Increased Frequency of Gastrointestinal Symptoms in Patients with Fibromyalgia and Associated Factors: A Comparative Study

ÖMER NURI PAMUK, HASAN ÜMIT, and ORBAY HARMANDAR

ABSTRACT. ***Objective.*** To determine the frequency and severity of gastrointestinal (GI) symptoms in patients with fibromyalgia (FM).

Methods. We included 152 women with FM (mean age 45.4 ± 12.2 yrs), 98 women with rheumatoid arthritis (RA; mean age 45.5 ± 12.3 yrs), and 60 healthy female controls (mean age 44 ± 11.3 yrs). All patients were questioned about the severity of their chronic widespread pain, symptoms of FM, symptoms of dyspepsia, using a visual analog scale (VAS), and anxiety-depression scale. Patients were asked self-reported (yes/no), symptom-based (≥ 2 criteria) constipation and severity of constipation questions, and about the severity of quality of life (QOL) disturbance secondary to dyspepsia and constipation.

Results. Patients with FM had higher symptom severities for belching, reflux, bloating, sour taste, and vomiting than patients with RA and controls (all p values < 0.01). Patients with FM had significantly more dyspepsia-related QOL disturbances than the other 2 groups ($p < 0.01$). FM and RA patients had more frequent self-reported constipation than controls (respectively, 42.1%, 48%, 21.7%; $p < 0.01$). The frequency of symptom-based constipation was significantly higher in the RA group (49%) than in FM (29.6%) and control groups (23.3%) ($p < 0.01$). Constipation-related QOL disturbance was significantly higher in patients with FM than in controls ($p < 0.01$).

Conclusion. In patients with FM, the severity scores of dyspepsia symptoms, constipation, and dyspepsia-related QOL disturbance were higher than in patients with RA and controls. The higher GI symptom severity in patients with FM might have negative effects on their QOL. (First Release July 1 2009; J Rheumatol 2009;36:1720–4; doi:10.3899/jrheum.090024)

Key Indexing Terms:
FIBROMYALGIA RHEUMATOID ARTHRITIS DYSPEPSIA
CONSTIPATION QUALITY OF LIFE

Fibromyalgia (FM) is a chronic pain syndrome and its main symptom is steadily fluctuating musculoskeletal pain. Psychiatric studies indicated that it was related to an anxiety disorder in a significant subgroup of patients and psychometric studies found an association between FM and chronic distress, anxiety, and depression[1-4]. Nevertheless, all patients with FM do not have those psychological features[5].

Functional dyspepsia (FD) is a relatively common functional illness and patients have dyspeptic symptoms, but no underlying physical or biochemical causes[6,7]. Similar to FM, FD is also associated with altered autonomic function, chronic distress, and anxiety[8,9]. Some recent psychiatric studies found a close relationship between FD and depressive disorders[1,10]. According to population-based surveys[11,12], functional gastrointestinal (GI) disorders are one of the most common problems in clinical practice, and their prevalence ranges from 12% to 25%. FM and FD are both somatic conditions, and both cannot be fully explained by objective medical findings.

Constipation is a common bowel disturbance with a social aspect. It is a combination of variable symptoms and some are classified as clinical entities, like the irritable bowel syndrome (IBS)[1,2]. Many studies reported an association between FM and IBS[13-15]. In particular, a different prevalence of bowel dysfunction in FM and the association of FM with particular patterns of the bowel disorder have been reported[13-15].

We determined the frequency and severity of FD symptoms and their effect on quality of life (QOL) in FM and rheumatoid arthritis (RA) patients. In addition, we evaluated the relationship between symptoms of FM and GI symptoms.

MATERIALS AND METHODS

One hundred fifty-two consecutive patients with FM who were admitted to the Rheumatology Outpatient Clinic of Trakya University Medical Faculty

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between January 2005 and December 2006 were included in our study. All patients were diagnosed with FM according to American College of Rheumatology (ACR) 1990 criteria[16]. The control group included 98 consecutive patients with RA who attended our clinic during the same period and 60 healthy volunteers matched for age. Patients with RA were diagnosed according to ACR 1987 criteria[17]. As FM is most prevalent in women and as it has been reported that content analysis scores from female subjects might allow a more correct prediction of psychological state than scores from men, we included only female subjects in our study[18]. Patients with a connective tissue disorder and patients who had psychiatric treatment within the last 6 months were not included in the FM group. Patients with history of abdominal surgery and chronic liver disease were excluded. The study protocol was in accord with the guidelines of our ethical committee. All patients were told the study design and all gave verbal consent to participate.

The sociodemographic features and clinical findings of the patients were recorded. They all underwent examination. They were questioned about their education level, history of psychiatric disorder, lifestyle habits (smoking and alcohol intake), their medication including nonsteroidal anti-inflammatory drugs (NSAID), proton-pump inhibitors (PPI), constipation medications, and marital status. The patients were questioned about the severity of chronic widespread pain (CWP), fatigue (0–100), sleep disturbance, paresthesia, and morning tiredness (0–10) by using a visual analog scale (VAS). In addition, FM and RA patients and control subjects were questioned for the severities of belching, reflux, gas, bloating, sour taste, vomiting, and halitosis (0–4) in the last month. Patients were also asked whether they considered themselves constipated during the last 12 months (self-reported constipation). In order to determine symptom-based constipation, a VAS numbered between 0 and 10 was used for each question, and evaluation was made according to the loose criteria. Subjects who met ≥ 2 of the following criteria for longer than 12 months without any laxative usage were considered to have constipation: < 3 defecations/week, pellety hard or big hard stools ≥ 25% of the time, straining for ≥ 25% of the defecation time, and incomplete evacuation ≥ 25% of the time. By means of the VAS, patients were also asked how much their QOL was disturbed because of dyspepsia and constipation (0: not at all affected; 100: affected negatively to the highest possible degree).

The Duke-Anxiety Depression (Duke-AD) scale[19] and physical function items of the FM Impact Questionnaire (FIQ) scale[20] were administered to all patients. Validation and reliability of the Turkish FIQ has been reported by Sarmer, *et al*[21]. The Duke-AD is the 7-item anxiety-depression subscale of the Duke Health Profile, and it has been validated separately as a screening instrument for anxiety and depression. The Duke-AD was translated into Turkish by 2 of the authors; back-translation of the questionnaire into English was performed by another translator. The initial and final English versions were similar.

For statistical analysis of the data, chi-squared, one-way analysis of variance, post-hoc Tukey test, unpaired t-test, and Pearson's correlation test were used. Multiple linear regression models were used to evaluate factors that influence constipation and dyspepsia-related QOL disturbance.

RESULTS

The general features of patients and controls are shown in Table 1. All groups were similar in age. Patients with FM had longer disease duration than patients with RA ($p = 0.026$). The number of smokers was higher in the FM group than in the RA group ($p = 0.043$). The frequencies of NSAID and PPI usage were significantly higher in RA and FM patients than in the control group (Table 1). The frequency of laxative usage was higher in patients with FM than in controls ($p = 0.03$).

Data for CWP and other pain-related scores of FM and RA patients are given in Table 2. Patients with FM had significantly higher CWP, fatigue, and Duke-AD mean scores than both RA and control groups (all p values < 0.01; Table 2). The CWP score of the RA group was significantly higher than the control group ($p < 0.001$). In addition, mean FIQ, paresthesia, morning tiredness, and sleep disturbance scores of patients with FM were significantly higher than subjects with RA ($p < 0.001$).

Patients with FM had higher symptom severities for belching, reflux, bloating, sour taste, and vomiting ($p < 0.01$) than patients with RA and controls. In addition, patients with FM had significantly higher dyspepsia-related QOL disturbances than the other 2 groups (p values < 0.01). Patients with FM and RA had more frequent self-reported constipation than controls (respectively, 42.1%, 48%, 21.7%; $p < 0.01$). The frequency of symptom-based (≥ 2 criteria) constipation was significantly higher in the RA group

Table 1. General characteristic features of patients with FM and RA and control subjects.

Feature	FM, n = 152	RA, n = 98	Controls, n = 60
Age, yrs	45.4 ± 12.2	45.5 ± 12.3	44 ± 11.3
Disease duration, mo	71.1 ± 89.3*	44.5 ± 65.1	—
Smoking, n (%)	47 (30.9)**	19 (19.4)	15 (25)
Alcohol, n (%)	6 (3.9)	1 (1)	3 (5)
Previous psychiatric therapy, n (%)	67 (44.1)†	21 (21.4)	12 (20)
Education level (> 9 yrs), n (%)	50 (32.9)	13 (13.3)††	20 (33.3)
Marriage, n (%)	142 (93.4)	89 (90.8)	56 (93.3)
NSAID usage, n (%)	114 (75)	88 (89.8)	3 (5)#
PPI usage, n (%)	52 (34.2)¶	56 (57.1)##	1 (1.7)
Laxative usage, n (%)	24 (15.8)§	11 (11.2)	3 (5)

* p = 0.026, RA group vs FM; ** p = 0.043, FM group vs RA; † p < 0.001, FM group vs RA and controls; †† p < 0.001, RA group vs FM and controls; # p < 0.001, controls vs RA and FM groups; ## p < 0.001, RA vs FM and controls; ¶ p < 0.001, FM vs controls; § p = 0.03, FM group vs controls. FM: fibromyalgia; RA: rheumatoid arthritis; NSAID: nonsteroidal antiinflammatory drugs; PPI: proton pump inhibitors.

Table 2. Severity of disease-related symptoms in patients with FM and RA and controls.

	Fibromyalgia	RA	Controls
CWP (0–100)	62.7 ± 20.9*	38.5 ± 30**	14.7 ± 22.9
Fatigue (0–100)	59.8 ± 27.4†	33.2 ± 31.6	24.8 ± 26.9
Duke-AD score (0–14)	6.8 ± 2.7††	5.3 ± 3.1	5.5 ± 2.6
FIQ score (0–3)	1.33 ± 0.8#	0.84 ± 0.8	—
Paresthesia (0–10)	3.6 ± 2.5#	1.9 ± 2.2	—
Morning tiredness (0–10)	5.1 ± 2.4#	2.6 ± 2.6	—
Sleep disturbance (0–10)	4.1 ± 2.8#	2.4 ± 2.5	—

* p < 0.001, FM group vs RA and controls; ** p < 0.001, RA group vs controls; † p < 0.001, FM group vs RA and controls; †† p < 0.01, FM group vs RA and controls; # p < 0.001, FM group vs RA. CWP: chronic widespread pain; Duke-AD: Duke-Anxiety Depression Scale; FIQ: Fibromyalgia Impact Questionnaire.

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(49%) than the FM (29.6%) and control groups (23.3%) ($p < 0.01$). Constipation-related QOL disturbance was found to be significantly higher in patients with FM than in controls ($p < 0.01$), as shown in Table 3. No significant differences in symptom severity and QOL disturbance scores were detected among FM and RA patients who took NSAID versus those who did not, or between those who took gastroprotective agents versus those who did not.

In the FM group, the severity of CWP correlated with dyspepsia-related QOL disturbance ($r = 0.25$, $p = 0.01$), bloating ($r = 0.26$, $p = 0.008$), gas ($r = 0.22$, $p = 0.03$), and sour taste scores ($r = 0.21$, $p = 0.04$). The severity of fatigue correlated with dyspepsia-related QOL disturbance ($r = 0.29$, $p = 0.004$), reflux ($r = 0.2$, $p = 0.045$), sour taste ($r = 0.23$, $p = 0.022$), and vomiting scores ($r = 0.29$, $p = 0.003$). FIQ scores of patients with FM had no correlation with the severities of any of the GI symptoms. Duke-AD scores correlated with dyspepsia-related QOL disturbance ($r = 0.31$, $p = 0.002$), bloating ($r = 0.28$, $p = 0.007$), sour taste ($r = 0.24$, $p = 0.018$), vomiting ($r = 0.28$, $p = 0.005$), and the severity of constipation ($r = 0.23$, $p = 0.03$).

Multivariate linear regression analysis revealed that dyspepsia-related QOL disturbance score was independently associated with CWP severity score (beta coefficient 0.23, $p = 0.028$), age (beta coefficient 0.19, $p = 0.047$), and Duke-AD score (beta coefficient 0.22, $p = 0.039$) in patients with FM. In addition, constipation-related QOL disturbance score was independently associated with age (beta coefficient 0.24, $p = 0.028$) and Duke-AD score (beta coefficient 0.21, $p = 0.046$) in FM.

In the RA group, CWP score had correlation only with sour taste score ($r = 0.35$, $p = 0.002$). Duke-AD in patients with RA correlated with dyspepsia-related QOL score ($r = 0.31$, $p = 0.004$), bloating ($r = 0.25$, $p = 0.023$), sour taste ($r = 0.38$, $p < 0.001$), and constipation severity scores ($r = 0.26$, $p = 0.025$). In multivariate linear regression analysis, it was observed that in patients with RA, both dyspepsia and constipation-related QOL disturbance scores were independently associated with the CWP score (beta coefficient 0.49 and 0.41, $p = 0.002$ and $p = 0.018$, respectively).

In the control group, Duke-AD scores had significant correlations with dyspepsia-related QOL disturbance severity scores ($r = 0.32$, $p = 0.015$), bloating ($r = 0.36$, $p = 0.006$), and constipation severity scores ($r = 0.48$, $p < 0.001$).

Table 3. The frequency and severity of gastrointestinal system-related symptoms in patients with FM and RA and control subjects.

Feature	Fibromyalgia	RA	Controls
Belching (0–4)	1.12 ± 1.2*	0.58 ± 0.9	0.55 ± 0.9
Reflux (0–4)	1.01 ± 1.17*	0.5 ± 0.9	0.34 ± 0.7
Bloating (0–4)	1.46 ± 1.1*	0.81 ± 1.1	0.96 ± 1
Gas (0–4)	0.98 ± 1.1	0.68 ± 0.9	0.89 ± 1.1
Sour taste (0–4)	1.01 ± 1*	0.58 ± 0.9	0.44 ± 0.8
Vomiting (0–4)	0.93 ± 1*	0.57 ± 0.9	0.32 ± 0.7
Halitosis (0–4)	0.57 ± 0.8	0.29 ± 0.6	0.69 ± 1**
Dyspepsia-related QOL disturbance (0–100)	28.3 ± 18.4*	16.1 ± 16.3	16.4 ± 18
Self-reported constipation, n (%)	64 (42.1)	47 (48)	13 (21.7)†
Symptom-based constipation (≥ 2 criteria), n (%)	45 (29.6)	48 (49)††	14 (23.3)
Constipation-related QOL disturbance (0–100)	31 ± 30.8#	24.4 ± 28.8	15.8 ± 28

* $p < 0.01$, FM group vs RA and controls; ** $p = 0.01$, controls vs RA; † $p < 0.01$, controls vs FM and RA groups; †† $p < 0.01$, RA group vs FM and RA groups; # $p < 0.01$, FM group vs controls.

DISCUSSION

We found that the symptom severities of dyspepsia subgroups and dyspepsia-related QOL disturbance severity scores were significantly higher in patients with FM compared to both RA and healthy control groups. To our knowledge, ours is the first study assessing the effect of GI symptoms on the QOL of patients with FM.

One interesting finding of our study was that although patients with RA took NSAID and other drugs with potential GI-related side effects quite frequently, their dyspepsia and QOL disturbance scores were not different from those of controls. One study pointed out that QOL was significantly impaired among RA and osteoarthritis patients with GI symptoms compared to asymptomatic patients[22]. In that study, dyspepsia and upper abdominal/epigastric pain were the GI symptoms most strongly associated with QOL measures and they were common among patients with arthritis[22].

In our study, the anxiety-depression score in patients with FM was higher than in patients with RA and controls. In addition, multivariate analysis revealed that dyspepsia-related QOL disturbance in FM was independently associated with severity of CWP and also with the anxiety-depression score. In patients with RA, on the other hand, only the CWP score was independently associated with the dyspepsia-related QOL disturbance score. As a result, we might assume that as FD-related symptoms are more severe in FM and are independently associated with anxiety-depression, and as symptom severity in RA patients is lower than in FM patients, and is similar to controls — in spite of a high frequency of NSAID usage we might conclude that FD-related symptoms were predominantly associated with anxiety-depression.

Up to 60% of patients with functional bowel disease have symptoms diagnosed as FM, and approximately half of patients with FM complain of symptoms of FD[23]. Therefore, FM and FD may be thought of as somatoform disorders. This does not mean that their origin is psychological, but both have high rates of psychological disturbances and psychiatric syndromes[1,9,10]. Psychiatric comorbidity might be a result of chronic illness, or it might be a kind of healthcare-seeking behavior[1]. The explanation for somatization

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might be sensitization, which means an increased reactivity to stimuli[24]. If patients are affected by functional symptoms from one organ system, they usually have other symptoms as well. There is considerable overlap of symptoms like fatigue, sleep disturbance, headache, depression, anxiety, and paresthesia between patients with FM and patients with chronic fatigue syndrome, another condition of unknown etiology[25,26]. A common underlying sensitization process influencing central processes like attention and health anxiety, changes in the hypothalamic-pituitary-adrenal axis, and possibly in the organs might underlie this overlap of symptoms. Within each diagnostic group, like FD, the contribution of each factor might vary. Some studies have stated that stress might play an important role by causing disturbances in the hypothalamic-pituitary-adrenal axis, the hypothalamic-pituitary-gonadal axis, and the autonomic system in FM[1,27].

One common feature of NSAID, which are the mainstay of RA and FM therapy, is GI toxicity. NSAID-associated GI symptoms might vary from mild epigastric discomfort immediately after ingestion, to asymptomatic or symptomatic ulcers, to life-threatening GI hemorrhages[28]. In addition to NSAID, medications like methotrexate and steroids that have GI side effects are commonly used in RA. In our study, an important proportion of FM and RA patients were using NSAID, and nearly half of patients with RA and one-third of patients with FM were using gastroprotective therapy. Patients using and not using gastroprotective therapy did not differ significantly in symptom severity.

In our study, there was a significantly higher incidence of self-reported constipation in both patients with FM and those with RA than in controls. One study from the USA reported a much lower incidence of constipation in FM (12%) than ours, and higher incidence of laxative usage (19%)[29]. In our previous study, the prevalence of self-reported constipation was found to be 3% in healthy Turkish people[30]. The frequency of constipation varies in different countries. In one large population-based US study, self-reported constipation was found in 20.8% of women and in 8% of men[31]. One Canadian study reported a 27.2% rate of self-reported constipation[32]. In our study, although nearly half of patients with RA had self-reported constipation, constipation-related QOL disturbance was not different from controls. Although patients with FM reported relatively less self-reported constipation than patients with RA, their constipation-related QOL disturbance score and frequency of constipation medication usage was significantly higher than other groups. This might be explained by patients with FM having more self-reported complaints as a result of a higher frequency of anxiety-depression. A confirmation of this was that when symptom-based (≥ 2 criteria) constipation was considered in RA, the frequency of constipation did not change (49%); nevertheless, patients with FM had a lower frequency of constipation than patients with RA (29.6%) and a frequency similar to healthy controls.

The limitation of our study was its cross-sectional design; it did not include longitudinal data. We evaluated dyspeptic complaints within the previous month of the study interview, and there were no data on followup. As a result, our patients with FM had significantly higher frequency of constipation, constipation and GI-related symptom severity scores, and constipation and dyspepsia-related QOL disturbances than patients with RA and controls. Anxiety and depression scores were independently associated with constipation and dyspepsia-related QOL disturbance. The higher GI symptom severity in patients with FM might have a negative effect on their QOL. The diagnosis of FM itself is arduous and the patients are frequently undertreated. GI symptoms should be questioned in patients with FM and should be taken into consideration.

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