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Subtypes of patients with fibromyalgia, psychopathological characteristics and quality of life

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Introduction. The main goal of this work was to identify subgroups of patients with fibromyalgia (FM) by means of a frequently used clinical tool, the Fibromyalgia Impact Questionnaire (FIQ).

Methodology. A total of 66 women diagnosed with FM participated in the study. Two subgroups of patients were identified by analysis of a hierarchical cluster of selected items from the FIQ (pain, fatigue, morning tiredness, stiffness, anxiety and depressive symptoms).

Results. The type I FM-group had very high levels of fatigue, morning tiredness and anxiety, and high levels of joint stiffness, pain and depressive symptoms, while the type II FM-group had predominantly moderate levels of fatigue and morning tiredness, with moderate low levels of pain and stiffness along with a low level of depression and anxiety.

Conclusions. Type I FM-group also had lower health-related quality of life, especially through emotional reactions and social isolation as well as more psychopathological affections than presented by type II FM-group.

Keywords:
Fibromyalgia, Subgroups, Health related quality of life, Psychopathology

Actas Esp Psiquiatr 2011;39(5):273-9

Subtipos de pacientes con fibromialgia, características psicopatológicas y calidad de vida

Introducción. El objetivo principal de este trabajo fue identificar subgrupos de pacientes con fibromialgia (FM) a

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partir de una herramienta clínica de uso frecuente, el Fibromyalgia Impact Questionnaire (FIQ).

Metodología. Un total de 66 mujeres con diagnóstico de FM participaron en este estudio. Mediante un análisis de conglomerados jerárquico de ítems seleccionados del FIQ (dolor, fatiga, cansancio matutino, rigidez, ansiedad y síntomas depresivos), se identificaron 2 subgrupos de pacientes con FM.

Resultados. El grupo de FM tipo I mostró niveles muy elevados de fatiga, cansancio matutino y ansiedad, y niveles altos en rigidez articular, dolor y síntomas depresivos. El grupo de FM tipo II presentó un predominio de niveles moderados de fatiga y cansancio matutino, con niveles moderadamente bajos de dolor y rigidez articular, junto a un nivel bajo en depresión y ansiedad.

Conclusiones. El grupo de FM tipo I se caracteriza también por tener una baja calidad de vida relacionada con la salud, especialmente en reacciones emocionales y aislamiento social, junto a una mayor afectación de la esfera psicopatológica que la presentada por el grupo de FM tipo-II.

Palabras clave:
Fibromialgia, Subgrupos, Calidad de vida relacionada con la salud, Psicopatología

Identification of psychopathological characteristics and impact on the health-related quality of life in subgroups of patients with fibromyalgia

Fibromyalgia (FM) is a multidimensional disease whose etiology is currently unknown. It is characterized by chronic generalized osteoarticular pain that the patient frequently describes as being located in locomotor apparatus areas. Other common clinical manifestations found in patients with FM, in variable grade, are: intense fatigue, sleep disorders, paresthesias in limbs, joint stiffness, headaches and sensation of numbness in the hands in addition to

depressive and anxiety symptoms and cognitive problems (decreased capacity of concentration and memory loss).¹

The prevalence of FM in Spain is estimated to be 2.4% of the general population over 20 years of age. This means, in absolute values, that there are 700,000 persons in Spain suffering FM. Prevalence in men is estimated at 0.2% versus 4.2% in women. This means a man-woman prevalence ratio of 1.21. By ages, FM is manifested in all the age groups studied, with maximum prevalence between 40 and 49 years (4.9%). Its frequency is very low in those over 80 years.² However, the symptomatic diversity of the FM picture and problems to reach a precise diagnosis directly affects the consensus on its prevalence. This consensus differs according to the studies, with figures going from 2-4% in the general population, from 2-6% in the primary care consultations, reaching up to 10-20% in rheumatology consultations.³

For more than one decade, an attempt has been made to identify different subgroups of this syndrome based on clinical criteria, differentiating between primary fibromyalgia with and without depression and the so-called secondary fibromyalgia, based on different therapeutical considerations and applications.

The complex clinical profile observed in patients with FM indicates a very heterogeneous disorder. The variability in the intensity of the symptoms related with the FM picture, which includes differences in the psychological functioning,^{2,4} altered cardiovascular reactivity,⁵ and distorted perception of the pain^{3,4,6} supports the heterogeneity of the picture. Recent studies have found that the individual differences shown by the patients in remission of the symptoms also make it possible to differentiate the functional profile of these patients. More recently, it has been found that a combination of psychological indicators and sensitivity to pain make it possible to better differentiate different subgroups of patients with FM.⁷ The cluster analysis made it possible to identify three different groups of patients with well-defined psychopathological profile: one group of patients with fibromyalgia characterized by predominance of elevated indices in the indicators of depression and anxiety, one group with predominance of cognitive factors of catastrophism and low control on the pain and finally a third group with greater sensorial reactivity to pain (hyperalgesia and painful perception). Each profile makes it possible to identify different strategies for the patient to confront the pain that would require a specific therapeutic approach. Other studies have also identified three subgroups of patients with similar characteristics.⁴ The authors called the first "dysfunctional," anxiety being the principal problem. The second subgroup was made up of patients with elevated interpersonal suffering, who would have associated psychiatric problems. Finally, there was a third group of persons with an adaptive coping strategy.

An empirical form of classification of the FM has been proposed, especially based on the psychopathological profile of the patient. This classification includes group 1 (without psychiatric disease), group 2 (FM with depression), group 3 (depression with FM) and group 4 (FM due to somatization).⁸

In a recent systematic review of the literature,⁹ the following classification groups were identified in the patients who fulfilled the criteria in force for FM: patients without concomitant disease (type I FM, patients with chronic rheumatic and autoimmune diseases (type II FM), patients with severe alteration in the psychopathological sphere (type III FM) and patients who simulated having FM (type IV FM).

Multifactorial studies having a biopsychosocial approach to FM show that the patients have significantly more psychological-type problems than the healthy controls and than patients with chronic pain disorders such as rheumatoid arthritis problems.¹⁰ In general, these patients also have more emotional-type disorders, poorer coping strategies to pain and a more limited social support network than the healthy control study. Some studies indicate that 47% of the patients with FM have an anxiety disorder while other studies indicate that 50% have a depressive picture.¹ The studies also indicate that there is a correlation between indicators of psychopathology with disease and pain duration.¹¹ FM has an important impact on health-related quality of life, that is even greater than other chronic diseases such as rheumatoid arthritis or arthrosis. The impact on family life is especially important, and affects activities of daily life and social relationships.⁶

Using the methodology proposed by Souza et al.¹² for the identification of subgroups of patients with different profiles of FM, this study has aimed to a) identify possible differences in quality of life indicators related with health and b) identify the possible differences in global indicators of psychopathology between groups of patients with different grades of FM involvement.

The Fibromyalgia Impact Questionnaire (FIQ) to identify subgroups of patients with FM was used. The FIQ is an adequate questionnaire to form groups. It is rapidly administered and evaluates the principal clinical characteristics of FM.¹² It is important to stress that the FIQ evaluates the psychological and physical symptoms, which makes an extensive measurement of the different indicators of FM possible.

MATERIAL AND METHODS

Patients

The patients were recruited from primary health care centers and local associations of patients with fibromyalgia.

A non-randomized sampling was performed by intentional selection of all candidates possible from the study population. Inclusion criteria: clinical rheumatological diagnosis of fibromyalgia according to the American College of Rheumatology,¹³ capacity to understand and respond to the questionnaires, signature on the informed consent form. Exclusion Criteria: diagnosis of physical or psychiatric disease. *Patients in whom compliance with the study protocol, in the opinion of the investigator, is unlikely. Patients who are participating in a clinical trial. Patients who have an unsolved work litigation related with fibromyalgia.*

The final sample was formed by 66 women diagnosed of FM, with ages from 28 to 62 years (MA =47.18; SD=8.52), and mean duration of the disease of 4.42 years (SD =1.72). A total of 75% of the patients were married (n=54), 8.3% (n=6) separated, 5.6% (n=4) widowed and 2.8% (n=2) single. Within the sample, 6.9% had no studies while 66.6% (n=48) had primary studies, 12.5% secondary and 5.6% upper studies (n=4). At the time of evaluation, 59.1% (n=39) of the patients were not working.

Instruments

Fibromyalgia Impact Questionnaire (FIQ) (14-16). This is a questionnaire formed by 10 items. The first item measures physical functioning and is made up of 10 subitems that are scored from 0 to 3, where 0 indicates "I am always capable of" and 3 "I am never capable of ...," and each one of the items refers to different activities of daily life such as "going shopping," "walking in the neighbor," "driving," etc. The next two items refer to the work situation, the first including the number of days of the week in which the subject felt well and the second the number of days of missed work due to fibromyalgia during the week prior to the evaluation. Finally, the last seven items measure, respectively, interference of the disease in work, pain, fatigue, daytime tiredness, stiffness, anxiety and depression. The FIQ has an acceptable test-retest reliability (with correlations that range from 0.56 for pain and 0.95 for physical functioning) and it has been used effectively in many investigations, both pharmacological¹⁷ and psychosocial.¹⁸ The FIQ is specific for women, given the greater prevalence of fibromyalgia syndrome in women than in men.

The *Nottingham Health Profile (NHP)*.^{19, 20} This is a generic instrument on health-related quality of life that evaluates physical, psychological and social distress associated to medical, social and emotional problems. It consists of 38 items having dichotomic response (yes/no) belonging to six dimensions of health: energy (3 items), pain (8 items), physical mobility (8 items), emotional reactions (9 items), sleep (5 items), and social isolation (5 items). The scores of each dimension are the percentages of affirmative

responses, with the range from 0 (no suffering) to 100 (maximum level of suffering), for each dimension. Thus, six different scores are obtained, corresponding to each one of the dimensions of the questionnaire, which provide a profile of the Patient's perceived health condition.²¹

Symptom Checklist-90-Revised (SCL-90-R).^{22,23} This is a multidimensional self-applied questionnaire made up of 90 items. The questionnaire provides information on nine dimensions of psychopathological symptoms (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism) and 3 general scales: the Global Severity Index (GSI), the *Positive Symptom Distress Index (PSDI)* and the *Positive Symptom Total (PST)*. The reliability indexes of the Spanish adaptation of the SCL-90-R are between 0.77 and 0.90. The SCL-90-R shows an elevated diagnostic sensitivity, from 80 to 90%, and specificity from 20 to 60%.

Procedure

The study protocol, together with the informed consent form, were approved by the Ethics Committee of the Institut d'Assistència Sanitaria (EC-IAS) of the Hospital Santa Caterina (Salt, Gerona). Informed consent was obtained from each participating patient. The administration of the evaluation protocol was individual and hetero-applied. All the participants selected completed the study protocol.

Data analysis

Descriptive analysis of the study variables. An analysis was made of the hierarchical clusters to identify FM subgroups. The groups were created with the scores obtained in six of the seven items of the FIQ. These items include clinical pain, fatigue, morning tiredness, stiffness, anxiety and depressive symptoms. The seventh item (pain interferes with work) was not included in the cluster analysis since 59.1% of the patients were not working at the time of the evaluation.

The *distances or dissimilarity matrix* between the centroids was obtained by the squared Euclidean distance, which is recommendable when the variables are homogeneous and measured in similar units.²⁴ The Ward method was used to determine which participants were assigned to each group. This method minimizes the intra-group variance and generates smaller and more homogeneous clusters.²⁵ The combination of the Calinski-Harabasz index,²⁶ maximization of the mean silhouette²⁷ and the detection of the elbow of the curve of representations²⁸ were used as stopping rules. A discriminant analysis was performed to study relative weight of each item in the discrimination between the

Table 1	Descriptives of the study variable	
	MA	SD
FIQ		
pain	6.88	2.36
fatigue	8.26	1.86
morning tiredness	8.26	2.32
joint stiffness	7.35	2.32
anxiety	7.48	2.71
depressive symptoms	6.98	2.84
NHP		
energy	88.88	26.38
pain	82.40	22.91
physical mobility	54.11	22.74
emotional reactions	59.97	27.48
sleep	59.74	28.44
social isolation	35.92	29.76
SCL-90-R		
somatization	2.43	0.71
obsessive-compulsive	2.17	0.85
interpersonal sensitivity	1.48	0.90
depression	2.30	0.87
anxiety	1.73	0.88
phobic anxiety	1.12	0.96
paranoid ideation	1.28	0.96
psychoticism	0.96	0.76
global severity index (GSI)	1.77	0.74
positive symptoms stress Index (PSDI)	2.38	0.57
positive symptoms total index (PST)	63.87	16.78

FIQ: Fibromyalgia Impact Questionnaire. NHP: Nottingham Health Profile; SCL-90-R: Symptom Checklist-90-Revised

groups of patients with FM and the multivariate analysis of the variance (MANOVA) of health-related quality of life study variables (NHP). For the stratified psychopathological variables per groups, the univariate contrasts for comparisons between groups were applied. The "pain" dimension of the NHP was not included in the analysis since it was specifically evaluated in the FIQ. In the multivariate analysis, only the global indexes of psychopathology of the SCL-90-R were used.

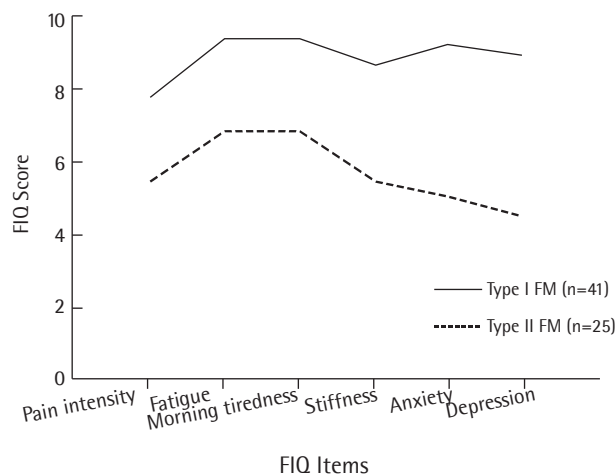


Figure 1 Clusters created from the FIQ items. Mean score of the items for each cluster: Type I

RESULTS

The characteristics of the sample and mean score of each one of the instruments used are shown in table 1. For the FIQ, only the mean scores of the 6 subscales used in the cluster analysis are shown (table 1).

The cluster analysis identified two groups of patients with differentiated profiles (figure 1). Table 2 shows the mean score and deviation of the study variables for each group. The first group (FM-I) included 41 patients with very high levels of fatigue, morning tiredness and anxiety and high levels of joint stiffness, pain and depressive symptoms. The second group (FM-II), formed by 25 patients, is characterized by a profile having predominance of moderate levels of fatigue and morning tiredness, with moderately low levels of pain and joint stiffness, together with a low level of depression and anxiety (figure 1).

After forming the clusters, a discriminant analysis was performed to study the relative weight of each item in the discrimination between the FM groups. The discriminant function obtained was significant ($\chi^2=80.84$; $gl=6$, $p<0.0001$). All the correlations (load saturation) superior to 0.35 were considered good predictors of the discriminant function. The results of the analysis of the discriminant function showed that the depressive symptoms, anxiety and joint stiffness better differentiated the two FM groups than fatigue, pain or morning tiredness (table 2).

The multivariate analysis showed that the results for the combined health group of indicators perceived and general indexes of psychopathology were significant between the

Table 2		Cluster characteristics. Discriminant Function Coefficients and Steps				
FIQ subscales	Type I FM (n=41) MA (SD)	Type II FM (n=25) MA (SD)	Classification function coefficients			
			Saturation	Type I FM	Type II FM	
Pain intensity	7.88(2.01)	5.24(1.96)	0.39	1.08	0.72	
Fatigue	9.20(0.98)	6.72(1.96)	0.51	2.85	2.35	
Morning tiredness	9.20(1.14)	6.72(2.90)	0.36	1.06	0.79	
Joint stiffness	8.56(1.07)	5.36(2.46)	0.54	-0.17	-0.23	
Anxiety	9.12(0.90)	4.80(2.56)	0.78	1.498	0.69	
Depression	8.73(1.16)	4.12(2.42)	0.78	1.841	0.78	
Constant				-36.86	-16.09	

Table 3		Results of multivariate analysis, effect size (d') and relative size of change percentage			
	Type I FM (n=41) MA (SD)	Type II FM (n=25) MA (SD)	F _{univariate} ;p	d' effect size (%)	
Energy					
physical mobility	95.12(14.06)	78.64 (37.15)	6.57;p<0.013	0.66(21)	
emotional reactions	60.05(19.56)	44.38(24.57)	8.19;p<0.006	0.75 (35)	
sleep	70.16(22.54)	43.26(27.02)	19;p<0.000	1.12 (62)	
social isolation	67.51(27.23)	47.00(26.14)	9.07;p<0.004	0.78(44)	
SCL-90-R	48.91(28.46)	14.60(16.95)	29.78;p<0.000	1.41 (100)	
SCL-90-R					
GSI	2.01(0.72)	1.37 (0.60)	13.45;p<0.001	0.96(47)	
PST	69.24(13.85)	55.08 (17.69)	13.12;p<0.001	0.93(26)	
PSDI	2.54(0.57)	2.11(0.45)	10.04;p<0.002	0.83(20)	

FM groups ($F_{\text{multivariate}} = 4.91$, $P = 0.0001$). The linear combination of the dependent variables accounted for 42% of the differences between groups. The univariate analysis showed significant differences between FM groups in all the dependent variables. The criteria proposed by Cohen²⁹ to interpret the typified effect size (values < 0.20 represents a small change; a value of 0.50 represents a moderate change and a value over 0.80 supposes an elevated change) were used for the interpretation of these statistics (table 3).

The effect size observed was elevated in the emotional reactions and social isolation variables and moderate in the remaining study variables.

DISCUSSION

The results obtained support the presence of different subgroups among women with FM. The subgroups were identified through a cluster analysis with selected items of the FIQ. Based on this analysis, the patients with FM can be divided into 2 groups: Type I-FM and Type II-FM. A total of 62.2% of the patients belonged to Type I-FM. The profile of the patients of this group showed very elevated levels of fatigue, morning tiredness and anxiety and high levels in joint stiffness, pain and depressive symptoms. The Type II group accounted for 37.8% of the sample. They had a

predominance of moderate levels of fatigue and morning tiredness, with moderately low levels of pain and joint stiffness, together with a low level of anxious and depressive symptoms. The comparisons between FM groups of the indicators of health-related quality of life showed that worse health was perceived in all the dimensions for the Type I-FM group. The emotional reactions to the disease and social isolation were the NHP dimensions having greater risk effect size and greater relative percentage of change. Regarding the differences in the psychopathological variables between groups, the Type I-FM group showed more alteration in the psychopathological sphere with greater severity (GSI) and intensity of the perceived symptoms (PSDI) and a greater number of psychopathological symptoms independently of their severity (PST) than those observed in the Type II FM group.

Coinciding with other studies,⁷ the data obtained suggest that the diagnostic heterogeneity that characterizes the FM patients may be due to significant differences in the anxious and depressive symptoms. These differences can be interpreted as there being an existence of more associated symptoms of anxiety or depression in the Type I-FM patients but not in those of Type II, even though these also have high levels of pain, tiredness and joint stiffness.⁴ The Type I-FM patient group has a greater impact on quality of life, especially on the emotional condition and social relationships, there being greater social isolation, results that partially coincide with those found in other investigations.³⁰⁻³²

The conclusions of this study support the existence of differentiated profiles of FM patients described in other investigations, with similar characteristics to those found in this study.^{8, 12}

In general, our study coincides in stressing that the heterogeneity characterizing FM is mainly due to differences in anxious and depressive symptoms, together with greater involvement of the psychopathological sphere. These differences can be considered as evidence that these symptoms may be indicators of psychiatric comorbidity in patients with Type I-FM, although not in patients with Type II-FM. The psychiatric comorbidity is frequent in different chronic organic diseases (e.g., coronary disease, diabetes or pulmonary hypertension). However, there are times in the clinical practice that the organicity of FM is still questioned in the clinical practice and that this is understood to be a form of masked depression. The profiles found in our study make it possible to maintain that the psychiatric symptoms would not be present in all patients with FM. However, hyperalgesia, fatigue, joint stiffness characteristic of the FM following would be present, but in different degree.

The results of this study also support the need to personalize and improve pharmacological treatments,^{33,34} although hyperalgesia, stiffness and tiredness, common to

both profiles, could be approached with the usual treatments in both FM subtypes.

One limitation of this study is the relatively short series of patients in the type of sampling performed, that limits the generalization of the results and can affect risk of over adjustment of the clusters obtained. However, the elevated effect size makes it possible to maintain that the results reflect the true inter-group differences found.

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