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Acupuncture effects on pain and health status in women with fibromyalgia: a randomized clinical trial

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ABSTRACT. This study aims to evaluate the effects of acupuncture on pain and health status in women with fibromyalgia. The present randomized, controlled, double-blind clinical trialwas carried out with one sample of 40 women diagnosed with fibromyalgia .They were randomized into one acupuncture group (n = 20; 51.7 ± 6.5 years old) and one sham acupuncture group (n = 20; 49.7 ± 7.2 years old). Acupuncture (points: pericardium 6, heart 7, large intestine 4, stomach 36, spleen-pancreas 6, and liver 2, variable depth with *Deqi* stimulation) and sham acupuncture (15mm lateral to the acupoint, outside the meridian line) were performed for 30min., once a week, and with a four-week follow-up. Pain (Visual Analogue Scale), algometry (lateral epicondyle, trapezius, suboccipital, 2nd rib), and health status (Fibromyalgia Impact Questionnaire) was assessed before the first and after the last intervention. Data were analyzed by the intention-to-treat.Acupuncture reduced pain by 16% ($p<0.001$) and improved health status by 21% ($p<0.001$). The improvement in health status ($p<0.001$) is due to the increased ability to work and go out, and reduced pain, fatigue, tiredness, and depression. Acupuncture reduced pain and improved health statusin women with fibromyalgia.

Keywords: fibromyalgia; acupuncture; chronic pain; quality of life; health status.

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Introduction

Fibromyalgia is a generalized chronic syndrome characterized by hypersensitivity and diffuse pain that causes fatigue, sleep disorders, cognitive dysfunction, myalgia, depression, and many other symptoms that impair the quality of life (Bazzichi et al., 2020; Sarzi-Puttini, Valeria Giorgi, Marotto, & Atzeni, 2020). On average, fibromyalgia affects between 2 to 3% of the Brazilian (Marques, Santo, Berssaneti, Matsutani, & Yuan, 2017) and world population, and occurs predominantly in women (Sarzi-Puttini et al., 2020). Many factors contribute to the development of disease, among them: genetic predisposition, personal experiences, emotional–cognitive factors, the mind–body relationship and a biopsychological ability to cope with stress (Sarzi-Puttini et al., 2020). Psychosocial factors can further aggravate the general symptoms of fibromyalgia, reducing the quality of life and health in general (Seto et al., 2019). The etiology of fibromyalgia is still unknown and several hypotheses have been suggested (Bazzichi et al., 2020). Among the hypotheses, one points to changes in the hypothalamic-pituitary-adrenal axis and central nervous system (CNS) in pain and sensory processing (Bellato et al., 2012).

According to European guidelines, the recommendation for the main intervention in the treatment of fibromyalgia is patient education and exercise (Macfarlane et al., 2017). However, many patients do not want or are unable to do the exercises due to pain, so acupuncture can promote relief of the symptoms so that the patient can perform the necessary exercises. Acupuncture is a complementary non-pharmacological therapeutic method that can reduce the symptoms of fibromyalgia, through neuromodulation mechanisms, increasing the release of endorphins and neurotransmitters that act in reducing pain (Sarzi-Puttini et al., 2020).Moreover, these mechanisms are reinforced by the results of a clinical trial that evaluated the acute effects (immediately after) of acupuncture in fibromyalgia patients and revealed that this procedure reduced

pain (4.36 points in Visual Analogue Scale) in these patients (Stival et al., 2014). On the other hand, previous studies have not demonstrated the benefits of acupuncture on pain and quality of life of fibromyalgia patients (Assefi et al., 2005; Harris et al., 2005).

Recent meta-analyses have shown promising evidences of acupuncture treatment in fibromyalgia patients (Kim, Kim, Lee, & Nam, 2019; Zhang et al., 2019b). Zhang et al. (2019b) who reported (acupuncture versus sham or medications) pain relief in the acupuncture group (moderate level of evidence) and improved quality of life (low level of evidence). Kim et al. (2019) confirmed improved qualities of sleep and life (high evidence), reduced pain (moderate evidence), and reduced fatigue (low evidence). However, these meta-analyses(Kim et al., 2019; Zhang et al., 2019b) have low number of randomized clinical trials and high heterogeneity of data (methodological bias, point selection, simulation method, stimulation use, and treatment frequency and duration), which suggests further research is needed to determine the effects of acupuncture on fibromyalgia.

Furthermore, there are various stimulation points (LI4, LI11, SI15, ST36, ST44, DU14, DU 20, RN6, LR3, GB41, GB34, BL40, among others) in acupuncture to treat fibromyalgia (Uğurlu et al., 2017; Karatay, Okur, Uzkeser, Yildirim, & Akcay, 2018), which leads to divergent results. Nevertheless, the stimulation point with the *Deqi* sensation activates the somatosensory pathwaysof the CNS, exciting themotor cortex (Sun et al., 2019) and active the brain regions associated with cognitive processing (with influence on pain) (Napadow et al., 2009).The hypothesis of the present study is that stimulation of these acupuncture points improves pain and health status for patients with fibromyalgia. In this context, the present study aimed to evaluate the effects of acupuncture (points: PC6, HT7, LI4, ST36, SP6, and LR2; with *Deqi* stimulation) on the pain,functional ability and health statusof women with fibromyalgia.

Material and methods

Design

The present randomized, controlled, double-blind clinical trial was carried out at the Laboratory of Functional Rehabilitation of the physiotherapy undergraduate program of the Federal University of Santa Maria (UFSM). Data were collected between April 2018 and December 2018. The study was approved by the Human Research Ethics Committee (No. 2097567) and registered in Brazilian Registry of Clinical Trials (ReBEC-6HVJNQ). The study was in accordance with the Declaration of Helsinki (2013) and Resolution 510/2016 of the National Health Council for research with human beings. All participants after explaining the study, signed the informed consent form.

Patients diagnosed with fibromyalgiawere evaluated and referred by the Rheumatology Service of the University Hospital of Santa Maria (HUSM). The patients' medication was unchanged throughout the experimental protocol. Initially, an evaluation was carried out to verify the eligibility criteria, and subsequently the patients were randomized (www.random.org) and homogeneously (1:1) allocated into two groups (acupuncture group and sham group) by independent evaluators. The evaluators and the patients were blinded to the interventions.

Subjects

The study included literate women aged between 20 and 60 years, diagnosed with fibromyalgia according to the American College of Rheumatology criteria (Stewart et al., 2019), and referred by the Rheumatology Service of the University Hospital of Santa Maria (HUSM). The exclusion criteria included patients with severe psychiatric illnesses with cognitive, neurological or sensitive deficits, cardiovascular and metabolic diseases, bleeding diathesis, infection, pregnant women or lactating women, and already undergoing acupuncture treatment.

Outcomes

The primary outcome was general pain and the secondary outcome was localized pain, functional ability and health status. All assessments were carried out before the first session and immediately after the last session,and two blinded assessorswere assigned to allocate each patient. The patients were not aware of the group in which they were allocated. The acupuncturist (G.U.B.) respected the sequence of allocation randomization, and had minimal contact with the patient and was blinded to the assessments (E.L.S. and B.S.L.D.).

In the evaluation, the participants answered a questionnaire to collect sociodemographic data. To assess the intensity of general pain, the Visual Analogue Scale was applied (Stival et al., 2014; Missau et al., 2018; Brito et al., 2022). A pressure algometer (Force Dial FDK/FDN Series, Wagner Instruments; Greenwich - USA) was used by a single evaluator to assess the pressure pain threshold ($kgcm^{-2}$). Pressure was applied to the evaluation points located in the suboccipital region, trapezius, second rib, and lateral epicondyle until the patient reported pain (Knapstad, Nordahl, Naterstad, Sture, & Goplen, 2018).

Functional ability and health status was assessed using the Fibromyalgia Impact Questionnaire (FIQ). The questionnaire contains 19 questions that are organized into 10 items, resulting in a progressive scale of the severity of the disorder(0 to 100 points). The items comprise the assessments of functional capacity, professional status, pain, psychological disorders, and physical symptoms in fibromyalgia patients (Marques et al., 2006).

Interventions

The patients underwent four 30 minutes sessions (acupuncture or sham) once a week for four consecutive weeks. Both groups received the same instructions to relax and concentrate on their breathing. An acupuncturist with over four years of experience applied the interventions.

The acupuncture group received treatment according to traditional Chinese medicine and based on the acupuncture points used by Stival et al. (Stival et al., 2014): pericardium 6 (PC6), heart 7 (HT7), large intestine 4 (LIG4), stomach 36 (ST36), spleen-pancreas 6 (SP6), and liver 2 (LR2). For this procedure, 12 disposable stainless steel needles (0.25x40mm, Hansol Medical CO., South Korea, lot 130321) were inserted perpendicularly at variable depths until stimulating the sensation of *Deqi* (sensation of pain, tingling, numbness, weight, fullness, coldness, heat, and pressure)(Hui et al., 2007).

The same treatment was applied to the sham group (needle size, number of insertion points, duration, and frequency), however, the insertions were superficial and covered a distance of 15 mm lateral to the acupoint and outside the meridian line (Lee et al., 2018).

Sample Calculation

Based on a previous study (Stival et al., 2014), the sample was estimated in 38 patients divided into two homogeneous groups. The sample calculation used the pain variable (assessed by Visual Analogue Scale) with a difference between average pain of 2.6 (±3.2 points), power of 90%, and the α error rate of 0.05.

Statistical Analysis

Data are presented in the form of mean, standard deviation (SD), absolute numbers (n), and their respective percentages (%). The primary efficacy analysis was done on an intention-to-treat (ITT) basis with all randomly assigned patients, being used as "MISSING" the baseline observation carried forward (BOCF). Data normality was verified by the Kolmogorov-Smirnov test. Categorical variables were evaluated by Fisher's exact test. The variables with two measures were compared using the Student's t-test and Mann-Whitney U test. For variables with more than two measurements, two-way ANOVA of repeated measurements followed by Bonferroni's *post hoc*were applied. The significant results are shown by mean difference (MD) and their respective 95% confidence intervals (95% CI). A significance level of 5% ($p < 0.05$) was considered.

Results

Initially, 50 patients were chosen and 10 were excluded (7 for not meeting the inclusion criteria and 3 for refusing to participate in the study) before randomization. Forty patients were allocated to the study (20 in each group). The sample loss over the course of the study was 20% (8 patients; in sham group: 4 did not return to the sessions and 1 doing acupuncture elsewhere; in acupuncture group: 1 did not return contact and 2 went through an acute crisis of lower back pain), therefore, 32 patients concluded the study. Design and flow chart of the study is shown in Figure 1. During the interventions, the patients reported no adverse events or complications.

Baseline of the physical, demographic characteristics and drug consumption of the patients are shown in Table 1. The patients were similar in both groups in terms of age, weight, height, BMI, time since diagnosis, and level of education. Consumption of painkillers, anti-inflammatories, and antidepressants throughout the study was similar.

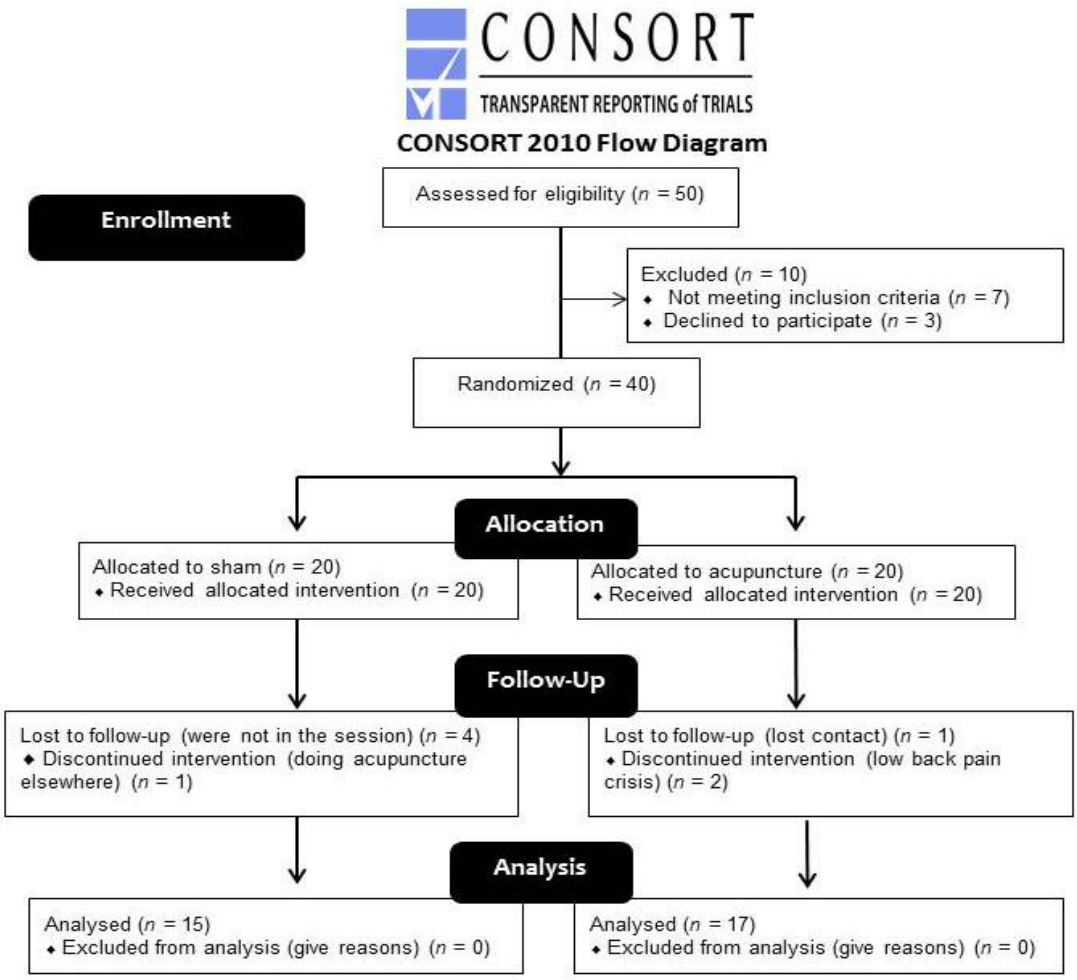

Figure 1. Design and flowchart of the study.

Legend: *n*: absolute numbers

Table 1. Baseline of the physical, demographic characteristics and drug consumption of the patients with fibromyalgia.

Variable	Intention-to-treat Analysis		p value
	Sham (n = 20)	Acupuncture (n = 20)	
Age (years)	51.7 ± 6.5	49.7 ± 7.2	0.338
Weight (kg)	74.4 ± 10.4	77.1 ± 14.8	0.505
Height (m)	1.60 ± 0.07	1.62 ± 0.06	0.719
BMI (kgm^{-2})	28.6 ± 4.9	29.2 ± 5.3	0.735
Time of diagnosis (years)	5.9 ± 5.2	4.3 ± 5.5	0.310
Education:			
Elementary school (n/%)	2 (10%)	5 (25%)	0.407
High school (n/%)	13 (65%)	11 (55%)	0.747
Higher education (n/%)	5 (25%)	4 (20%)	0.999
Drugs:			
Analgesics (n/%)	18 (90 %)	18 (90 %)	0.999
Anti-inflammatories (n/%)	5 (25 %)	3 (15 %)	0.695
Antidepressants (n/%)	13 (65 %)	16 (80 %)	0.480

Values expressed as mean ± standard deviation (SD) and in absolute numbers (*n*) and their respective percentages (%). BMI: body mass index.

The results of pain are shown in Figure 2. Pain was similar between the groups before (MD: 0.20; 95%CI: -1.12 to 1.52 points) and after (MD:-0.05[95%CI: -1.37 to 1.27] points) interventions. The pain in the sham group did not change (MD: -1.15 [95%CI: 0.18 to -2.48] points) throughout the experiment (before vs after), but in the acupuncture group, this variable decreased by approximately 16% (MD: -1.4[95% CI: -0.06 to 2.74] points).

Algometry results are shown in Table 2. The threshold for pain stimulated by pressure on the Lateral Epicondyles (Right and Left) and Suboccipital did not change over the course of the study. This variable

did not change in the region of the Left Trapezius, although there was an apparent change in time in the Right Trapezius (p = 0.015) despite not being confirmed by the Bonferroni's Test (p > 0.05) and confidence intervals in the sham (MD: 0.23[95% CI: -0.11 to 0.58]kgcm^{-2}) and acupuncture (MD: 0.29[95% CI: -0.05 to 0.64]kgcm^{-2}) groups. The 2nd Right and Left Ribs also showed an apparent change over time (p = 0.046 and p = 0.026, respectively), although this was not confirmed by the Bonferroni's Test (p > 0.05) andthe confidence intervals in the groups. In the sham group the 2nd Right Rib (MD: 0.16[95% CI: -0.09 to 0.43]kgcm^{-2}), 2nd Left Rib (MD: 0.15[95% CI: -0.04 to 0.35]kgcm^{-2}), and in the Right Acupuncture group (MD: 0.16[95% CI: -0.09, 0.42]kgcm^{-2}) and the Left (MD: 0.12[95% CI: -0.07 to 0.32]kgcm^{-2}).

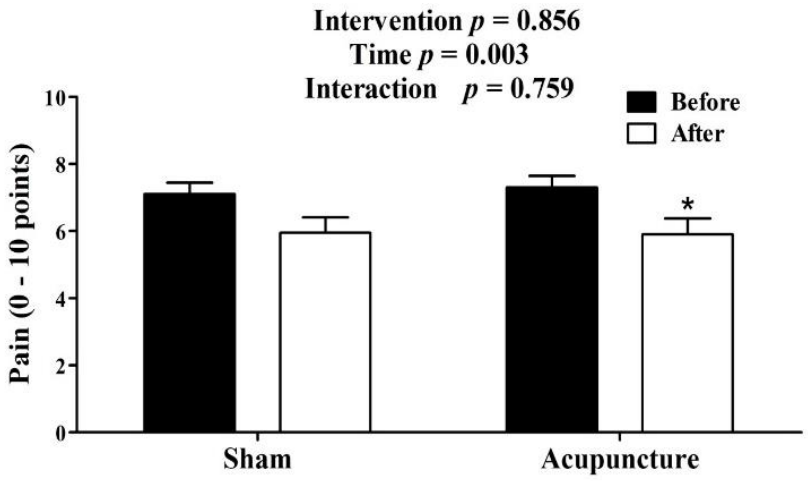

Figure 2. Pain values before and after intervention protocols.
Values expressed as mean ± standard deviation (SD).

Table 2. Algometry for pressure pain threshold in patients with fibromyalgia.

Point		Intention-to-treat Analysis				p value		
		Sham (n = 20)		Acupuncture (n = 20)				
		Before	After	Before	After	Intervention	Time	Interaction
Lateral Epicondyle (kgcm^{-2})	R	2.5 ± 1.1	2.6 ± 1.2	2.8 ± 0.8	2.6 ± 0.8	0.658	0.730	0.382
	L	2.6 ± 1.2	2.6 ± 1.0	2.8 ± 1.2	2.0 ± 1.0	0.665	0.642	0.811
Trapezius (kgcm^{-2})	R	2.1 ± 0.7	2.4 ± 0.9	2.0 ± 0.6	2.3 ± 0.7	0.558	0.015	0.776
	L	2.0 ± 0.8	2.2 ± 0.7	2.0 ± 0.6	2.2 ± 0.7	0.961	0.059	0.595
Suboccipital (kgcm^{-2})	R	1.7 ± 0.8	1.8 ± 0.8	1.7 ± 0.5	1.8 ± 0.6	0.849	0.137	0.771
	L	1.7 ± 0.7	1.8 ± 0.8	1.8 ± 0.6	1.9 ± 0.6	0.791	0.216	0.716
2ndRib (kgcm^{-2})	R	1.4 ± 0.5	1.5 ± 0.6	1.4 ± 0.5	1.6 ± 0.5	0.667	0.046	0.999
	L	1.4 ± 0.5	1.5 ± 0.6	1.5 ± 0.6	1.7 ± 0.6	0.474	0.026	0.806

Values expressed as mean ± standard deviation (SD); R: Right; L: Left; *n*: absolute numbers.

The results of the functional ability and health status of fibromyalgia patients throughout the study are shown in Table 3. The general functional ability and health status showed no difference in interventions (p = 0.796) and interactions (p = 0.45). The over health status in the sham group did not change over the course of the study. However, the functional ability and health status in the acupuncture group (MD: -15[95% CI: -4.2 to -25.8] points) improved by 21% over the course of the study. This improvement in functional ability and health status is due to a 28% improvement in the ability to accomplish work (MD: -2.1[95% CI: -0.8 to-3.4] points), 28% of pain relief (MD: -2.8 [95% CI: -4.4 to-1.1] points), 28% of fatigue (MD: -2.1[95% CI: -1.0 to-3.8] points), 25% in tiredness (MD: -2.1[95% CI: -0.8 to-3.2] points), and 23% in depression (MD: -1.80[95% CI: -0.4 to-3.2] points).

Functional capacity, overall well being, absence from work, rigidity, and anxiety did not change during the study (Table 3). Notably, changes in the time of the sub-items overall well being (p= 0.034), absence from work (p = 0.027), rigidity (p = 0.041), and anxiety (p = 0.026) were not confirmed by the *post hoc* Bonferroni's test (p > 0.05), and their respective confidence intervals (MD: - 1.1[95% CI: -3.2 to 1.1]; MD: -1.8[95% CI: -3.9 to0.4]; MD:-1.4[95% CI: 0.4 to-3.1]; MD: -0.9[95% CI: 0.5 to -2.3] points). All patients reported no side effects after treatments.

Table 3. Assessment of functional ability and health status in patients with fibromyalgia.

Variable	Intention-to-treat Analysis	Sham (n = 20)	Acupuncture (n = 20)	p value Intervention	Time	Interaction
General FIQ(points)	Before	71.1 ± 12.1	72.8 ± 13.8	0.938	<0.001	0.595
	After	57.7 ± 22.2	55.1 ± 24.4*			
			FIQ (points):			
Physical function	Before	4.7 ± 2.1	5.2 ± 2.1	0.239	0.515	0.377
	After	4.2 ± 2.0	5.3 ± 1.9			
Wellbeing	Before	8.1 ± 2.7	6.8 ± 3.4	0.408	0.031	0.491
	After	5.7 ± 3.6	5.6 ± 3.5			
Absence from work	Before	4.5 ± 3.9	6.6 ± 3.4	0.077	0.029	0.768
	After	2.9 ± 3.3	4.5 ± 3.9			
Work done	Before	7.8 ± 1.8	7.8 ± 1.9	0.510	<0.001	0.307
	After	6.2 ± 2.6	5.3 ± 2.8*			
Pain	Before	7.8 ± 1.7	8.8 ± 1.0	0.798	<0.001	0.095
	After	6.7 ± 2.5	6.0 ± 3.1*			
Fatigue	Before	7.9 ± 2.0	8.2 ± 1.8	0.630	<0.001	0.131
	After	6.8 ± 2.7	5.8 ±3.1*			
Rested	Before	6.9 ± 2.1	7.4 ±2.2	0.713	<0.001	0.791
	After	5.4 ± 2.9	5.5 ± 3.2*			
Stiffness	Before	7.4 ± 1.7	7.2 ± 3.0	0.544	0.044	0.695
	After	6.3 ± 3.0	5.5 ± 3.3			
Anxiety	Before	8.1 ± 1.4	7.2 ± 2.6	0.317	0.024	0.699
	After	6.7 ± 3.1	6.1 ± 2.9			
Depression	Before	7.9 ± 1.6	7.7 ± 2.1	0.368	0.004	0.331
	After	6.8 ± 2.9	5.6 ± 3.4*			

Values expressed as mean ± standard deviation (SD); VAS: visual analog scale; FIQ: fibromyalgia impact questionnaire; *n*: absolute numbers* $p < 0.05$ vs before.

Discussion

The present study showed that the acupuncture applied to points (PC6, C7, IG4, E36, BP6, and F2) reduced pain and improved functional ability and health status. Pain reduction was confirmed by two protocols (VAS and FIQ) and is supported by previous studies (Vas et al., 2016; Uğurlu et al., 2017; Karatay et al., 2018). Acupuncture reduced pain compared to the sham group without needle penetration(Uğurlu et al., 2017). Karatay et al. (2018) showed that acupuncture was better than sham with needle penetration, relieving pain up to three months after treatment, in addition to increasing serum levels of serotonin and reducing substance P. A multi-center study using individualized acupuncture showed a 41% reduction in pain in the treated group compared to the sham group. Moreover, there was still an improvement in functional capacity at the end of the study that persisted for a year after treatment, although there was also increased use of antidepressants (Vas et al., 2016). These studies corroborate our results, as they also observed pain relief and an overall improvement of functional ability and health status.

A previous study showed that a difference of 14% is necessary to demonstrate clinical relevance in improving the functional ability and health status of patients with fibromyalgia evaluated by the FIQ (Bennett, Bushmakin, Cappelleri, Zlateva, & Sadosky, 2009). The results of the present research show clinical relevance in improving functional ability and health status, as the acupuncture-treated group improved the results of this questionnaire by 21%. Previous studies have also shown that acupuncture improves functional ability and health status compared to the sham group(Uğurlu et al., 2017; Karatay et al., 2018). Martins et al. (2006) reported improved scores in the FIQ and in fatigue and anxiety symptoms in the acupuncture group. However, our study shows that the improvement in functional ability and health status is not only due to favorable results on fatigue and anxiety, but also on improving work capacity and reducing pain, tiredness and depression.

In contrast to the results reported herein, acupuncture and three types of sham acupuncture did not yield any differences in pain between groups of fibromyalgia patients (Assefi et al., 2005; Harris et al., 2005). These results are in accordance with a previous study (Harris et al., 2005), which found no differences in pain, fatigue, and physical function between the groups regarding the location or stimulation point. These divergences in results are due to different methodologies applied in real acupuncture and sham groups. In the study by Harris (Harris et al., 2005), the reduction of pain and fibromyalgia symptoms did not depend on the point of manipulation, showing that minimal acupuncture may not be inert and the points work as *Ashi* points (localized pain point). Assefi et al. (2005) reported that the non-specific response may be associated with the

presence of the acupuncturist, the relaxing environment, psychological response, and fluctuations in the clinical history, are aspects that may have influenced the results, in addition to different acupuncturists and points used in the study. In sham acupuncture, with needle penetration, effects similar to real acupuncture can occur (Vickers et al., 2018), and superficial needling (sham) can activate brain regions associated with pain (Harris et al., 2009), as well as stimulation of the sensory nerve system (Uğurlu et al., 2017). Moreover, sham acupuncture can be seen as a less effective form of therapeutic needles, because depending on the location and point, similar results can occur, such as local analgesia and even the stimulation of a region similar to acupuncture in the brain (Choi, Jiang,& Longhurst, 2012).

Acupuncture-induced analgesia starts in activation of acupoints by the needles, these stimuli are transmitted to the spinal cord and to the CNS, where is activated the descending pain modulation system (including the anterior cingulated cortex, the periaqueductal gray, and the rostral ventromedial medulla) to relieve pain (Chen, Zhang, Chu, & Wang, 2020), that results in reduced symptoms of fibromyalgia. Needle stimulation at the acupuncture point may reflect different stimuli that lead to different results. In acupuncture, stimulation of the point with the sensation of *Deqi* activates regions of the brain associated with cognitive processing (influencing pain), with more complex and lasting stimuli. On the other hand, areas associated with sensorimotor processing are activated by sham acupuncture (Napadow et al., 2009). *Deqi* stimulation can (through the somatosensory pathway) modulate the CNS, increasing motor cortical excitability (Sun et al., 2019) and provoking patterns of sensations that extend farther from the stimulated location by the needle (Jung et al., 2016).

In the present study, the sensation of *Deqi* was stimulated, which benefited the functional ability and health status assessed by the FIQ. The FIQ is a tool developed to assess functional ability and health status through various symptoms present in fibromyalgia patients (Marques et al., 2006). Previous studies have already shown the benefits of acupuncture in improving symptoms of fatigue (Zhang et al., 2019a), depression (Smith, Armour, Lee, Wang, & Hay, 2018), and pain (Vickers et al., 2018), which impacts the quality of life, as demonstrated herein.

Among the limitations of the study are: out sample loss, small sample size, groups of only women, low number of acupuncture sessions, evaluation of the outcomes immediately after the last session and absence of inflammatory markers assessment. Another limitation to be considered is the segment loss in the sham group (5/20: 25%) and in the acupuncture group (3/20: 15%), however, analysis by "intention-to-treat analysis" attenuates the impact of this effect on the results.

Conclusion

Acupuncture performed once a week, for four weeks, and applied to points (PC6, C7, IG4, E36, BP6, and F2) with *Deqi* stimulation, reduced pain, improved the functional ability and health status of women with fibromyalgia, what did not happen in the sham group. The increased health status of these patients is due to the ability to perform their work, in reducing pain, fatigue, tiredness, and depression. The present study showed that this therapy is safe and improves the level of clinic evidence of its application associated with other therapies usually used to treat patients with fibromyalgia.

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References

Assefi, N. P., Sherman, K. J., Jacobsen, C., Goldberg. J., Smith, W. S., & Buchwald, D. (2005). A randomized clinical trial of acupuncture compared with sham acupuncture in fibromyalgia. *Annals of Internal Medicine*, *143*(1), 10-19. DOI: https://doi.org/10.7326/0003-4819-143-1-200507050-00005

Bazzichi, L.Giacomelli, C., Consensi, A., Giorgi, V., Batticciotto, A., & Di Franco, M.(2020). One year in review 2020: fibromyalgia. *Clinical and Experimental Rheumatology*, *38*(Suppl. 123), 3-8. Retrieved from https://www.clinexprheumatol.org/a.asp?IDArchivio=234

Bellato, E., Marini, E., Castoldi, F., Barbasetti, N., Bonasia, D. E. & Blonna, D. (2012). Fibromyalgia Syndrome: Etiology, Pathogenesis, Diagnosis, and Treatment. *Pain Research and Treatment*, 1-17. DOI: https://doi.org/10.1155/2012/426130

Bennett, R. M., Bushmakin, A. G., Cappelleri, J. C., Zlateva, G., & Sadosky, A. L. (2009). Minimal clinically important difference in the fibromyalgia impact questionnaire. *The Journal of Rheumatology*, *36*(6), 1304-1311. DOI: https://doi.org/10.3899/jrheum.081090

Brito, E., Teixeira, A. O., Righi, N. C., Paulitcth, F. S., Silva, A. M. V., & Luis, L. U. (2022). Vitamins C and E associated with cryotherapy in the recovery of the inflammatory response after resistance exercise: a randomized clinical trial. *Journal of Strength and Conditioning Research*, *36*, 135-141. DOI: https://doi.org/10.1519/JSC.0000000000003342

Chen, T., Zhang, W. W., Chu, Y., & Wang, Y. (2020). Acupuncture for Pain Management: Molecular Mechanisms of Action. *The American Journal of Chinese Medicine*, *48*(4), 793-811. DOI: https://doi.org/10.1142/S0192415X20500408

Choi, E. M., Jiang, F., & Longhurst, J. C. (2012) Point specificity in acupuncture. *Chinese Medicine*,*7*(4). DOI: https://doi.org/10.1186/1749-8546-7-4.

Jung, W. M., Shim, W., Lee, T., Park, H-J., Ryu, Y., Beissner, F., & Chae, Y. (2016). More than DeQi: Spatial patterns of acupuncture-induced bodily sensations. *Frontiers in Neuroscience*, *10*, 1-8. DOI: https://doi.org/10.3389/fnins.2016.00462

Harris, R. E., Zubieta, J-K., Scott, D. J., Napadow, V., Gracely, R. H., & Clauw, D.J. (2009). Traditional Chinese acupuncture and placebo (sham) acupuncture are differentiated by their effects on μ-opioid receptors (MORs). *Neuroimage*,*47*(3), 1077-1085. DOI: https://doi.org/10.1016/j.neuroimage.2009.05.083

Harris, R., Xiaoming, T., Williams, D., Tian, T. X., Cupps, T. R., Petzke, F., ... Clauw, D. J. (2005). Treatment of fibromyalgia with formula acupuncture: investigation of needle placement, needle stimulation, and treatment frequency. *The Journal of Alternative and Complementary Medicine*, *11*(4), 663-671. DOI: https://doi.org/10.1089/acm.2005.11.663

Hui, K. K. S., Nixon, E. E., Vangel, M. G., Liu, J., Marina, O., Napadow, V., ... Kennedy, D. N. (2007). Characterization of the 'deqi' response in acupuncture. *BMC Complementary and Alternative Medicine*, *7*(33),1-16. DOI: https://doi.org/10.1186/1472-6882-7-33

Karatay, S., Okur, S. C., Uzkeser, H., Yildirim, K.,& Akcay, F. (2018). Effects of acupuncture treatment on fibromyalgia symptoms, serotonin, and substance P levels: A randomized sham and placebo-controlled clinical trial. *Pain Medicine (United States)*, *19*(3), 615-628. DOI: https://doi.org/10.1093/pm/pnx263

Kim, J., Kim, S. R., Lee, H., & Nam, D-H. (2019) Comparing verum and sham acupuncture in fibromyalgia syndrome: a systematic review and meta-analysis. *Evidence-based Complementary Alternative Medicine*, *25*, 8757685.DOI: https://doi.org/10.1155/2019/8757685

Knapstad, M. K., Nordahl, S. H. G., Naterstad, I. F., Ask, T., Sture, J. S., & Goplen, F. K. (2018). Measuring pressure pain threshold in the cervical region of dizzy patients - The reliability of a pressure algometer. *Physiotherapy Research International*, *23*(4), e1736. DOI: https://doi.org/10.1002/pri.1736

Macfarlane, G. J., Kronisch, C., Dean, L. E., Atzeni, F., Häuser, W., Fluß, E,.& Jones, G. T. (2017) EULAR revised recommendations for the management of fibromyalgia. *Annals of the Rheumatic Diseases*,*76*(2), 318-328. DOI: https://doi.org/10.1136/annrheumdis-2016-209724

Marques, A. P., Santos, A. M. B., Assumpção, A., Matsutani, L. A., Lage, L. V., & Pereira C. A. B. (2006). Validation of the Brazilian version of the Fibromyalgia Impact Questionnaire (FIQ). *Revista Brasileira de Reumatologia*, *46*, 24-31. DOI: https://doi.org/10.1590/S0482-50042006000100006

Marques A. P., Santo A. S. E., Berssaneti, A. A., Matsutani, L. A., & Yuan S. L. K. (2017). Prevalence of fibromyalgia: literature review update. *Revista Brasileira de Reumatologia (English Edition)*, *57*(4), 356-363. DOI: https://doi.org/10.1016/j.rbre.2017.01.005

Missau, E., Teixeira, A. O., Franco, O. S., Martins, C. N., Paulitsch, F. S., Peres, W., ...Signori, L. U. (2018). Cold water immersion and inflammatory response after resistance exercises. *Revista Brasileira de Medicina do Esporte*, *24*(5) DOI: https://doi.org/10.1590/1517-869220182405182913

Napadow, V., Dhond, P. R., Kim, J., LaCount, L., Vangel, M., Harris, R. E., ...Park, K. (2009). Brain encoding of acupuncture sensation - coupling on-line rating with fMRI. *Neuroimage*, *47*(3),1055-1065. DOI: https://doi.org/10.1016/j.neuroimage.2009.05.079

Sarzi-Puttini, P., Valeria Giorgi, P., Marotto, D., & Atzeni, F. (2020). Fibromyalgia: an update on clinical characteristics, aetiopathogenesis and treatment. *Nature Reviews Rheumatology*, *16*(11), 645-660. DOI: https://doi.org/10.1038/s41584-020-00506-w

Seto, A., Han, X., Price, L. L., Harvey, W. F., Bannuru, R. R., & Wang, C. (2019). The role of personality in patients with fibromyalgia. *Clinical Rheumatology*, *38*, 149-157. DOI: https://doi.org/10.1007/s10067-018-4316-7

Smith, C. A., Armour, M., Lee, M. S., Wang, L. Q.,& Hay, P. J. (2018). Acupuncture for depression. *Cochrane Database of Systematic Reviews*. DOI: https://doi.org/10.1002/14651858.CD004046.pub4

Stival, R. S. M., Cavalheiro, P. R., Stasiak, C., Galdino, D. T., Hoekstra, B. E., & Schafranski, D. M. (2014).Acupuncture in fibromyalgia: a randomized, controlled study addressing the immediate pain response. *Revista Brasileira de Reumatologia (English Edition)*, *54*(6), 431-436. DOI: https://doi.org/10.1016/j.rbre.2014.06.002

Sun, Z. G., Pi, Y. L., Zhang, J., Wang, M., Zou, J., & Wu, W. (2019) Effect of acupuncture at ST36 on motor cortical excitation and inhibition. *Brain and Behavior*, *9*(9), 1-8. DOI: https://doi.org/10.1002/brb3.1370

Uğurlu, F. G., Sezer, N., Aktekin, L., Fidan, F., Tok, F.& Akkuş, S. (2017). The effects of acupuncture versus sham acupuncture in the treatment of fibromyalgia: A randomized controlled clinical trial. *Acta Reumatologica Portuguesa*, 32-37. Retrieved from http://www.arprheumatology.com/article_download.php?id=1225

Vas, J., Santos-Rey, K., Navarro-Pablo, R., Modesto, M., Aguilar, I., Campos, M. Á., ... Rivas-Ruiz, F. (2016). Acupuncture for fibromyalgia in primary care: a randomised controlled trial. *Acupuncture in Medicine*, *34*(4), 257-266. DOI: https://doi.org/10.1136/acupmed-2015-010950

Vickers, A. J., Vertosick, E. A., Lewith, G., MacPherson, H., Foster, N. E., Sherman, K. J., ... & Linde, K. (2018). Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis. *The Journal of Pain*, *19*(5), 455-474. DOI: https://doi.org/10.1016/j.jpain.2017.11.005

Zhang, X. C., Chen, H., Xu, W. T., Xu, S., Wang, W., & Huang, G. (2019a). Acupuncture therapy for fibromyalgia: A systematic review and meta-analysis of randomized controlled trials. *Journal of Pain Research*, *12*, 527-542. DOI: https://doi.org/10.2147/JPR.S186227

Zhang, Q., Gong, J., Dong, H., Song, Y-Y., Gu, Y-H., & Ni, G-X.(2019b). Acupuncture for chronic fatigue syndrome: a systematic review and meta-analysis.*AcupunctureinMedicine*, *37*(4), 211-222. DOI: https://doi.org/10.1136/acupmed-2017-011582