İstanbul Med J 2015; 16: 18-22
DOI: 10.5152/imj.2015.75436

Original Investigation

The Effect of Fibromyalgia on Disease Activity in Patients with Rheumatoid Arhritis

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Abstract

Objective: The aim of the study is to determine the effect of fibromyalgia (FM) on disease activity and quality of life in patients with rheumatoid arthritis (RA).

Methods: This was a randomized and prospective study conducted in 96 RA patients admitted to our rheumatic diseases outpatient clinic, diagnosed according to the American College of Rheumatology (ACR) 1987 criteria at least for 2 years. Data composed of demographical properties, painful and swollen joints, duration of morning stiffness, level of pain by Visual Analog Scale (VAS), number of used disease-modifying antirheumatismal drugs (DMARDs), and disease duration of all patients. In addition C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), and anticyclic citrullinated peptide (anti-CCP) levels were measured. Disease Activity Score 28 (DAS28) was used to assess disease activity and Health Assessment Questionnaire (HAQ) and short form (SF-36) were used to assess the quality of life. FM diagnosis was primarily made on the basis of the ACR 1990 FM criteria. After then, two groups were generated as FM-positive and FM-negative patients. Disease activity (DAS28), quality of life (HAQ and SF-36), morning stiffness durations, numbers of painful and swollen joints, pain levels by VAS, number of DMARDs used, duration of disease, and laboratory diagnosis as well as activity parameters (CRP, ESR, RF, and anti-CCP) were compared between the two groups.

Results: There was no significant difference in the duration of morning stiffness, duration of disease, number of used DMARDs, CRP, ESR, RF, and anti-CCP ($p>0.05$) between the two groups. RA patients with FM showed significantly higher scores of VAS, HAQ, and DAS28 and more painful joints than RA patients without FM; SF 36 scores were significantly lower in FM patents ($p<0.05$).

Conclusion: FM adversely affects disease activity and quality of life in patients with RA. It may be help full to consider FM while evaluating disease activity in RA patients.

Keywords: Fibromyalgia, rheumatoid arthritis, disease activity, quality of life

Introduction

Rheumatoid arthritis (RA), the etiology of which is not completely known and which begins with pathological changes of synovial tissues, primarily results in the destruction of peripheral joints and tissues characterized with chronic polyarticular joint involvement, and it is a systemic inflammatory autoimmune disease (1-3). The most important impacts of RA on patients are persistent pain and functional impairment caused by synovitis and progressive joint damage (3). Because of the chronic course of the disease and functional insufficiency caused by the disease, the patients' physical, emotional, and social functions are affected from the early stages of the disease and functional insufficiency and decrease in the quality of life occurs (4, 5).

Fibromyalgia syndrome (FMS), the etiology of which is not certain, is a rheumatic disease characterized with widespread body pain, tenderness at specific anatomic regions, decreased pain threshold, sleep disorders, fatigue, and frequent associations with psychological distress (6). Although the etiology and mechanisms of FM are not fully understood, the most important factors for its emergence seem to be charecterized by neuroendocrine dysfunction, central pain mechanisms, and central sensitization (7). Although there is widespread musculoskeletal pain, physical examinations, laboratory findings, and radiological examinations are normal. The disease is mostly seen in women between 40 and 50 years of age (8).

Although there is no objective evidence such as inflammation and joint damage, FM can reduce the quality of life to a similar extent as RA. A study conducted by Sivas et al. (9) revealed that FM, which is not an inflammatory disease, could lead to high Disease Activity Scores (DAS) 28 because of the subjective symptoms such as tenderness and pain (9).

The aim of the study was to determine the effect of FM on disease activity and the quality of life in patients with in patients with RA.

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Received:
12.08.2014

Accepted:
27.12.2014

Methods

Our study involved 96 patients with RA in the age group of 18–75 years who had been admitted to our rheumatic diseases outpatient clinic between January 2012 and April 2012 and who had been diagnosed according to the American College of Rheumatology (ACR) 1987 criteria for at least 2 years. Ethics committee approval was received for this study from the ethics committee of İstanbul Training Research Hospital Clinic Research and Ethical Committee. Patients were informed orally and in written form about the purpose of the study. Written informed consent was obtained from patients who partipicated in this study. Cases with malignancy, active infection, significant neurological deficits, and any other inflammatory rheumatic diseases; those who do not have the mental ability to understand and answer the questions; and those with an insufficient intellectual level for the questionnaire were excluded.

The patients' age, gender, occupation, marital status, medication they take [non-steroidal anti-inflammatory drugs (NSAIDs)], disease-modifying antirheumatic drugs (DMARDs), corticosteroids (CS), anti-tumor necrotizing factor alpha inhibitors (anti-TNF inhibitors), disease duration, and duration of morning stiffness were recorded. Laboratory diagnosis and activity parameters (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor(RF), anti- cyclic citrullinated peptide (CCP) antibody) levels were recorded.

DAS28 score was used to assess disease activity. The results that were obtained were evaluated according to the schedule as follows: >5.1, high disease activity; >3.2–≤5.1, moderate disease activity; ≥2.6–≤3.2, low disease activity; and <2.6, remission (1, 2).

In our study, pain level was assessed using the visual analog scale (VAS) (10). The two ends of VAS is numbered differently; the left end is numbered as 0, meaning there is no pain; and the right end is numbered as 10, representing the most severe pain. The patient was asked about the pain level s/he felt in the last week and to mark the line on the VAS scale.

Patient's quality of life was assessed using Short-Form (SF)-36. SF-36 was developed to be used in clinical practice and research to evaluate the quality of life (11). SF-36 consists of eight subscales and 36 questions, including questions on physical functioning, physical role limitations, body pain, general state of health, vitality, social function, emotional role limitations, and mental health. The SF-36's validity study for the Turkish language was conducted by Koçyiğit et al. (11).

The health assessment questionairre (HAQ) was used to measure the patients' functional ability degree. HAQ is a good indicator of future disability and loss. Over the past week, patient's daily skills were assessed (5). HAQ's reliability and validity study for the Turkish language was conducted by Küçükdeveci et al. (12).

In all patients included in the study, the presence of FM was investigated using the ACR 1990 diagnostic criteria for FM (13). Patients were divided into two groups: FMS-positive and FMS-negative patients. Disease activity, quality of life, morning stiffness durations, numbers of painful and swollen joints, pain levels, number of DMARDs used, duration of disease, laboratory diagnosis, as well as activity parameters were compared between the two groups.

Statistical analysis

For descriptive statistics of the data, mean, standard deviation, rate, and frequency values were used. The Kolmogorov–Smirnov test was used for the distribution of the data. According to the distribution of the data, Mann-Whitney U-test and independent sample t-test were used. Chi-square test was used for the proportional data analysis. Fisher's exact test was used when the conditions of the chi-square test could not be provided. The agreement between the diagnostic protocol conducted on two different years was measured by kappa analysis of agreement. The Statistical Package for the Social Sciences (SPSS) ver. 20.0 software was used in the analysis. Statistical significance was taken as $p<0.05$.

Results

The study included 82 female and 14 male patients who had been diagnosed with RA in accordance with the ACR 1987 diagnostic criteria for at least 2 years. Of these patients, 63 (65.6%) were housewives, 24 (25%) were employed, and 9 (9.4%) were retired. In total, 21 (21.8%) of the 96 patients were diagnosed with FM. All the cases diagnosed with FM were female (100%). None of the male patients (0%) was diagnosed with FM. There was a statistically significant difference in the sex ratio among FM-positive and FM-negative patients ($p=0.032$, $p<0.005$). No significant difference was detected in terms of average age and occupational status ($p<0.05$) (Table 1).

The ratio for morning stiffness was 76.2% among FM-positive patients, whereas it was 36.0% in FM-negative patients; it was considered statistically significant ($p<0.05$). There was no statistically significant differences in terms of duration of morning stiffness and swollen joint count (SJC) between FM-positive and FM-negative patients ($p>0.05$) (Table 2).

Sensitive spot ratio for FM-positive patients (100%) was significantly higher than that for FM-negative patients (54.7%). Similarly, the number of sensitive spots in FM-positive patients (12.76±1.51) was significantly higher than that in FM-negative patients (3.68±2.26) ($p<0.05$) (Table 2).

No statistically significant difference was observed in FM-positive patients with RA in terms of duration of disease, average utilization rate of DMARD, and number of used DMARDs ($p>0.05$) (Table 3).

The average VAS pain score of FM-positive patients was found to be 6.0±2.4, whereas that for FM-negative patients was 3.9±2.7. The VAS, DAS28, and HAQ scores were significantly higher in FM-positive patients with RA than those in FM-negative patients with RA, and the SF-36 scores were significantly lower in patients with FM ($p<0.05$) (Table 4).

The average physical component summary (PCS) score , which is one of the two subscales of the SF-36 quality of life scores, in FM-positive patients was 33.52±10.74, whereas the average score in FM-negative patients was 41.16±10.31. The average mental component score (MCS), another subscale of SF-36, in FM-positive patients was 33.81±9.82, whereas that in FM-negative patients was 43.17±11.30. PCS and MCS scores were significantly lower in FM-positive patients ($p<0.05$) (Table 4).

There was no statistically significant difference in CRP, ESR, RF, and anti-CCP ($p>0.05$) scores between FM-positive and FM-negative patients ($p>0.05$).

Table 1. Comparison of the demographic characteristics of the patients

		Fibromyalgia diagnosis ACR-1990				
		Yes		No		
		Mean±SD / n (%)		Mean±SD / n (%)		p
Sex	Female	21	100.0%	61	81.3%	0.032
	Male	0	0.0%	14	18.7%	
Age		49.43±9.14		49.19±9.78		0.919
Occupation	Housewife	15	71.4%	48	64.0%	
	Employed	4	19.0%	20	26.7%	0.771
	Retired	2	9.5%	7	9.3%	

Chi-square test/Independent samples t-test
ACR: American College of Rheumatology

Table 2. Comparison of morning stiffness and the number of painful and swollen joints of FM-positive and -negative patients with RA

	Fibromyalgia diagnosis ACR-1990				
	Yes		No		
	Mean±SD / n (%)		Mean±SD / n (%)		p
Morning stiffness	16	76.2%	27	36.0%	0.001
Duration of morning stiffness (min)	45.31±41.05		41.30±36.55		0.741
Swollen joint	7	33.3%	23	30.7%	0.816
Number of swollen joints	3.71±2.56		4.04±3.40		0.940
Painful joints	21	100.0%	57	76.0%	0.013
Number of painful joints	9.24±5.44		4.04±5.75		0.000
Sensitive spot	21	100.0%	41	54.7%	0.000
Number of sensitive spots	12.76±1.51		3.68±2.26		0.000

Chi-square test/Independent samples t test/Mann–Whitney U-test
FM: fibromyalgia; RA: rheumatoid arthritis; ACR: American College of Rheumatology

Discussion

Present treatment options can neither prevent nor treat RA completely. Therefore, the main objective in the treatment of the disease is to minimize the negative impact of the disease by improving the quality of life and by reducing limitations on the patient's life (14). To plan an effective treatment program, the symptoms and the relationship between functional status and quality of life should be well understood (4). Knowing these relationships will help to establish an individualized rehabilitation program during the clinical course of the disease.

On the other hand, it has been reported in many studies that allodynia and hyperalgesia-associated FMS, which is a multidimensional disease, affects the quality of life in a negative way and is characterized with chronic widespread pain and sensitive spots in specific anatomical regions. According to the 1990 ACR diagnostic criteria for FMS diagnosis, there has to be widespread pain for at least 3 months on the four quadrants of the body (including axial skeleton), and pain should also be detected in 11 of 18 sensitive spots by palpation in physical examination. Because FMS is associated with comorbidities such as fatigue, stiffness, sleep disorders, depression, and anxiety, classification and treatment is very difficult (15, 16).

Table 3. Comparison of duration of disease and number of DMARDs used in FM-positive and -negative patients with RA patients

	Fibromyalgia diagnosis ACR-1990				
	Yes		No		
	Mean±SD / n (%)		Mean±SD / n (%)		p
Duration of disease	8.05±7.32		9.07±8.32		0.745
DMARDs used	21	100.0%	71	94.7%	0.573
Number of DMARDs used	1.33±0.66		1.33±0.54		0.461

Chi-square test/Mann–Whitney U-test
DMARDs: disease-modifying antirheumatic drugs; FM: fibromyalgia; ACR: American College of Rheumatology

Table 4. Comparison of the VAS, DAS28, HAQ, and SF-36 parameters of FM-positive and -negative patients with RA

		Fibromyalgia diagnosis ACR-1990				
		Yes		No		
		Mean±SD / n (%)		Mean±SD / n (%)		p
VAS		6.0±2.4		3.9±2.7		0.002
DAS28		4.33±0.91		3.46±1.11		0.001
DAS28	In remission	0	0.0%	12	16.0%	
	Low activity	4	19.0%	31	41.3%	0.006
	Moderate-high activity	17	81.0%	32	42.7%	
HAQ Score		16.05±9.54		9.25±8.27		0.002
PCS		33.52±10.74		41.16±10.31		0.004
MCS		33.81±9.82		43.17±11.30		0.001

Chi-square test/Mann–Whitney U-test
VAS: Visual Analog Scale; DAS28: Disease Activity Score 28; HAQ: Health Assessment Questionnaire; PCS: physical component summary; MCS: mental component score; FM: fibromyalgia; SF: short form; ACR: American College of Rheumatology

Although there is no objective evidence such as inflammation or joint damage, FMS can have a similar negative affect as RA in terms of SF-36 and HAQ scores, which are quality of life measures (17).

In our study, the effect of FM on RA disease activity was investigated. The assessment of this effect was based on DAS28, one of the most important parameters that we use in the evaluation of disease activity in RA. Since SF-36 and HAQ, which are quality of life criteria, are the parameters used to evaluate the quality of life of patients in both RA and FM, we also used these criteria when investigating the effect of FM on RA. In addition, two groups were compared in terms of morning stiffness, pain scores (VAS), the number of DMARDs used, the number of painful and swollen joints, and the effect of FM on RA.

There have been many studies conducted on the relationship between RA and FM and the effects of FM on the disease activity and quality of life of patients with RA. In the study conducted by Sivas et al. (9) in 2010, it was stated that elevated DAS28 scores had been identified on FM. The intervening infections during the evaluation of disease activity in RA or concomitant diseases like FM might cause fluctuations in the DAS28 scores.

In the study conducted by Kapoor et al. (18) in 2011, with 285 patients with RA, on the FM frequency in patients with RA and the ef-

fects of FM on DAS28, one of the disease activity criteria stated that DAS28 scores were significantly higher in the group with FM. In the studies that investigated the FM frequency in patients with RA and the impact of FM on RA, DAS28 scores were also found to be high (19-22). Because the number of tender joints, which is one of the subjective components on DAS28 and VAS, had higher scores than FM, DAS28 scores in patients with RA were higher. In our study, 21 (21.8%) out of the 96 patients were diagnosed with FM, and the results were compatible with previous studies. We measured significantly higher DAS28 scores in FM-positive patients with RA than those in the group without FM.

The measurement of DAS28, which is the most important disease activity criteria of RA, is based on four components: the number of painful and swollen joints, ESR, and VAS. In similar studies investigating the effects of FM on RA disease activity, in FM-positive patients with RA, the number of painful and swollen joints and VAS values were found to be significantly higher than those in FM-negative patients with RA. In the same studies, patients were compared in terms of sedimentation and the number of painful and swollen joints, and no significant differences were observed between the two groups (19-22).

Similar to the studies that had been performed previously, although we could not observe significant differences in terms of the number of painful and swollen joints and ESR scores between FM-positive patients with RA and FM-negative patients with RA, the number of painful and swollen joints and VAS scores were found to be significantly higher in FM-positive patients with RA. These results support the hypothesis that FM has an impact on the number of painful and swollen joints and VAS, the subjective components of DAS28, and cause high disease activity in patients with RA.

In earlier studies, it was reported that both FM and RA cause low SF-36 scores and high HAQ scores by negatively affecting HAQ and SF-36, quality of life measures (9, 17-21). In another study conducted by Kolahi et al. (23), in both the FM and RA group, the mental and physical component scores, the subscales of SF-36, were significantly lower than those in the healthy control group.

In compliance with earlier studies, we found that HAQ, one of the quality of life measures, was significantly higher in FM-positive patients with RA, and FM has a negative impact on the quality of life of patients with RA.

One of the important results we have reached is the impact of FM on the duration of morning stiffness, which is one of the RA remission criteria. The duration of morning stiffness did not differ significantly in FM-positive patients with RA compared with FM-negative patients with RA. However, the presence of morning stiffness was significantly higher in patients diagnosed with FM. Ranzolin et al. (21) reported that the duration of morning stiffness was found to be significantly longer in FM-positive patients with RA in their study. Although it is stated that FM has a negative effect on patients with RA in terms of the presence and duration of morning stiffness, more studies are required on this subject.

Previous studies indicated that FM, which is reported to have negative impacts on disease activity and quality of life in patients with RA, also affects the number of DMARDs, the main therapy administered to patients with RA. It was reported that FM-positive patients with RA utilized more DMARD (21, 24). In contrast to other studies, we could not observe significant differences in the number of DMARDs used between the FM-positive patients with RA and FM-negative patients with RA. This might be due to the small number of patients compared with earlier studies.

Conclusion

It was observed that although FM-positive patients with RA had higher DAS28, HAQ, and VAS scores and lower SF-36 scores than FM-negative patients with RA, FM adversely affects disease activity and quality of life in patients with RA. In addition, it may be helpful to consider FM while establishing a treatment protocol for patients with RA with high DAS28 scores.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul Training and Research Hospital Clinic Research and Ethical Committee.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.B., N.S.Ç.; Design - S.Ç.O., Y.P.D.; Supervision - E.A., T.A.; Funding - E.Ç., İ.H.E.; Materials - Ö.A., A.B.; Data Collection and/or Processing - N.S.Ç., E.A.; Analysis and/or Interpretation - Y.P.D., S.Ç.O.; Literature Review - İ.H.E., E.Ç.; Writer - A.B., S.Ç.O.; Critical Review - E.A., E.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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