM, 25% of IBS patients without FM, and in 13% of control patients.

Sicca Complex

Symptoms of dry eyes and dry mouth were more common in the IBS patient group (25/46; 54%) than in the controls (4/46; 9%) ($p < 0.001$) (Table 1), a difference of 45% (95% CI, 29–62%). Thirty-three percent (15/46) of patients compared with 7% (3/46) of controls had an abnormal Schirmer test ($p = 0.004$), a difference of 26% (95% CI, 11–41%). Rose-Bengal staining was positive in all patients with an abnormal Schirmer test and only one of them had antibody to Ro (SSA) and La (SSB), which is what would be expected in the general population.

DISCUSSION

The results of this study indicate that, compared with healthy controls, patients with IBS have a significantly higher prevalence of SC (6% *vs* 33%, $p = 0.004$) and a weaker association with FM (11% *vs* 28%, $p = 0.06$). Although this latter association is of borderline significance, the IBS patients were more than twice as likely to have FM than controls. It is important to emphasize that this study was undertaken in secondary care patients and the prevalence of these syndromes in the primary care setting may be different. However, patients attending hospital are, by definition, harder to treat and so the complexities of these patients need to be fully appreciated.

There is now mounting evidence that there are two forms of sicca syndrome, the first conforming to classic Sjogren's syndrome and associated with immunological abnormalities and the second without an immune component (9, 19). The latter has been called seronegative Sjogren's syndrome (9) but is probably more appropriately labelled sicca complex (SC). Patients with SC appear to have other features, including chronic fatigue, pelvic pain, dyspareunia, headaches, parasthesiae, irritable bladder, nonulcer dyspepsia, anxiety, and depression (17, 20), which are also well known to be associated with FM (21) and IBS (22). Whether this reflects a common etiological component or not remains to be determined.

There is currently considerable interest in the possibility of disordered perception in IBS patients, with as many as 70% of subjects demonstrating visceral hypersensitivity as reflected by lowered thresholds to balloon distension of the rectum (23). It has previously been established that IBS patients suffer from bladder symptoms and disordered visceral sensing has been suggested as a cause for this feature (24, 25). If IBS and FM are associated, then it is possible to speculate that some disorder of perception may also contribute to the symptoms of FM, possibly accounting for the presence of widespread tender points.

Sicca complex appears to be unequivocally associated with IBS ($p = 0.004$), with control values being remarkably close to those previously reported (10). The observation that the Schirmer and Rose-Bengal tests are positive indicates that tear production is objectively reduced, rather than the findings all being related to a perceptual abnormality. The mechanism by which tear production could be affected is unclear but a neuroendocrine cause is a possibility, particularly as disturbances of this system are currently very topical in both FM (26) and IBS (27).

Patients attending hospital with IBS exhibit an increased prevalence of psychopathology, which is on the order of 50–60% (28). In light of this finding, the distribution of abnormal HAD scores in IBS patients with and without FM is noteworthy. It appears that the coexistence of IBS and FM is associated with a strikingly high prevalence of psychopathology (85%), whereas patients with IBS alone are not affected as frequently (25%). There are a number of possible explanations for this observation ranging from a psychological, either cause or effect, to a more fundamental abnormality of the neuroendocrine system. Whatever the reason for this observation, it is clearly of considerable importance from the point of view of treatment. It could be that the earlier use of psychotropic agents in such patients might be justified.

It has been suggested that there is a spectrum of related and overlapping syndromes that share many features and probably a common pathophysiology; the name Dysfunctional Spectrum Syndrome has been proposed (29). FM and IBS, as well as chronic fatigue syndrome, migraine, primary dysmenorrhea, and possibly SC may be examples of such a disorder. A central disturbance of the neuroendocrine/immune system may explain the overlap between these conditions (26).

So-called functional disorders are frequently encountered in most medical specialties, leading to unexplained symptoms in the system of interest. To date, these conditions have tended to be considered in isolation and the potential for overlap has been largely ignored. The results of this study emphasize the importance of this concept of overlap not only from a clinical standpoint but also from the point of view of a better understanding of their pathophysiology.

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