

Impact of Tobacco Use in Patients Presenting to a Multidisciplinary Outpatient Treatment Program for Fibromyalgia

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Objectives: This study examined the relationship between the severity of fibromyalgia symptoms and current tobacco use in patients evaluated at a specialized fibromyalgia treatment program.

Methods: Demographic and clinical data from 984 consecutive patients evaluated at the Mayo Clinic Fibromyalgia Treatment Program including the Fibromyalgia Impact Questionnaire (FIQ) were prospectively collected and stored in an electronic medical record and an electronic database. Univariate analyses were performed comparing tobacco users and nonusers. A post-hoc analysis of covariance was conducted for tobacco use, using group differences of confounding clinical and demographic variables. A P value ≤ 0.05 was accepted as the level of significance.

Results: One hundred and forty-five patients were identified as tobacco users (14.7%). Tobacco use was associated with greater pain intensity as measured by pain scales and the pain component of the FIQ. Tobacco users had a greater FIQ composite score 70.0(15.1) versus 61.8(16.8), $P < 0.001$. By univariate analysis, tobacco users had higher scores on all the FIQ components and fewer good days and more days of work missed per week. Tobacco use was associated with several confounding clinical and demographic variables including lower education, higher unemployment, not being married or widowed, and history of abuse. After adjusting for these confounding variables, tobacco users continued to have greater pain intensity, a higher total and component FIQ scores except for fatigue. Smoking was not associated with a higher number of tender points.

Discussion: Current tobacco use was associated with more severe fibromyalgia symptoms in patients presenting to a specialized fibromyalgia treatment program.

Key Words: fibromyalgia syndrome, smoking, fibromyalgia impact questionnaire

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There is increasing evidence in the literature that there is an association between smoking status in patients with chronic pain and pain intensity and functional status.^{1–5} Fibromyalgia (FM) is a chronic pain condition characterized by widespread pain for greater than 3 months and the presence of 11 of 18 specific tender points.⁶ Yunus et al⁵ reported that among patients evaluated for FM at a rheumatology clinic ($N = 233$) that smokers with FM ($N = 51$) had greater pain intensity, patient global severity, functional disability, and numbness than nonsmokers. Similar studies have not been undertaken by other investigators to confirm these findings in patients with FM. The purpose of this study is to determine the overall prevalence of smoking in a large cohort of patients with FM and to determine if smoking status has an impact on the clinical features of FM.

METHODS AND MATERIALS

This study was approved by the Mayo Clinic Institutional Review Board. Participants consisted of 1016 patients with FM who consecutively participated in the multidisciplinary outpatient treatment program for FM at the Mayo Clinic, Rochester, MN from May 2001 to April 2004. Data were incomplete on tobacco use in 4 patients and incomplete on the number of FM tender points in another 4 patients, and these 8 patients were excluded from further analysis. An additional 24 patients had fewer than 11 FM tender points and were also excluded from further analysis. All participants provided written consent to participate in research protocols. Participants underwent a standardized preliminary evaluation with a registered nurse where demographic and social variables, 11 point numeric pain scores assessing for worst, least, and average pain, and the number of FM tender points were ascertained and entered into the electronic medical record. During this nursing evaluation, participants were asked if they were currently smoking cigarettes or using tobacco products. Participants who affirmed current use of tobacco products were classified as tobacco users and participants who denied current use of these products were classified as tobacco nonusers. A psychiatrist or rheumatologist saw the patients after the nurse's evaluation and diagnosed FM based on the American College of Rheumatology criteria.⁶ Participants completed the FM Impact Questionnaire (FIQ) to assess and quantify pain severity and life interference, and responses to individual questions were stored in an electronic database.^{7–10} The FIQ contains 10 items measuring physical functions, symptoms of pain, fatigue, morning tiredness, stiffness, job difficulty,

depression and anxiety, and days of worked missed and overall well-being in the previous week. Scoring as described by Bennett¹¹ is carried out in such a way that higher scores indicate a greater impact of FMS on the patient, with a possible range of 0 to 100. It is a brief self-administered instrument that takes approximately 5 minutes to complete. The FIQ was compared with the Arthritis Impact Measurement Scale, a well-known and clinically sound instrument used to measure health status of patients with rheumatic disease.⁷ Both scales are self-administered. The test-retest reliability of the FIQ was 0.56 to 0.95, and the Arthritis Impact Measurement Scale was 0.64 to 0.91 when 64 women with the diagnosis of FMS using the American College of Rheumatology criteria completed the scales.⁷ The conclusion was that the FIQ had sufficient test-retest reliability and could be a valuable outcome measure in FMS patients.⁷ An analytical review of outcome studies in FMS recommended the use of the FIQ as a measurement of outcomes.¹²

Statistical Analysis

The differences in mean scores of the FIQ score and scales, pain scores, and number of FM tender points between patients currently using or not using tobacco products were calculated by univariate analysis of variance. Categorical variables were compared using 2-sided χ^2 tests. A post-hoc analysis of covariance was conducted for tobacco use status using significant group differences including age, sex, marital status, abuse history, employment status, and educational level as covariates. Adjustments were not made in the *P* values to account for multiple comparisons. In all cases, a 2-tailed *P* value of ≤ 0.05 was considered significant. All analyses were completed using SPSS (version 15.0).

RESULTS

Current tobacco use was reported by 14.7% of the study population. Tobacco users were younger (43 ± 10 vs. 49 ± 13 , $P < 0.0001$), less educated ($P = 0.008$), less frequently married or widowed ($P = 0.006$), and more frequently unemployed ($P < 0.0001$) (Table 1). Also tobacco users reported a prior history of physical, sexual, emotional, or verbal abuse (37.2% vs. 28.2%, $P = 0.03$). The percent of participants who used alcohol was lower among participants who used tobacco, but this observation was not significant.

Tobacco users reported greater pain intensity as measured by 3 numeric rating scores obtained during the nursing interview and the pain component of the FIQ (Table 2). These findings remained significant even after adjusting for conflicting variables. Tobacco users had a higher FIQ score and scored higher on all components of the FIQ than tobacco nonusers by both univariate and adjusted analysis with the exception that report of fatigue lost significance with adjusted analysis. Tobacco users also had fewer good days and missed more days of work than tobacco nonusers by univariate analysis, but these observations lost significance with adjusted analysis. No difference was found between the number of FM tender points between tobacco users and nonusers.

DISCUSSION

Tobacco use was found to be associated with self-report of significantly greater pain intensity on the 3 pain

TABLE 1. Demographic and Social Characteristics of Tobacco Users and Nonusers With FM

	N/ Mean (%/SD)		<i>P</i>
	Tobacco Users N = 145	Tobacco Nonusers N = 839	
Sex			0.011
Female	131 (14.1)	801 (85.9)	
Male	14 (26.9)	38 (73.1)	
Age	43 (10)	49 (13)	< 0.0001
Physical/emotional/ sexual/verbal abuse history			0.026
Yes	54 (37.8)	236 (28.5)	
No	89 (62.2)	591 (71.5)	
Current alcohol use			0.54
Yes	57 (39.3)	352 (42.1)	
No	88 (60.7)	485 (57.9)	
Marital status			0.006
Married	99 (68.3)	640 (76.3)	
Nonmarried	46 (31.7)	179 (21.3)	
Widowed	0 (0)	20 (2.4)	
Employment status			< 0.0001
Employed	78 (53.8)	447 (53.3)	
Homemaker	9 (6.2)	73 (8.7)	
Retired	4 (2.8)	114 (13.6)	
Unemployed	54 (37.2)	205 (24.4)	
Education Level			0.008
< 12 grade	8 (5.6)	29 (3.5)	
High school diploma or equivalent	47 (32.9)	255 (30.8)	
Some college/technical college degree	57 (39.9)	251 (30.4)	
College graduate	31 (21.7)	292 (35.3)	

scales and the pain component of the FIQ. Yunus et al⁵ also found that among patients with FM, smokers had greater pain intensity as measured by a visual analog pain scale than nonsmokers (62.3 ± 18.6 vs. 69.5 ± 16.7 , $P = 0.02$).

The functional impact of FM was greater in tobacco users as evidenced by the higher FIQ composite score. All the components of the FIQ except the number of good days and the number of days of work missed per week, and fatigue were elevated in tobacco users suggesting that the greater functional impact of FM felt by these patients was broad-based. Other studies have demonstrated that chronic pain patients who smoke suffer greater functional impairment secondary to pain. Yunus et al⁵ found smokers with FM had greater patient global severity and worse Health Assessment Questionnaire scores. Smokers enrolled in the national spine network database had more severe back pain and lower scores on all the SF-36 subscales.⁴ Population-based studies in Great Britain, Norway, and Germany also found that tobacco use was associated with more severe symptoms from musculoskeletal disorders.^{2,13,14} The redundancy of findings among these different studies suggests

TABLE 2. FM Symptoms by Tobacco Use Status

	Tobacco Users, N = 145 Mean (SD)	Tobacco Nonusers N = 839, Mean (SD)	Univariate Analysis	Adjusted Analysis*
Fibromyalgia Impact Questionnaire				
Total score	70.0 (15.1)	61.8 (16.8)	[F(1,978) = 29.892, P < 0.001]	[F(1,951) = 15.640, P < 0.001]
Physical impairment (0-3)	5.32 (2.09)	4.53 (2.27)	[F(1,979) = 15.522, P < 0.001]	[F(1,952) = 11.624, P = 0.001]
Good d/wk	1.28 (1.37)	1.62 (1.62)	[F(1,971) = 5.514, P = 0.02]	[F(1,944) = 2.516, P = 0.113]
Missed work, d/wk	3.47 (2.61)	2.76(2.51)	[F(1,948) = 9.378, P = 0.002]	[F(1,921) = 3.428, P = 0.064]
Work interference	7.48 (2.32)	6.72 (2.41)	[F(1,971) = 12.261, P < 0.001]	[F(1,944) = 4.298, P = 0.038]
Pain	7.74 (1.78)	7.05 (2.09)	[F(1,973) = 13.745, P < 0.001]	[F(1,946) = 6.700, P = 0.010]
Fatigue	8.56 (1.66)	8.10(2.08)	[F(1,974) = 6.287, P = 0.012]	[F(1,947) = 3.358, P = 0.067]
Awakened refreshed	8.49 (1.86)	7.75 (2.34)	[F(1,976) = 13.040, P < 0.001]	[F(1,949) = 6.257, P = 0.013]
Stiffness	8.08 (1.93)	7.18 (2.34)	[F(1,976) = 18.834, P < 0.001]	[F(1,949) = 12.352, P < 0.001]
Anxiety	5.73 (2.93)	4.86 (3.04)	[F(1,976) = 10.062, P = 0.002]	[F(1,949) = 5.375, P = 0.021]
Depression	5.45 (3.19)	3.91 (3.16)	[F(1,975) = 28.673, P < 0.001]	[F(1,948) = 18.108, P < 0.001]
Pain Numeric Rating Scale (0-10)				
Average	6.46 (1.60)	5.95 (1.79)	[F(1,959) = 10.119, P = 0.002]	[F(1,935) = 6.306, P = 0.012]
Best	4.18 (1.89)	3.65 (1.86)	[F(1,959) = 9.604, P = 0.002]	[F(1,935) = 6.271, P = 0.012]
Worst	9.57 (2.31)	9.15 (1.45)	[F(1,958) = 8.226, P = 0.004]	[F(1,934) = 4.651, P = 0.031]
FM tender points	16.4 (2.17)	16.1(2.17)	[F(1,982) = 2.453, P = 0.118]	[F(1,955) = 1.171, P = 0.280]

*Adjusted for clinical and demographic variables.

that our observation that tobacco users with FM had more subjective impairment than tobacco nonusers may generalize to other chronic pain conditions.

The overall rate of current tobacco use in the study group was 14.7% and for women 14.1%, which is lower for the overall national prevalence of tobacco use of 20.6% and lower for the national prevalence rate among women of 19.2%.¹⁵ This rate is considerably lower than the 21.9% reported by Yunus et al, but is comparable to the 15.3% smoking rate among 25,417 patients with rheumatic diseases who are enrolled in the National Data Bank for Rheumatic Diseases and the 15.0% smoking rate among 13,961 female patients who are enrolled in the National Spine Network Database.^{4,5,16} As our study population was not community based, the lower rate may reflect a selection bias or regional differences. The current rate of tobacco consumption in community patients with FM is unknown and it is unknown if exposure to tobacco products is a risk factor for the development of FM.¹⁷ Population-based

studies of nonspecific musculoskeletal disorders found that smoking was associated with greater risk of having a painful disorder.^{2,13,14} However, the relationship between smoking and the development of low back pain is less clear. Two large systematic reviews of the literature regarding the association of low back pain and smoking status had somewhat conflicting results. The Goldberg et al¹⁸ review of 38 studies concluded that smoking was associated with an increased incidence of nonspecific low back pain, but the Leboeuf-Yde¹⁹ review of 41 studies concluded that smoking was a weak risk indicator but not a cause for low back pain. If tobacco use was a strong risk factor for the development of FM, the percentage of patients who use tobacco in our clinic should have been greater than observed.

Tobacco use in our cohort was associated with several confounding variables including a history of physical, sexual, emotional, or verbal abuse, lower rates of current marriage and widowhood, and educational and employment variables associated with lower socioeconomic class.

These variables have previously been reported to have a higher prevalence among patients with FM or be associated with worse FM symptoms.^{20–25} Despite tobacco's association with these confounding variables, a multivariate analysis demonstrated that smoking was still associated with a higher FIQ score.

Interestingly, the number of FM tender points did not vary between tobacco users and nonusers in our study, a similar observation made by Yunus et al.⁵ Furthermore, in our cohort the number of FM tender points correlated poorly with the total FIQ score ($r = 0.049$). Currently, there are no widely accepted measurable biologic or physiologic abnormalities found in patients with FM that correlates with disease severity.²⁶

A major limitation of this study was lack of data on former use of tobacco products. A population study from Great Britain of 21,000 adults demonstrated that even a history of past tobacco use was a risk factor for developing musculoskeletal pain.¹⁴ Data on the quantity or duration of tobacco use, or information on the degree of nicotine dependence were not obtained. Such information could have been used to determine if FM symptoms correlated with severity of nicotine dependence. Yunus et al⁵ did demonstrate a dose-response relationship between packs of cigarettes smoked per day and FM symptoms. Another limitation of this study is the lack of formal testing for depressive disorders in our study cohort. Depression has been associated with more severe FM symptoms and smoking is associated with depressive disorders.^{27–29} In this study, smokers had higher depression scores on the FIQ. The FIQ depression score has been shown to correlate with the Arthritis Impact Measurement Scales depression scale.⁷ Potentially, depression could be an unmeasured confounding factor that accounts for the observed relationship between tobacco use and FM symptoms. Our patient population consists of patients with FM that were referred to a tertiary clinic that specializes in that disorder. This represents selection bias and our results may not generalize to community-based patients with milder forms of the disorder.

A mechanistic explanation for our results cannot be determined in a cross-sectional observational study. Tobacco use and nicotine have several interesting characteristics in regard to pain. Smoking has been shown to have antinociceptive properties in experimental pain models using electrical, cold pressor, thermal, and ischemic pain stimuli.^{30–38} However, in female participants, smoking did not have an analgesic effect in electrical or cold pressor experimental pain models.^{31,32,39,40} Smoking was associated with higher levels of substance P in the cerebral spinal fluid in patients with FM.⁴¹ Smokers also have lower plasma β -endorphin levels than nonsmokers.^{31,42} β -endorphin levels have been shown to be lower in patients with FM.⁴³ Both smokers and patients with FM have demonstrated perturbations of the hypothalamic-pituitary-adrenal axis.^{31,42,44} Functional neuroimaging studies have demonstrated that both smoking and FM result in similar alterations of endogenous opioid activity in pain modulating regions of the brain including the nucleus accumbens, amygdala, and dorsal cingulate.^{45,46} Other potential mechanisms by which tobacco use could impact FM are associations between tobacco use and psychologic disorders and behavioral characteristics. Smokers have a higher incidence of major depression.^{27,28} Concurrent depression and FM are common and together associated with more severe FM

symptoms.²⁹ Also smokers treated in a chronic pain rehabilitation facility were more likely to have personality disorders than nonsmokers.⁴⁷ Unfortunately, our study did not assess patients for major depression, other mood disorders, or personality disorders; but tobacco users did have a higher score on the depression FIQ subscale. Smoking is associated with multiple economic variables such as lower education level, higher rates of divorce, and unemployment that can also have an impact on FM symptoms.^{48–50} Interestingly in this cohort, the rate of current alcohol use is not associated with current tobacco use. Smokers enrolled in a chronic pain rehabilitation program have been shown to have higher rates of alcohol consumption.⁴⁷ Our study did not quantify the amount of alcohol consumption or attempt to identify the problem of drinking. Such data would be useful to determine if smoking in FM is associated with different rates of alcohol abuse than nonsmokers.

It is unknown if tobacco users with FM respond differently to treatment for FM than tobacco nonusers. It is also unknown, if smokers with FM have more difficulty quitting tobacco than smokers without FM, and if abstinence from tobacco influences FM symptoms. However, it has been shown that the presence of pain does not affect the readiness to quit among patients.⁵¹ Prospective studies are needed to evaluate these questions and to establish a causal relationship between tobacco use and FM symptoms. Regardless of the mechanism(s) or how tobacco users respond to treatment, our findings add further evidence that current tobacco use is associated with worse symptoms in patients with FM and it is probably prudent to offer these patients tobacco cessation therapy for general health reasons and to eliminate any theoretical deleterious effects from tobacco.

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