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Original article

Acupuncture in fibromyalgia: a randomized, controlled study addressing the immediate pain response



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ARTICLE INFO

Article history:

Received 23 March 2013

Accepted 8 June 2014

Available online 27 October 2014

Keywords:

Acupuncture

Fibromyalgia

Visual analogue pain scale Chronic pain

ABSTRACT

Objective: To evaluate the efficacy of acupuncture in the treatment of fibromyalgia, considering the immediate response of the visual analogue pain scale (VAS) as its primary outcome. **Methods:** Randomized, controlled, double-blind study including 36 patients with fibromyalgia (ACR 1990) selected from the outpatient rheumatology clinic, Santa Casa de Misericórdia, Ponta Grossa, PR. Twenty-one patients underwent an acupuncture session, under the principles of the traditional Chinese medicine, and 15 patients underwent a placebo procedure (sham acupuncture). For pain assessment, the subjects completed a Visual Analogue Scale (VAS) before and immediately after the proposed procedure. The mean change in VAS was compared among groups.

Results: The variation between the final and initial VAS values was -4.36 ± 3.23 ($P = 0.0001$) in the treatment group and -1.70 ± 1.55 in the control group ($P = 0.06$). The difference in terms of amplitude of variation of VAS (initial – final VAS) among groups favored the actual procedure ($P = 0.005$). The effect size (ES) for the treatment group was $d = 1.7$, which is considered a large effect. Although small, the statistical power of the sample for these results was very relevant (94.8%).

Conclusion: Acupuncture has proven effective in the immediate pain reduction in patients with fibromyalgia, with a quite significant effect size.

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DOI of original article: <http://dx.doi.org/10.1016/j.rbr.2014.06.001>.

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<http://dx.doi.org/10.1016/j.rbre.2014.06.002>

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Acupuntura na fibromialgia: um estudo randomizado-controlado abordando a resposta imediata da dor

R E S U M O

Palavras-chave:

Acupuntura
Fibromialgia
EVA
Dor crônica

Objetivo: Avaliar a eficácia da acupuntura no tratamento da fibromialgia, considerando-se como desfecho primário a resposta imediata da escala visual analógica (VAS) para avaliação da dor.

Material e métodos: Estudo randomizado, controlado e duplo-cego incluindo 36 pacientes portadores de fibromialgia (ACR 1990) selecionados no ambulatório de Reumatologia da Santa Casa de Misericórdia de Ponta Grossa, PR. Vinte e um pacientes foram submetidos a uma sessão de acupuntura, nos moldes da Medicina Tradicional Chinesa, e 15 pacientes foram submetidos a um procedimento placebo (acupuntura *sham*). Para avaliação da dor, os indivíduos preencheram uma Escala Visual Analógica (VAS) antes e imediatamente após o procedimento proposto. As médias na variação da VAS foram comparadas entre os grupos. **Resultados:** A variação entre o valor da EVA final e da EVA inicial foi de $-4,36 \pm 3,23$ ($P=0,0001$) no grupo de tratamento e de $-1,70 \pm 1,55$ no grupo de controle ($P=0,06$). A diferença na amplitude de variação da EVA (EVA inicial – final) entre os grupos favoreceu o procedimento verdadeiro ($P=0,005$). O tamanho de efeito (*effect size* – ES) para o grupo de tratamento foi de $d=1,7$, o que é considerado um efeito grande. Embora com uma amostra reduzida, seu poder estatístico para esses resultados foi bastante relevante (94,8%).

Conclusão: A acupuntura mostrou ser eficaz na redução imediata da dor em pacientes portadores de fibromialgia, com um tamanho de efeito (*effect size*) bastante significativo.

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Introduction

Fibromyalgia is a non-inflammatory syndrome manifested primarily on the musculoskeletal system by a chronic widespread pain, often associated with other symptoms such as fatigue, sleep disturbance and mood disorders.¹⁻³ The pain usually exacerbates after physical activity and there are patients who complain of its intensification when exposed to cold and humidity.³

The etiology of fibromyalgia remains unknown, being considered by some authors as a somatisation syndrome.⁴ But, mostly from the 1980s on, this condition came to be understood as a chronic pain syndrome in which the sensitization of the central nervous system (CNS) to pain plays a major role. Its diagnostic criteria have been defined by the American College of Rheumatology in 1990, and in 1992 the World Health Organization (WHO) recognized fibromyalgia as a disease.⁴

The available treatments for this disease are only partially effective and focus on the relief of symptoms; and its cure, like other rheumatic diseases, constitutes a still elusive task.^{5,6} Acupuncture has been applied as a therapeutic modality in a wide variety of painful conditions.⁷ Its neurobiological effects, that interfere on neurotransmitters related to pain and depression, qualify this as a proper technique for the treatment of chronic pain.^{7,8}

In this study, we sought to evaluate the efficacy of acupuncture in treating fibromyalgia, considering the immediate response of the visual analogue scale of pain as the primary outcome.

Material and methods

Patients and controls

Thirty-six patients with fibromyalgia diagnosed according to the 1990 American College of Rheumatology classification criteria seen at the outpatient rheumatology clinic at the Hospital Santa Casa de Misericórdia, Ponta Grossa (University Hospital, UEPG) were selected. Volunteers selected for the study were randomly distributed into two groups. Patients with contraindication to acupuncture, for instance, individuals with needle phobia, bleeding diathesis, pregnant or lactating women, were excluded.

The sample size calculation was performed by estimating a Cohen's *d* coefficient = 1.2 (effect size) for an α -error of 5% and a sample power of 80%, and we inferred that the required sample size was at least 12 patients in each group.

The randomization followed a computer generated table of random numbers by Research Randomizer (www.randomizer.org). The study was approved by the Universidade Estadual de Ponta Grossa (UEPG) Ethics Committee on Human Research (COEP) and all individuals involved signed an informed consent form.

Table 1 shows the baseline characteristics of the selected patients. There was no statistically significant difference between the two groups.

Intervention

The acupuncture methods applied were identically standardized and implemented in all subjects studied, according to

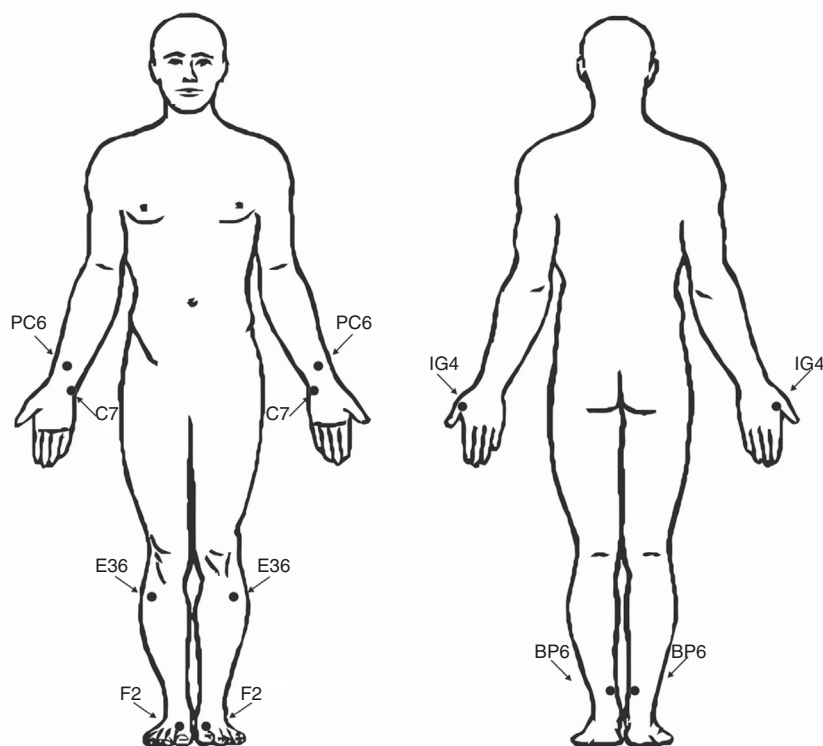


Figure 1 – Acupuncture points. Pericardium 6 (PC6), Heart 7 (C7), Spleen 6 (BP6), Large Intestine 4 (IG4), Liver 2 (F2), Stomach 36 (E36) points were used bilaterally.

their intervention group. The chosen sites to the treatment were the points: the large intestine 4, stomach 36, liver 2, spleen 6, pericardium 6 and heart 7 bilaterally, according to what is recommended by Traditional Chinese Medicine.^{9,10} Fig. 1 shows, schematically, the acupuncture points employed.

A group of 21 patients underwent acupuncture with needles of 0.20 × 40 mm inserted perpendicularly at the points described above, i.e., precisely respecting the anatomical location described in Traditional Chinese Medicine. A group of

15 patients received sham acupuncture, which comprises the use of the needles as placebo. In this procedure, needles of 0.18 × 8 mm were used to stimulate points on the surface 15 mm to the left of the true points.^{11,12}

The same acupuncturist, not a physician, but at the time with the appropriate qualification to perform this therapeutic modality, led the proceedings. Both conversations between the acupuncturist and the patient as any contact beyond what was considered strictly necessary for the acupuncture procedure, were restricted. The session of acupuncture lasted 20 minutes.

Outcome assessment

Immediately before and after the intervention, patients completed a visual analog scale (VAS) for pain, which consists of a ruler with a scale of 0 to 10 cm, with the number zero representing no pain, and the number 10 being the worst pain ever experienced by the subject. Within the proposed protocol (a double-blind study), the professionals who collected the responses of VAS for pain were unaware of the randomization status of each individual. Only the acupuncturist knew the intervention groups.

Statistical analysis

The sample was properly tested for normality of distribution (Shapiro-Wilk test). Parametric distributions were analyzed

Table 1 – Baseline characteristics of patients.

	Sham Acupuncture n = 15	Acupuncture n = 21	P
Age	49.2 ± 11.8	52.0 ± 7.57	0.38 ^a
Gender			
Male	1 (6.6%)	4 (19.5%)	0.28 ^b
Female	14 (93.3%)	17 (80.4%)	
VAS, initial	5.72 ± 2.50	7.27 ± 2.66	0.08 ^a
Duration of disease	9.07 ± 6	7.3 ± 5.98	0.5 ^c

Data are presented as mean ± standard deviation, except where indicated by ^c, that for reasons of non-parametric distribution, the interquartile range (IQR, comparison performed by Mann-Whitney test) was used.

^a Student's t test.

^b Student's exact test.

Table 2 – Change in VAS in both intervention groups.

	Sham acupuncture n = 15	Acupuncture n = 21	P
VAS, initial	5.72 ± 2.50	7.27 ± 2.66	
VAS, final	4.01 ± 2.43	2.91 ± 2.38	
Change	-1.70 ± 1.55	-4.36 ± 3.23	0.005 ^a

^a Paired Student's t test.

using the Student's t test (unpaired for basal characteristics and matched for the results) and non-parametric distributions were tested using the Mann-Whitney test. For comparison of categorical variables, the two-tailed Fisher exact test was applied. Data are presented as mean ± standard deviation, except where indicated (mean ± interquartile range – IQR). P values <0.05 were considered statistically significant. The effect size is demonstrated by Cohen's d coefficient, that considers 0.2 as a small effect; 0.5 as a medium effect; and 0.8 as a large effect. To estimate the observed statistical power of the sample, it was considered as appropriate an α -error (type I) of 5% and an β -error (type II) of 20%. All analyzes were performed using MedCalc software, version 12.4.0 (Ostend, Belgium).

Results

Both groups showed improvement in the outcome analysis of VAS after the proposed intervention (Table 2). In the treatment group, there was a change of -4.36 ± 3.23 between initial and final VAS values, which was statistically significant ($P=0.0001$). In the sham group, although a considerable change was observed in VAS (-1.70 ± 1.55), this difference did not reach the threshold of statistical significance ($P=0.06$).

However, in relation to the effect size measured by the Cohen's d coefficient, the acupuncture procedure has been shown effective in both groups: the sham intervention resulted in an effect considered medium ($d=0.69$) and the acupuncture resulted in a large effect ($d=1.7$).

And finally, with respect to the amplitude of VAS variation (initial – final VAS), the difference among groups favored the actual procedure with statistical significance ($P=0.005$), with a Cohen's d coefficient = 1.05 (large effect).

Despite the relatively small sample size, estimating an α -error of 5%, the observed statistical power demonstrated by the sample was 94.8%, with a consequent β -error (type II) of only 5.2%, which confirms the robustness of our findings.

Discussion

The present study aimed to evaluate the immediate response of VAS for pain in fibromyalgia patients, diagnosed according to ACR criteria (1990), after a single session of acupuncture, comparing to controls subjected to a sham procedure after a randomization process.

It is known that acupuncture can promote physiological changes in the body, such as changes in blood pressure and in brain and thalamus electrical activity.^{6-8,13} There are several theories to explain the analgesia subsequent to the acupuncture treatment. Mackenzie's theory states that the sensory stimulation by the needle causes functional reactions to the muscles, ligaments and vessels innervated by the same myelotome.⁷ The stimulation of skin areas can influence the organs functionally, by being connected by the same neurotome.^{7,14} Some studies have shown that acupuncture stimulates the release of endorphins and enkephalins, which leads to a modulating pain response, resulting in analgesia.^{7,15} Other studies have shown that acupuncture may block the pain afferents by two mechanisms: the first by inhibiting the activity of pain transmission neurons at a medullary level; the second by inhibiting nociceptive afferent stimuli through the activation of segmental and suprasegmental pain suppressor systems.^{6,7} The concept of sensitive or tender points, although today controversial in the diagnosis of fibromyalgia, has a close relationship with the concept of acupuncture points. The stimulation of these points with needles can promote pain control.¹⁶ The effects of acupuncture on brain activity have been demonstrated through imaging studies, which showed that, after the acupuncture needling, there is an intensification of cerebral blood flow.^{6,7} Thus, many patients with chronic pain turn to treatment by this technique.^{7,10,17}

The studies on acupuncture specifically for treating fibromyalgia have shown quite controversial results.

Assefi et al.,¹¹ in a randomized, controlled, double-blind study, evaluated the efficacy of acupuncture in relieving pain in 100 fibromyalgia patients. These subjects were divided into four groups according to the intervention: acupuncture program that was specifically designed to treat fibromyalgia, according to the principles of Traditional Chinese Medicine; acupuncture use for other conditions, except for fibromyalgia; use of placebo needles in different points of Energy Meridians; and stimulation of the skin with a toothpick, simulating needle insertion. The authors concluded that acupuncture treatment is not superior to sham treatment for pain relief.

Sanchez et al.¹⁸ performed a systematic review on the effectiveness of acupuncture in treating fibromyalgia. After a critical analysis of studies indexed at PubMed, the Cochrane Library, EMBASE, CINAHL and at Pascal Biomed, six studies were selected from 59 found. The analysis of these six studies led to the conclusion that there is no evidence of benefit of acupuncture compared to sham acupuncture in the treatment of fibromyalgia.

On the other hand, in a randomized single-blind study Deluze et al.¹⁹ evaluated the efficacy of electroacupuncture in patients with fibromyalgia. In a group of 70 patients, 36 received electroacupuncture at points recommended by the Traditional Chinese Medicine and 34 received sham acupuncture (the needling was made in points 20 mm away from the true points and with reduced electrical stimulation). In the electroacupuncture group there was a significant improvement of symptoms. In five of the eight parameters analyzed, the improvement in patients treated with

electroacupuncture was more significant than in the control group.

Itoh and Kitakoji,²⁰ in a preliminary randomized controlled study, evaluated the impact of acupuncture on pain and quality of life in 16 patients with fibromyalgia. The patients were divided into two groups of eight patients who underwent 10 weekly acupuncture sessions. The control group received the actual therapy only after the first five weeks. A clear improvement in both FIQ (Fibromyalgia Impact Questionnaire) and VAS in the control group which was perceived only after the application of the actual procedure suggested that acupuncture treatment is effective in relieving pain in patients with fibromyalgia.

Martin et al.¹⁰ conducted a randomized, partially blinded, controlled study in which 50 patients with fibromyalgia were subjected to six treatment sessions in two groups: actual vs. sham (stimulation of the skin by the needle, but without penetrating the skin) acupuncture. The authors concluded that acupuncture is effective in treating the symptoms of fibromyalgia, especially with regard to anxiety and fatigue.

The present study, carried out by a double-blind randomized design, favors the acupuncture in terms of an immediate pain improvement in patients with fibromyalgia. This conclusion was obtained by a significantly robust difference in VAS variation, observed in patients undergoing the actual procedure. It is noteworthy to observe that both intervention groups showed a significant and immediate improvement in pain, with expressive Cohen's *d* coefficients, representing a medium effect size for sham acupuncture and a large effect size for the actual acupuncture. This fact is in agreement with Pariente et al.,²¹ who examined the pain response to acupuncture vs. a sham procedure using functional MRI, and demonstrated that both procedures activate cortical regions related to analgesia, such as the dorsolateral prefrontal cortex and the anterior singular cortex, but the actual procedure results in an insular activation that is not seen after the simulation.²¹

Despite the reduced sample size, the statistical power observed was high, with an almost expressionless β -error, in face of the important difference in response among the groups evaluated.

From the findings of this study, it appears that acupuncture performed in accordance of traditional Chinese Medicine has an important effect on the immediate reduction of pain in patients with fibromyalgia, compared to the effects of sham acupuncture. More studies with different protocols are needed to confirm this hypothesis, with a larger number of individuals and with a longer follow-up, mainly to evaluate more accurately the duration of the analgesic effect.

Funding

The researchers Patrícia Rechetello Cavalheiro and Camila Stasiak received an educational grant from CNPq (PIBIC) to implement the project. The researcher Bianca Eliza Hoekstra received a support grant from Araucaria Foundation (BIC) for the same purpose.

Conflicts of interest

The authors declare no conflicts of interest.

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