Evaluating obesity in fibromyalgia: neuroendocrine biomarkers, symptoms, and functions

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Abstract

The aim of this study was to investigate the associations between obesity and fibromyalgia syndrome (FMS). This study was conducted at the University of Utah Pain Management and Research Center, Salt Lake City, Utah. Thirty-eight FMS patients were included in this study. Neuroendocrine indices (catecholamines, cortisol, C-reactive protein [CRP], and interleukin-6), symptom measures (Fibromyalgia Impact Questionnaire), sleep indices (Actigraph), and physical functioning (treadmill testing) were measured. Body mass index (BMI) provided the primary indicator of obesity. Approximately 50% of the patients were obese and an additional 21% were overweight. Strong positive associations were found between BMI and levels of IL-6 ($r=0.52$) and epinephrine ($r=0.54$), and somewhat weaker associations with cortisol ($r=0.32$) and CRP ($r=0.37$). BMI was also related to maximal heart rate ($r=0.33$) and inversely related to distance walked ($r=−0.41$). BMI was associated with disturbed sleep: total sleep time ($r=−0.56$) and sleep efficiency ($r=−0.44$). No associations between self-reported symptoms and BMI were found. This study provides preliminary evidence suggesting that obesity plays a role in FMS-related dysfunction.

Keywords

Catecholamine; Cortisol; Cytokine; Fibromyalgia; Obesity; Sleep

Introduction

Fibromyalgia syndrome (FMS) is a prevalent musculoskeletal pain disorder affecting 3–5% of the population [1]. The cardinal features of FMS are widespread pain and hyperalgesia to palpation on at least 11 of 18 specific tender points (TP) [2]. FMS typically hosts a range of comorbidities, including chronic fatigue, nonrestorative sleep, functional disability, and mood disturbance [2]. FMS is not progressive or fatal but FMS patients report severe disability and are high utilizers of healthcare resources [3]. The etiology of FMS is unknown. A number of factors are thought to contribute to the pathophysiology of FMS. They include abnormal regulation of the central pain modulation system [4], dysregulated hypothalamic–pituitary–adrenal axis (HPA) [5], and immunological vulnerability [6].

One of the factors that contribute to FMS may be obesity. These aforementioned factors are also implicated in obesity. Obese individuals typically exhibit abnormalities in the regulation of neuroendocrine function. Obesity is related to the dysregulated HPA axis [7] and excessive cortisol levels [8]. Recent evidence also suggests that obesity may be characterized by a low-

grade chronic inflammatory state as reflected by elevated levels in a number of inflammatory markers in the serum, such as interleukin-6 (IL-6) and C-reactive protein (CRP) [9].

Clinically, obesity may augment FMS-related symptoms [10]. Obesity may also be a risk factor for chronic pain disorders in general. Primary headaches are more common in obese individuals [11], and obesity is associated with the severity of headaches in migraine patients [12]. Cross-sectional as well as longitudinal studies show that obesity is a risk factor for chronic back pain [13].

This report presents a pilot study to examine the relationship between obesity and neuroendocrine indices that are implicated in FMS. In addition, the objectives of the study included a preliminary examination of the relationship between obesity and FMS-related symptoms and disabilities.

Materials and methods

The research protocol was approved by the Institutional Review Board at the University of Utah. All subjects provided written consent prior to entering the study.

Participants

Thirty-eight FMS patients, who were initially recruited for a larger clinical study, participated in this study. Their FMS status was confirmed at the time of the initial evaluation for the larger study (see below). A nurse practitioner conducted TP examinations to assure that participants met the FMS classification criteria [2] recommended by the American College of Rheumatology. There were five male and 33 female participants with an average age of 44 years old (SD=11.44) and average pain duration of 10.55 years (SD=8.66). Table 1 lists the basic background information of the participants.

Procedures

As part of the larger clinical study, participants were asked to undergo a comprehensive FMS evaluation. This evaluation included in-clinic assessment by our medical, physical therapy, and psychology staff, as well as a function assessment performed at home for 7 days.

Medical evaluation—Medical evaluations were provided by a nurse practitioner under the supervision of a physician specializing in pain medicine. The nurse practitioner took a detailed medical history and conducted the standardized TP examination protocol [14]. Following each palpation of TP, participants indicated whether the palpation was painful, and the degree of painfulness on a scale of 0 to 10 (0=no pain, 10=worst pain).

Physical therapy evaluation—A licensed physical therapist evaluated each participant's fitness level. A walking test was performed on a treadmill set to the patient's preferred speed. Patients were instructed to walk as long as they are able, up to 20 min. Distance walked was calculated based on the walking speed and time.

Psychological evaluation—A licensed psychologist conducted a semistructured interview to assess pain history, current functioning, psychosocial history, and mood. A part of this interview assessed symptoms of depression and anxiety, based on the diagnostic criteria [15].

In addition to in-person evaluations, each participant completed the Fibromyalgia Impact Questionnaire (FIQ) to assess their FMS-related symptoms and mood. The FIQ has three parts, each assessing FMS-related dysfunctions and symptoms. The first part consists of Likert-type ratings of 10 questions related to various functional tasks. A few work-related questions are

also included. The FIQ also contains a series of visual analog scales to assess pain, fatigue, sleep quality, stiffness, anxiety, and depression. The validity and reliability of the instrument has been extensively reviewed [16].

On completing the evaluation, patients were escorted to a phlebotomy service located in the same building for collection of 10 mL blood samples. Blood sample analyses measured levels of epinephrine, norepinephrine, cortisol, IL-6, and CRP using standard protocols.

Home sleep assessment—For 7 days following evaluation, patients were asked to continuously wear a Micro Mini Motionlogger Actigraph (Ambulatory Monitoring, Ardsley, NY, USA), a wristwatch-type device that measures three-dimensional movement and provides algorithm-based sleep quality scores [17].

Results

Obesity categories

Body mass index (BMI, in kilograms per square meter) was calculated for each participant, based upon their height and weight ([weight in pounds×703]/[height in inches]^2). The mean height and weight of the patient sample were 66.06 in. (SD=3.39) and 189.58 lb (SD=44.33), respectively, yielding an average BMI of 30.78 (SD=7.81). Using the 1998 clinical guideline proposed by the National Institutes of Health, BMI scores were categorized as "normal" (BMI less than 25), "overweight" (BMI over 25 but less than 30), and "obese" (BMI greater than 30). In our sample, 11 patients fell in the normal range, eight in the overweight range, and 19 in the obese range. Thus, 50% of our patients were obese and an additional 21% were overweight. Groups did not differ on any of these parameters.

Neuroendocrine indices

The mean values of CPR, IL-6, cortisol, epinephrine, and norepinephrine by BMI group are listed in Table 2. The sample size for CRP was smaller because we started collecting assays midway through the study. Given the small size of the normal and overweight groups, we opted to use correlational analyses to evaluate the relationship between BMI and assay values. BMI was positively associated with IL-6 ($r=0.52$, $p<0.001$) and epinephrine ($r=0.54$, $p<0.001$). Somewhat weaker relationships were also observed with cortisol ($r=0.32$, $p<0.05$) and CRP ($r= 0.37$, $p<0.06$).

FMS symptoms and dysfunctions

Table 2 shows the mean values of FMS-related symptoms and functional indices as well as correlation coefficients for associations between these variables and BMI. There was no difference in rates of depressive and anxiety disorders across groups ($\chi^2(2)=0.23$ for depression, $\chi^2(2)=0.46$ for anxiety). Obesity does not seem to affect pain and other related symptoms. However, higher BMI was significantly related to shorter distance on the treadmill test and higher maximal heart rate during the test ($r=-0.41$, $p<0.01$ and $r= 0.33$, $p<0.05$, respectively).

Sleep parameters

The following sleep parameters were analyzed: total time spent sleeping (in minutes), sleep efficiency, sleep latency, how many minutes per night were spent awake after sleep onset, and activity index during sleep. Table 2 shows the mean values of these sleep parameters for each group. Descriptively, obese patients showed an overall trend toward more troubled sleep. Indeed, there are significant correlations between BMI and total sleeping time ($r=-0.56$, $p<0.001$), sleep efficiency ($r=-0.44$, $p<0.006$), waking minutes after sleep onset ($r=0.36$, $p<0.03$), and activity index ($r=0.41$, $p<0.01$).

Discussion

The results of this study provide a preliminary indication that obesity may play some role in FMS-related dysfunction. The prevalence of obesity in our sample (50%) was higher than that found in the general population (approximately 30%) [18]. Obesity in FMS seems to be linearly related to greater levels of inflammatory markers, specifically IL-6 and CRP. These results also suggest a significant impact of obesity on HPA regulation. FMS patients having greater BMI showed greater levels in the stress indicators cortisol and epinephrine. However, our results do not show a clear association between neurophysiological indices and symptom burden in FMS. BMI in this study showed little relation to the common symptoms of FMS. This may be due to insufficient statistical power; a study with a larger sample size is needed to clarify this issue.

Sample size notwithstanding, our results showed that obesity in FMS may be related to greater physical dysfunction and sleep disturbance. Obese patients showed a significantly lower degree of fitness as evidenced by shorter treadmill walking distance combined with higher maximum heart rate. Clearly, obesity may impede successful implementation of activating therapy, a method that consistently shows encouraging efficacy [19]. Obese patients also had shorter sleeping times with greater waking after sleep onset, suggesting that both quantity and quality of sleep is adversely impacted by obesity. Since sleep is known to influence FMS symptoms [20], weight management may be an important aspect of treatment for obese FMS patients.

This brief report presents a preliminary study to examine the relationship between obesity and FMS from neurophysiological, symptomatic, and functional perspectives. The results support the need to consider obesity as a significant comorbid condition in FMS.

Acknowledgements

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Table 1

Patient characteristics (*n*=38)

Characteristics	Percentage
Sex (female)	87
Race (white)	95
Education (>HS)	97
Marital (married)	76
Pain onset (insidious)	55
Medications	
Nonopioid analgesics	58
Opioid analgesics	34
Tricyclics	18
SSRI/SNRI	47
Antiepileptic	18
Muscle relaxant	16
Benzodiazepine	26

Table 2

Mean values of the neuroendocrine indices, FMS symptoms, and functions by group

	Normal (*n*=11)	Overweight (*n*=8)	Obese (*n*=19)	Correlation coefficients with BMI
IL-6 (pg/mL)	3.41 (1.09)	3.28 (.78)	4.35 (1.39)	0.52
Cortisol (μg/dL)	8.77 (2.70)	6.50 (3.29)	9.35 (4.33)	0.32
Norepinephrine (pg/mL)	476.00 (217.53)	466.75 (221.37)	509.21 (291.53)	0.05
Epinephrine (pg/mL)	21.78 (13.70)	20.25 (9.27)	30.07 (17.41)	0.54
CRP[a] (mg/dL)	0.18 (0.13)	0.34 (0.25)	0.73 (0.64)	0.37
TP counts	17.72 (0.65)	17.25 (2.12)	17.84 (0.50)	0.17
TP severity	5.41 (0.78)	5.17 (1.99)	5.52 (1.26)	0.13
FIQ disability	1.40 (0.60)	1.82 (0.47)	1.44 (0.70)	0.26
FIQ pain	76.91 (18.70)	66.00 (17.42)	69.74 (17.22)	−0.06
FIQ fatigue	74.27 (28.96)	78.75 (16.94)	85.53 (10.66)	0.26
FIQ AM not refreshed	75.55 (20.57)	83.00 (17.66)	86.84 (10.64)	0.27
FIQ AM stiffness	58.00 (34.33)	84.50 (12.74)	75.10 (17.32)	0.22
FIQ anxiety	69.73 (25.88)	79.63 (16.57)	54.44 (27.99)	−0.19
FIQ depression	50.64 (24.90)	55.25 (25.23)	43.37 (28.04)	−0.03
Walking distance (mile)	0.71 (0.29)	0.45 (0.25)	0.47 (0.30)	−0.41
Max heart rate	100.50 (33.14)	95.63 (14.58)	116.56 (13.34)	0.33
Total sleep minutes	427.21 (36.32)	414.24 (40.23)	391.57 (55.61)	−0.56
Sleep efficiency (%)	95.69 (2.08)	91.93 (5.98)	91.53 (4.30)	−0.44
Sleep latency (min)	9.63 (3.32)	13.23 (9.05)	16.43 (12.64)	0.21
Waking after sleep onset	21.83 (10.52)	39.48 (28.48)	37.92 (17.80)	0.36
Activity index during sleep	48.82 (11.87)	54.48 (13.87)	59.43 (13.35)	0.41

[a]*n*=6 for normal weight, *n*=5 for overweight, *n*=15 for obese