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Gender Differences Among Patients with Fibromyalgia Undergoing Multidisciplinary Pain Rehabilitation

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ABSTRACT

Objective. This study was conducted to test the hypothesis that gender differences in physical and emotional functioning are present among patients with fibromyalgia undergoing multidisciplinary pain rehabilitation.

Design. Retrospective case-matched series.

Setting. Multidisciplinary pain rehabilitation center at a tertiary referral medical center.

Patients. Thirty-three consecutive men with fibromyalgia admitted from January 2002 through June 2005 were matched to 33 women with fibromyalgia for age, treatment dates, and program completion status.

Interventions. A 3-week outpatient multidisciplinary pain rehabilitation program based on a cognitive-behavioral model that incorporates analgesic medication withdrawal.

Outcome Measures. Multidimensional Pain Inventory (MPI), Short Form-36 Health Status Questionnaire (SF-36), Coping Strategies Questionnaire-Catastrophizing subscale (CSQ-C), and the Center for Epidemiologic Studies-Depression scale (CES-D) were administered before and after treatment. The numbers of patients using opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and benzodiazepines before and after treatment were compared.

Results. Pretreatment MPI and SF-36 scores revealed men had lower health perception ($P = 0.017$) and more physical limitations ($P = 0.004$) while women had greater life interference due to pain ($P = 0.005$). Mean differences in all pre- and post-treatment outcome measures demonstrated a statistically significant treatment response. However, men had lower post-treatment scores on the SF-36 health perception ($P = 0.023$), role limitations-physical ($P = 0.021$), and social functioning ($P = 0.033$) subscales. Significant within-gender reductions in opioid analgesic, NSAID, and benzodiazepine use were observed but no significant between-gender differences were identified.

Conclusions. These results support the hypothesis that pretreatment gender differences are present among fibromyalgia patients undergoing multidisciplinary pain rehabilitation and post-treatment gender differences persist despite improvements in physical and emotional functioning.

Key Words. Fibromyalgia; Multidisciplinary Pain Rehabilitation; Gender Differences

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Introduction

The clinical hallmark of fibromyalgia (FM) is diffuse musculoskeletal pain. The predominance of women with FM has been repeatedly demonstrated in epidemiological studies. In a community sample of persons living in the United States, the prevalence of FM was 3.4% (95% confidence interval [CI], 2.3–4.6) for women and 0.5% (95% CI, 0.0–1.0) for men [1]. Similar gender differences in prevalence have been reported in population samples from Bangladesh, Canada, Italy, Japan, and Turkey [2–6]. These consistent epidemiological findings across various populations have provided the impetus for investigating differences in symptoms and psychosocial functioning among men and women with FM.

Clinical differences in FM symptoms among men and women have been previously described. In a prospective study of 391 FM patients from the United States, women, compared with men, had more tender points (odds ratio 9.6, 95% CI, 2.0–46.3) and lower pain thresholds, as measured by dolorimetry [7]. Women were also more likely to experience fatigue, irritable bowel, sleep disturbance, and diffuse pain [7]. These results were replicated in a separate study involving a consecutive series of 536 (men = 67) patients diagnosed with FM in a U.S. university-based rheumatology clinic [8]. In this study, women had significantly more tender points and were more likely to have fatigue and generalized pain compared with men [8]. While these two studies provide evidence that women with FM experience more severe symptoms compared with men, contradictory findings were identified in a cohort of Israeli men and women. In this retrospective study, where 40 men and women with FM were matched for age and educational level, men reported significantly more pain, fatigue, stiffness, sleep disturbance, and irritable bowel [9].

Whereas significant differences in clinical symptoms among U.S. cohorts of men and women with FM have been reported, no significant differences in measures of comorbid depressive symptoms or anxiety have been identified among these patients. However, in the Buskila et al. study of Israeli men and women, men reported increased levels of depression, as measured by an 11-point Likert scale [9]. In this same study, standardized measures of depressive symptoms and anxiety, using subscales of the Arthritis Impact Measurement Scale, failed to detect significant differences between men and women. Moreover, the assessment of functioning, using the Fibromyalgia Impact Questionnaire and Short Form-36 Health Status Questionnaire (SF-36), demonstrated men had reduced levels of physical functioning and more limitations related to emotional problems, respectively [9]. Consistent with these measures of impaired physical and emotional functioning, the self-reported health status and quality of life for men were lower compared with women [9].

Reported variations in physical and emotional functioning among men and women with FM could be due in part to differences in study design and patient populations. While gender differences have been characterized for various groups of patients with FM, differences in physical and emotional functioning among men and women undergoing multidisciplinary pain rehabilitation have not been well studied. Furthermore, among patients with FM, the impact of gender differences on clinical outcomes following multidisciplinary pain rehabilitation has been underinvestigated. This study was conducted to test the hypothesis that pre- and post-treatment gender differences in physical and emotional functioning are present among patients with FM undergoing multidisciplinary pain rehabilitation.

Patients and Methods

Procedures

This retrospective case-matched series included 33 consecutive men with a diagnosis of FM admitted to the Mayo Clinic Comprehensive Pain Rehabilitation Center from January 2002 through June 2005. Thirty-three women with FM were matched for age, treatment dates, and program completion status. All patients were diagnosed with FM according to the American College of Rheumatology 1990 diagnostic criteria [10]. Consent was provided by all patients for use of their medical records for research purposes and the study protocol was approved by the Mayo Foundation Institutional Review Board.

The outpatient pain rehabilitation program is of 3-week duration. Admissions to the rehabilitation program occur on a revolving basis and patients attend 8 hours daily for 15 consecutive working days. Prior to admission, patients were receiving medical care from a physician and experienced incomplete symptomatic relief from multiple pharmacological trials, repeated courses of physical therapy, or interventional pain procedures. A cognitive-behavioral model serves as the

basis for treatment and incorporates physical reconditioning, biofeedback and relaxation training, stress management, chemical health education, activity moderation, and elimination of pain behaviors. Patients are involved in daily physical and occupational therapy as well as daily cognitive-behavioral group educational sessions where the aforementioned aspects of pain rehabilitation are addressed.

The primary goal of treatment is functional restoration. A secondary treatment goal is discontinuation or reduction in benzodiazepines and analgesic medications including opioid analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), and muscle relaxants. These medications are eliminated or reduced in patients with FM because they have no proven efficacy or provide limited symptomatic relief [11–14]. Medication discontinuation is not recommended for patients who use these drugs to treat comorbid medical or psychiatric illnesses. All medication tapers are initiated and coordinated by a physician following admission to the rehabilitation program.

Relevant clinical data were collected, including age, duration of illness, marital status, years of education, and the frequency of pre- and post-treatment medication use. Additionally, at the time of admission and dismissal, patients completed four standardized questionnaires to assess physical and emotional functioning.

Measurements

Multidimensional Pain Inventory

The Multidimensional Pain Inventory (MPI) is widely used to quantify the psychosocial impact of chronic pain [15]. The 52-item self-report questionnaire contains 12 subscales and responses to each item are scored by the patient on a seven-level Likert scale. The MPI has proven reliability and construct validity [16]. The raw scores are converted to standardized T-scores with a normative value of 50 and a standard deviation of 10 [17]. For purposes of the current study, five MPI subscales were used including pain severity, life interference due to pain, perceived life control, affective distress, and general activity. The selected MPI subscales are the measures for which the 3-week outpatient programming is expected to have the greatest impact immediately following treatment. These five subscales have been previously used to measure psychosocial functioning among patients undergoing multidisciplinary pain rehabilitation at our institution [18–20]. The pain severity subscale quantifies pain intensity and pain-related suffering while the life interference subscale assesses the interference of pain in relationships and daily activities. Life control and problem management are assessed by the perceived life control subscale and the affective distress subscale provides a measure of overall mood, irritability, and anxiety. The general activities subscale assesses participation in home tasks and social activities. Lower scores on the pain severity, life interference, and affective distress subscales signify less psychosocial impairment. Conversely, higher scores on the life control and general activity subscales are desirable and indicate less psychosocial impairment.

Short Form-36 Health Status Questionnaire

The SF-36 is a scale that was developed for use in clinical practice and research to assess physical and emotional health attributes during the past month [21–23]. The self-administered 36-item questionnaire contains eight subscales and each item is scored on a five-level Likert scale. The raw scores are converted to T-scores with a normative value of 50 and a standard deviation of 10. Standardized T-scores were calculated with the use of published age- and gender-specific mean scores and standard deviations for the SF-36 scales in the general U.S. population [24]. Higher scores reflect a more favorable health status. For purposes of the current study, five subscales were used including health perception, physical functioning, role limitations related to physical problems, role limitations from emotional problems, and social functioning. The selected SF-36 subscales are the measures for which the 3-week outpatient programming is expected to have the greatest impact immediately following treatment. These five subscales have been previously used to measure health attributes in patients undergoing pain rehabilitation at our institution [19,20]. Higher scores on the health perception subscale reflect a belief that personal health is excellent. Individuals involved in vigorous physical activities would score higher on the physical and social functioning subscales. Similarly, individuals who are able to work and perform other daily activities without limitations due to physical or emotional problems would score higher on both the physical and emotional role limitations subscales.

Pain Catastrophizing

The Catastrophizing subscale from the Coping Strategies Questionnaire (CSQ-C) assesses negative pain-related cognitions and emotions [25]. The validated self-administered questionnaire

contains six items scored on a Likert scale. Higher scores indicate negative expectancies regarding the capacity to cope with pain. Pain catastrophizing has been described as an "exaggerated negative 'mental set' associated with actual or anticipated pain experiences" [26].

Center for Epidemiologic Studies-Depression Scale

The Center for Epidemiologic Studies-Depression (CES-D) scale provides a measure of depressive symptoms that have occurred in the past week [27]. Four factors comprise the composite CES-D score including measures of general depressive and somatic symptoms, positive affect, and interpersonal difficulties. The 20-item self-administered questionnaire has established reliability and validity and is scored on a four-point Likert scale [28]. Total scores range from 0 to 60 where higher scores indicate greater levels of depression. A cutoff score of 16 or greater has been used to identify patients with minor depressive symptoms [29] while a cutoff score of 27 or greater has been used to identify major depression in patients who have chronic pain [30].

Statistical Analysis

Each man with FM was matched 1:1 to a woman with FM based on age (±1 year), treatment dates (±1 year), and program completion status with the optimal set of matched pairs identified using the approach described by Rosenbaum [31]. Patient characteristics, medication use, and survey responses at baseline, follow-up, and the proportional change from baseline were compared between men and women using a paired signed rank test for continuous variables and conditional logistic regression for categorical variables [32]. The frequency of pre- and post-treatment medication use within each group was compared using a sign test. In all analyses, P values ≤ 0.05 were considered statistically significant.

Results

Demographic information for men (N = 33) and women (N = 33) are contained in Table 1. The mean age of men was 46.9 years and the mean age of women was 46.7 years. The majority of men and women were white (90.6%), married (68.2%), and had completed high school (97.0%). Men had been diagnosed with FM for a mean of 11.3 years (SD 12.7) while women had been diagnosed for a mean of 9.5 years (SD 8.9). No significant gender differences in age, education, or pain duration were identified.

Table 1 Characteristics of men and women with fibromyalgia admitted to the Mayo Comprehensive Pain Rehabilitation Center

Characteristics	Men (N = 33)	Women* (N = 33)
Age, mean years (SD)	46.9 (11.4)	46.7 (11.2)
Ethnicity, white (%)	93.5	87.5
Marital status, married (%)	68.8	66.7
Education, mean years (SD)	14.7 (3.8)	14.5 (1.7)
Completed high school (%)	93.8	100.0
Pain duration, mean years (SD)†	11.3 (12.7)	9.5 (8.9)
Completed treatment (%)	29 (87.9)	29 (87.9)

* Women matched for age, treatment dates, and program completion status.
† Data were missing for one matched set.

The level of attrition was low where 29 of 33 (88%) men completed the 3-week rehabilitation program. The comparison group was also matched for program completion and contained four women who did not complete treatment. These eight patients were dismissed from the outpatient program after a mean of 6.3 days (SD 3.7). The indication for early dismissal included discrepant expectations of treatment (N = 3), acute medical illness (N = 3), frequent absences (N = 1), and the reason for early dismissal was undetermined for one patient.

Table 2 contains the mean pre- and post-treatment MPI subscale T-scores for men and women. The pretreatment assessment of psychosocial functioning revealed men and women had similar levels of pain severity, perceived life control, affective distress, and general activity. However, compared with men, women reported greater life interference due to pain ($P = 0.005$). The mean difference in pre- and post-treatment MPI subscale scores demonstrated significant within-gender improvements ($P < 0.001$ in each case) in psychosocial functioning. Paired signed rank tests did not show significant between-gender differences when post-treatment scores for men and women were compared. However, analysis comparing the proportional change from pre- to post-treatment, while accounting for the 1:1 matched study design, revealed women experienced greater improvement on the life interference subscale compared with men ($P = 0.022$).

Table 3 contains the mean pre- and post-treatment subscale T-scores for the SF-36. A comparison of the pretreatment scores showed men and women had similar levels of physical functioning, social functioning, and role limitations related

Table 2 Pre- and post-treatment subscale T-scores from the Multidimensional Pain Inventory for men and women with fibromyalgia

	Pre-Treatment					Post-Treatment							
	Men (N = 33)		Women (N = 33)		Between Subjects*	Men (N = 24)		Within Subjects†	Women (N = 24)		Within Subjects†	Between Subjects*	Between Subjects Percentage Change‡
Subscale	Mean	SD	Mean	SD	*P* Value	Mean	SD	*P* Value	Mean	SD	*P* Value	*P* Value	*P* Value
Pain severity	49.9	8.6	51.8	8.6	ns	38.7	12.6	<0.001	37.1	9.4	<0.001	ns	ns
Interference with life	48.8	8.3	53.6	6.9	0.005	38.1	10.8	<0.001	34.8	12.7	<0.001	ns	0.022
Perceived life control	47.6	7.9	46.0	7.2	ns	56.2	7.0	<0.001	57.9	6.4	<0.001	ns	ns
Affective distress	48.2	9.5	49.7	9.2	ns	37.5	9.8	<0.001	39.9	8.7	<0.001	0.061	ns
General activity level	50.5	10.4	50.9	8.1	ns	57.0	9.7	0.001	57.2	10.7	<0.001	ns	ns

* Paired signed rank test comparing men and women.
† One-sample signed rank test comparing the change from baseline to 0.
‡ Paired signed rank test comparing the proportional change from baseline between men and women.
ns = not statistically significant ($P > 0.1$).

Table 3 Pre- and post-treatment subscale T-scores from the Short Form-36 Health Status Questionnaire (SF-36) for men and women with fibromyalgia

	Pre-Treatment					Post-Treatment						
	Men (N = 33)		Women (N = 33)		Between Subjects*	Men (N = 21)		Within Subjects†	Women (N = 21)		Within Subjects†	Between Subjects*
Subscale	Mean	SD	Mean	SD	*P* Value	Mean	SD	*P* Value	Mean	SD	*P* Value	*P* Value
Health perception	29.1	13.0	35.8	11.5	0.017	36.4	15.9	<0.001	47.2	10.5	<0.001	0.023
Physical functioning	26.7	10.7	25.7	13.5	ns	38.6	11.2	<0.001	39.2	9.9	<0.001	ns
Role-physical	24.4	9.4	28.3	4.3	0.004	34.8	15.9	<0.001	43.7	11.1	<0.001	0.021
Role-emotional	35.7	13.6	36.7	12.8	ns	45.9	13.5	0.005	48.7	9.1	0.001	ns
Social functioning‡	26.5	10.5	28.2	10.9	ns	38.4	12.9	<0.001	45.2	9.7	<0.001	0.033

* Paired signed rank test comparing men and women.
† One-sample signed rank test comparing the change from baseline to 0.
‡ N = 22 at post-treatment.
ns = not statistically significant ($P > 0.1$).

to emotional problems. However, compared with women, men had significantly more limitations on the health perception ($P = 0.017$) and role limitations-physical ($P = 0.004$) subscales. The mean difference in all pre- and post-treatment subscale scores of the SF-36 demonstrated significant within-gender improvements in functioning ($P \leq 0.005$ in all cases). However, compared with women, paired signed rank tests revealed men had more post-treatment limitations on the health perception ($P = 0.023$), role limitations-physical ($P = 0.021$), and social functioning ($P = 0.033$) subscales. Further analysis comparing the proportional change from pre- to post-treatment, while accounting for the 1:1 matched study design, demonstrated no significant gender differences.

Table 4 contains the mean pre- and post-treatment scores from the CES-D and CSQ-C. A

Table 4 Pre- and post-treatment scores from the Center for Epidemiological Studies-Depression scale (CES-D) and Coping Strategies Questionnaire catastrophizing subscale (CSQ-C) for men and women with fibromyalgia

	Pre-Treatment					Post-Treatment						
	Men (N = 32)		Women (N = 32)		Between Subjects*	Men (N = 24)		Within Subjects†	Women (N = 24)		Within Subjects†	Between Subjects*
Scale or Subscale	Mean	SD	Mean	SD	*P* Value	Mean	SD	*P* Value	Mean	SD	*P* Value	*P* Value
CES-D	25.7	10.1	26.4	11.4	ns	14.9	13.0	<0.001	16.2	8.6	<0.001	ns
CSQ-C	13.3	6.5	13.8	6.2	ns	8.3	6.1	0.004	5.8	5.9	<0.001	ns

* Paired signed rank test comparing men and women.
† One-sample signed rank test comparing the change from baseline to 0.
ns = not statistically significant ($P > 0.1$).

Table 5 Frequency of pre- and post-treatment medication use for men and women with fibromyalgia

	Pre-Treatment			Post-Treatment				
Drug Class	Men (N = 33) n (%)	Women (N = 33) n (%)	Between Subjects* *P* Value	Men (N = 33) n (%)	Within Subjects† *P* Value	Women (N = 33) n (%)	Within Subjects† *P* Value	Between Subjects* *P* Value
Opioids	10 (30)	11 (33)	ns	0 (0)	0.002	1 (3)	0.002	ns
Benzodiazepines	10 (30)	13 (39)	ns	5 (15)	ns	4 (12)	0.004	ns
NSAIDs	14 (42)	12 (36)	ns	4 (12)	0.002	4 (12)	0.008	ns
Muscle relaxants	6 (18)	3 (10)	ns	2 (6)	ns	1 (3)	ns	ns
Antidepressants								
SSRI	14 (42)	15 (45)	ns	11 (33)	ns	15 (45)	ns	ns
Tricyclic	8 (24)	6 (18)	ns	7 (21)	ns	4 (12)	ns	ns

* Conditional logistic regression comparing men and women.
† Sign test.
ns = not statistically significant ($P > 0.1$); NSAIDs = nonsteroidal anti-inflammatory drugs; SSRI = selective serotonin reuptake inhibitor; tricyclic = tricyclic antidepressants.

comparison of pre-treatment scores showed men and women had similar levels of depression and pain catastrophizing. The mean difference in pre- and post-treatment scores revealed significant within-gender improvements in depressive symptoms and catastrophizing ($P < 0.004$ in all cases). At program completion, a comparison of post-treatment scores showed no significant between-gender differences.

Table 5 contains the pre- and post-treatment medication use patterns for the study cohort. The mean morphine equivalence for men (N = 10) was 63.6 mg/day (SD 86, range 11–300). One man was taking 300 mg/day, another was taking 90 mg/day, and the remaining 8 patients were taking less than 45 mg/day. The mean morphine equivalence for women (N = 11) was 39.1 mg/day (SD 51.6, range 7.5–165). One woman was taking 165 mg/day, another was taking 112.5 mg/day, and the remaining patients were taking less than 37.5 mg/day. The frequency of pre- and post-treatment medication use was compared and the number of men taking opioids ($P = 0.002$) and NSAIDs ($P = 0.002$) was significantly reduced at the time of program completion. Similarly, compared with program admission, the number of women taking opioids ($P = 0.002$), NSAIDs ($P = 0.008$), and benzodiazepines ($P = 0.004$) was significantly reduced at program completion. Conditional logistic regression comparing men and women, while accounting for the 1:1 matched study design, demonstrated no significant between-gender differences in the pretreatment use of opioid analgesics, benzodiazepines, NSAIDs, muscle relaxants, selective serotonin reuptake inhibitors (SSRI), or tricyclic antidepressants. Similar analysis at program completion revealed no significant between-gender differences in medication use.

Discussion

The results of this study support the hypothesis that pre- and post-treatment differences in physical and emotional functioning are present among men and women with FM undergoing multidisciplinary pain rehabilitation. A comparison of pre-treatment scores from the SF-36 revealed men had more limitations related to health perception and physical problems while women had greater life interference due to pain, as measured by the MPI. Despite improvements in all outcome measures, statistically significant post-treatment gender differences were identified. When post-treatment outcomes were compared, men had persistently more limitations on the health perception and role limitations-physical subscales of the SF-36. Whereas men and women had similar pretreatment levels of social functioning, men had more limitations on the SF-36 social functioning subscale at program completion. Although men had more favorable pre-treatment scores on the MPI life interference subscale, the proportional change on this outcome measure was greater for women.

When speculating about the basis of gender difference among patients with FM, two aspects of this study require further consideration. First, what gender differences are directly related to FM and, second, what are the gender-related treatment effects of multidisciplinary pain rehabilitation. The pre-treatment gender differences identified herein were not demonstrated in previous studies of men and women with FM from the United States [7,8]. However, similar gender differences were reported in the aforementioned study by Buskila and colleagues, where more limitations in health status, emotional functioning, and physical functioning were identified among

Israeli men compared with women [9]. The similarities between our results and the findings of Buskila et al. [9] could be due in part to use of similar research methodologies in that both studies were conducted at tertiary referral medical centers and a case-matched retrospective design was used. While biological and psychological factors have been proposed to account for some observed gender-related differences [33], our findings suggest sociological influences could, in part, contribute to pretreatment differences in functioning. We hypothesize that as a result of sociological influences, men are expected to be involved in more physically tasking activities. Due to these sociological expectations, FM-related limitations in role-physical functioning among men could lead to more limitations in health perception compared with women.

Following multidisciplinary pain rehabilitation, gender differences in pain intensity and physical functioning have been reported for heterogeneous groups of chronic pain patients [34–36]. However, gender differences following pain rehabilitation for FM have not been well characterized. In a recent Norwegian study, 208 patients with "chronic widespread pain" were randomized to light or extensive multidisciplinary treatment vs a usual care–control group [37]. The primary outcome measure was work status 1 year following completion of treatment. For purposes of this randomized trial [37], FM was considered to represent a chronic widespread pain disorder but not all patients in the trial fulfilled the American College of Rheumatology diagnostic criteria for FM [10]. At 1-year follow-up, women, but not men, randomized to the extensive rehabilitation group had fewer absent days from work compared with the usual care group [37]. These differences in occupational functioning are consistent with our post-treatment findings that showed men had more severe limitations in role-physical functioning, social functioning, and health perception. Persistent limitations in these functional domains among men could adversely impact occupational performance compared with women. Furthermore, these findings support our speculation that sociological influences may contribute significantly to gender differences among patients with FM. As other investigators have noted, it is premature to recommend "gender-specific" interventions for FM [34]. However, incorporating treatments that focus on gender-specific sociological circumstances may improve treatment outcomes for men.

While the sample size in the current study precludes a comparison of men and women taking opioids vs those not taking opioids, the findings reported herein may further extend previous outcomes research related to medically directed withdrawal of analgesic medications and benzodiazepines during multidisciplinary pain rehabilitation [18,20]. In these two studies, the number of patients taking opioid analgesics, benzodiazepines, NSAIDs, and muscle relaxants at program admission was significantly reduced at the time of program completion. Despite significant reductions in a broad range of analgesic and psychotropic medications, mean differences in pre- and post-treatment scores from the MPI, SF-36, CES-D, and CSQ-C scales and subscales demonstrated statistically significant improvements in all measured domains of physical, emotional, and social functioning [18,20]. In the current study, the number of men and women taking opioid analgesics and NSAIDs was significantly reduced during the course of treatment but no post-treatment between-gender differences were identified. Conversely, whereas the number of women taking benzodiazepines was significantly reduced, no significant change in the number of men taking benzodiazepines was detected.

Our study has several limitations. The use of multiple comparisons in this small sample could increase the risk of a Type I error. However, these findings provide important preliminary data that could help guide the focus of future investigations regarding the basis and impact of gender differences among patients with FM. All patients were specifically referred for multidisciplinary treatment. Following referral, patients were self-selected and had the health care resources and motivation to participate in a daily 3-week outpatient rehabilitation program. As a result of this selection bias, the study results may not be applicable to all patients with FM. However, the level of pretreatment functioning, as assessed on the MPI and CES-D, is similar to a cohort of FM patients treated at our institution's FM clinic [38,39]. In this series of 100 FM patients, which included seven men, the mean pre-treatment pain severity and life interference subscales of the MPI were 46.2 (SD 8.8) and 42.8 (SD 11.7), respectively [38]. The mean values for the other MPI subscales, including life control, affective distress, and general activity level, were similar to the findings reported herein [38]. The mean pre-treatment CES-D score was 23.0 (11.2), which is also comparable to our current findings [39].

Finally, while the immediate post-treatment outcomes reported herein were favorable, 6- and 12-month outcome measures are needed to establish the duration of treatment response and the persistence of gender differences in physical and emotional functioning.

Among patients with FM undergoing multidisciplinary pain rehabilitation, recognition of gender differences could foster incorporation of specific treatments aimed at gender-specific impairments. Further research is needed to identify specific clinical interventions that could attenuate gender-related differences and thereby improve treatment outcomes. Moreover, experimental pain models and neuroendocrine outcome measures should be incorporated into clinical research protocols to elucidate the specific mechanisms that mediate the differential gender effects of multidisciplinary pain rehabilitation.

References

1 Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995; 38:19–28.

2 Choudhury AK, Yunus MB, Haq SA, et al. Clinical features of fibromyalgia syndrome in a Bangladeshi population. J Musculoskelet Pain 2001;9:25–33.

3 White KP, Speechley M, Harth M, Ostbye T. The London Fibromyalgia Epidemiology Study: Comparing the demographic and clinical characteristics in 100 random community cases of fibromyalgia versus controls. J Rheumatol 1999;26:1577–85.

4 Salaffi F, De Angelis R, Grassi W. Prevalence of musculoskeletal conditions in an Italian population sample: Results of a regional community-based study. I. The MAPPING study. Clin Exp Rheumatol 2005;23:819–28.

5 Nishikai M. Fibromyalgia in Japanese. J Rheumatol 1992;19:110–4.

6 Topbas M, Cakirbay H, Gulec H, et al. The prevalence of fibromyalgia in women aged 20–64 in Turkey. Scand J Rheumatol 2005;34:140–4.

7 Wolfe F, Ross K, Anderson J, Russell IJ. Aspects of fibromyalgia in the general population: Sex, pain threshold, and fibromyalgia symptoms. J Rheumatol 1995;22:151–6.

8 Yunus MB, Inanici F, Aldag JC, Mangold RF. Fibromyalgia in men: A comparison of clinical features with women. J Rheumatol 2000;27:485–90.

9 Buskila D, Neumann L, Alhoashle A, Abu-Shakra M. Fibromyalgia syndrome in men. Semin Arthritis Rheum 2000;30:47–51.

10 Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis Rheum 1990;33:160–72.

11 Yunus MB, Masi AT, Aldag JC. Short term effects of ibuprofen in primary fibromyalgia syndrome: A double blind, placebo controlled trial. J Rheumatol 1989;16:527–32.

12 Goldenberg DL, Felson DT, Dinerman H. A randomized, controlled trial of amtriptyline and naproxen in the treatment of patients with fibromyalgia. Arthritis Rheum 1986;29:1371–7.

13 Russell IJ, Fletcher EM, Michalek JE, McBroom PC, Hester GG. Treatment of primary fibrositis/fibromyalgia syndrome with ibuprofen and alprazolam. A double-blind, placebo-controlled study. Arthritis Rheum 1991;34:552–60.

14 Tofferi JK, Jackson JL, O'Malley PG. Treatment of fibromyalgia with cyclobenzaprine: A meta-analysis. Arthritis Rheum 2004;51:9–13.

15 Kerns RD, Turk DC, Rudy TE. The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). Pain 1985;23:345–56.

16 Bernstein IH, Jaremko M, Hinkley BS. On the utility of the West Haven-Yale Multidimensional Pain Inventory. Spine 1995;20:956–63.

17 Rudy TE. Multiaxial Assessment of Pain Multidimensional Pain Inventory: Computer Program User's Manual, Version 2.0. Pittsburgh, PA: University of Pittsburgh; 1989.

18 Rome JD, Townsend CO, Bruce BK, et al. Chronic noncancer pain rehabilitation with opioid withdrawal: Comparison of treatment outcomes based on opioid use status at admission. Mayo Clin Proc 2004;79:759–68.

19 Townsend CO, Sletten CD, Bruce BK, et al. Physical and emotional functioning of adult patients with chronic abdominal pain: Comparison with patients with chronic back pain. J Pain 2005;6:75–83.

20 Hooten WM, Townsend CO, Sletten CD, Bruce BK, Rome JD. Treatment outcomes after multidisciplinary pain rehabilitation with analgesic medication withdrawal for patients with fibromyalgia. Pain Med 2006 (in press).

21 Ware JE, Sherbourne CD. The MOS 36-Item Short Form Health Survey (SF-36): 1. Conceptual framework and item selection. Med Care 1992;30:473–83.

22 McHorney CA, Ware JE, Rogers W, Raczek AE, Lu JFR. The validity and relative precision of MOS Short- and Long-Form Health Status Scales and Dartmouth COOP charts: Results from the Medical Outcomes Study. Med Care 1992;30:MS253–65.

23 McHorney CA, Ware JE, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–63.

24 Ware JE. SF-36 Health Survey Manual & Interpretation Guide. Boston, MA: Health Institute, New England Medical Center; 1993.

25 Sullivan MJL, Pivik J. The Pain Catastrophizing Scale: Development and validation. Psychol Assess 1995;7:524–32.
26 Sullivan MJ, Thorn B, Haythornthwaite JA, et al. Theoretical perspectives on the relation between catastrophizing and pain. Clin J Pain 2001;17:52–64.
27 Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. J Appl Psychol Meas 1977;1:385–401.
28 Radloff LS, Locke BZ. The community mental health assessment survey and the CES-D Scale. In: Weissman M, Myers J, Ross C, eds. Community Surveys. Piscataway, NJ: Rutgers University Press; 1977:177–89.
29 Weissman MM, Sholomskas D, Pottenger M, Prusoff BA, Locke BZ. Assessing depressive symptoms in five psychiatric populations: A validation study. Am J Epidemiol 1977;106:203–14.
30 Geisser ME, Roth RS, Robinson ME. Assessing depression among persons with chronic pain using the Center for Epidemiological Studies-Depression Scale and the Beck Depression Inventory: A comparative analysis. Clin J Pain 1997;13:163–70.
31 Rosenbaum PR. Optimal matching for observational studies. J Am Stat Assoc 1989;84:1024–32.
32 Breslow NE, Day NE. Statistical Methods in Cancer Research. Volume 1—The Analysis of Case–Control Studies. IARC Scientific Publications, No. 32. Lyon: International Agency for Research on Cancer; 1980.
33 Yunus MB. Gender differences in fibromyalgia and other related syndromes. J Gend Specif Med 2002;5:42–7.
34 Keogh E, McCracken LM, Eccleston C. Do men and women differ in their response to interdisciplinary chronic pain management? Pain 2005;114:37–46.
35 Edwards RR, Doleys DM, Lowery D, Fillingim RB. Pain tolerance as a predictor of outcome following multidisciplinary treatment for chronic pain: Differential effects as a function of sex. Pain 2003;106:419–26.
36 Jensen IB, Bergstrom G, Ljungquist T, Bodin L, Nygren AL. A randomized controlled component analysis of a behavioral medicine rehabilitation program for chronic spinal pain: Are the effects dependent on gender? Pain 2001;91:65–78.
37 Skouen JS, Grasdal A, Haldorsen EMH. Return to work after comparing outpatient multidisciplinary treatment program versus treatment in general practice for patients with chronic widespread pain. Eur J Pain 2006;10:145–52.
38 Worrel LM, Krahn LE, Sletten CD, Pond GR. Treating fibromyalgia with a brief interdisciplinary program: Initial outcomes and predictors of response. Mayo Clin Proc 2001;76:384–90.
39 Pfeiffer A, Thompson JM, Nelson A, et al. Effects of a 1.5-day multidisciplinary outpatient treatment program for fibromyalgia: A pilot study. Am J Phys Med Rehabil 2003;82:186–91.