

Treatment with low-intensity transcranial magnetic stimulation in women with fibromyalgia improves diagnostic variables up to 6 months after treatment completion

J.L. Pareja¹, O. Cáceres², P. Zambrano², F. Martín³, F.J. Berral⁴, M. Blanco²

¹School of Sciences, Universidad Mayor, Santiago de Chile, Chile;

²SHC Medical, Viamed Santa Ángela de la Cruz Hospital, Seville, Spain;

³Department of Molecular Biology and Biochemistry Engineering, University Pablo Olavide, Seville, Spain; ⁴Department of Sports and Informatic, University Pablo Olavide, Seville, Spain.

Abstract

Objectives

Fibromyalgia (FM) is a disease treated with various therapeutic approaches that have limited success. Pulsed electromagnetic field therapy has been proposed as a possible solution to reduce several symptoms. This study aims to analyse the therapeutic effects of transcranial low-intensity magnetic stimulation (LIMS) in women diagnosed with FM at 2, 12 and 24 weeks from the last LIMS administration treatment session.

Methods

560 women (53.7 ± 11.3 years) diagnosed with FM according to the ACR 2016 criteria were randomly allocated in two groups: 280 received standard pharmacological treatment and 280 received the same treatment plus eight sessions of LIMS, 20 minutes long, once a week. The variables analysed were the widespread pain index (WPI), symptoms severity score (SS score) and the Spanish-validated version of the FM impact questionnaire (S-FIQ). The evaluations were performed at the beginning of LIMS treatment and at 2, 12 and 24 weeks after the end of the last LIMS treatment session.

Results

From the second week after the last LIMS session, there was significant improvement ($p < 0.001$) in the variables WPI, SS score and S-FIQ. This improvement was maintained throughout the 24 weeks of monitoring after the last intervention. The age of the patients and the severity of the symptoms at the time of diagnosis did not affect the improvement observed in the three variables studied.

Conclusions

Treatment with LIMS for eight weeks resulted in significant improvement in FM diagnostic variables, which was maintained up to 24 weeks after the last treatment session. This therapy could be recommended as a part of a multimodal approach for FM treatment.

Key words

fibromyalgia, repetitive transcranial magnetic stimulation, transcranial low-intensity magnetic stimulation

Jose L. Pareja, MSc
Oscar Cáceres, PhD
Paola Zambrano, MSc
Franz Martín, PhD
Francisco J. Berral, PhD
Manuel Blanco, MD

Please address correspondence to:
Dr. Francisco José Berral de la Rosa,
Department of Sports and Informatic,
Ctra. de Utrera Km 1,
41013 Sevilla, Spain.
E-mail: fjberde@upo.es

Received on January 11, 2021; accepted in
revised form on October 18, 2021.

© Copyright CLINICAL AND
EXPERIMENTAL RHEUMATOLOGY 2021.

Introduction

Fibromyalgia (FM) is a component of central sensitisation syndrome (1-3) and is understood as a nondegenerative chronic disorder of unknown cause and characterised by generalised hyperalgesia, nonrestorative sleep and morning stiffness (4, 5). Other clinical conditions such as chronic fatigue syndrome, irritable bowel syndrome, headaches, interstitial cystitis, temporomandibular joint dysfunction syndrome, anxiety and depression may also be related to FM (6, 7). In 2016, the American College of Rheumatology (ACR) modified the criteria for its diagnosis, which considers the association between the WPI and SS score. Since 1990, the use of these two questionnaires together has correctly classified 88.1% of patients diagnosed using the ACR criteria (8, 9). The prevalence worldwide is estimated to be between 1.78% and 4.43% and mainly affects the female population (10). Some studies have shown a genetic predisposition to this disease and potential candidate genes have been found (11, 12). Therefore, its aetiology is still unknown and is associated with regulatory dysfunction between the nervous, endocrine and immune systems and is triggered by exposure to environmental and infectious agents (13). Its treatment is varied and considers pharmacological support (14), physical activity (15), physiotherapy (16), behavioural therapy (17), nutritional (18) and alternative or natural therapies (19) to reduce pain and fatigue and improve sleep quality, mood disorders and the level of activation and functionality of people suffering from this disease.

The above therapies have not been able to definitively eradicate the symptoms, which significantly affect the quality of life of these individuals (20). Since the 1990s, repetitive transcranial magnetic stimulation (rTMS) has been successfully added to the aforementioned options (21, 22), favouring the modulation of neural networks, which has been linked with a decrease in clinical manifestations of FM (23). Several studies have shown that transcranial low-intensity magnetic stimulation (LIMS) therapy maintains its effects on

the control and improvement of symptoms, adding safety and eliminating the side effects described with rTMS (24, 25). However, until now, the efficacy and safety of treatment with LIMS has not been studied in the medium and long term; therefore, the effectiveness of this therapy for treating this disease is unknown.

The objective of this study was to analyse the effects of the application of LIMS in women diagnosed with FM on the diagnostic criteria of the ACR at 2, 12 and 24 weeks from the last LIMS treatment session.

Materials and Methods

Patients

The sample consisted of 560 women (age: 53.7 ± 11.3 years; 95% CI: 95.2-51.4; range 35 to 75 years) selected from 1200 women treated at the Fibromyalgia Unit of the Viamed Hospital in Seville, Spain, across 3 years. The inclusion criteria were as follows: i) women aged between 35-75 years and diagnosed with fibromyalgia, at least 12 months before the start of the study, according to the 2010 ACR diagnostic criteria; ii) WPI value of 19 points; and iii) at the time of inclusion, a pharmacological treatment scheme consisting of analgesics (paracetamol 600 mg/day), nonsteroidal anti-inflammatories (dexketoprofen 25 mg/day), anxiolytics (lorazepam 2 mg/day) and antidepressants (amitriptyline 75 mg/day). The exclusion criteria were as follows: i) medical diagnosis of other rheumatic diseases or serious diseases such as cancer and heart disease; ii) mental illnesses such as schizophrenia, bipolar disorder, depression and cognitive impairments (not having passed the Mini-Mental State Examination); iii) pacemaker and implants with electric current conduction in the brain; and iv) pregnant. Patients were stratified into four groups according to: i) age (older patients: above 50 years old and with menopause and younger patients: below 50 years old and without menopause; $Q_{1E} = 64.3 \pm 4.7$ years, and $Q_{4E} = 37.9 \pm 2.4$ years) and ii) WPI scores (patients with high WPI scores and patients with low WPI scores; using a cut-off value of 10, which is the

Funding: this study was funded by
PAI BIO-311 and CTS-595
(Junta de Andalucía).
Competing interests: none declared.

mean value of the WPI scale; $Q1_w = 18.1 \pm 1.6$ points; 95% CI: 17.4-18.5 points; $Q4_w = 6.5 \pm 1.6$ points; 95% CI 6.2-7.4 points). All participants were informed about the objectives of the study and its methodology. In addition, they signed an informed consent form following the criteria approved at the 18th World Medical Association, Helsinki, Finland, June 1964, and its subsequent modifications. The protocol was approved by the Ethics Committee of Pablo de Olavide University (Seville, Spain) (n°. 12632-Y) and by the Spanish Agency for Medicines and Medical Devices [2010 02 0783 CD], in regard to LIMS. The procedures followed were in accordance with the Helsinki Declaration of 1975/83.

Procedure

Patients received an initial evaluation in which the FM severity level was determined and were randomly assigned into two groups (280 patients followed the pharmacological treatment and another 280 patients followed the pharmacological treatment plus LIMS sessions). For this purpose, all subjects were evaluated with the ACR 2010 criteria (WPI and SS score), which consider that a patient meets the diagnostic criteria for FM if WPI ≥ 7 and SS score ≥ 5 or if WPI 3-6 and SS score ≥ 9 . Jointly with the aforementioned, the S-FIQ was used to measure the extent of functional capacity and quality of life of the participants. The scores for this questionnaire range from 0 to 100; scores above 70 points indicate severe impact. These same measurements were performed two weeks after the last application of LIMS to analyse the acute effects of LIMS on the central nervous system and its impact on the systemic somatization of the organism. All tests were performed from 9:00 a.m. to 12:00 p.m. in the Fibromyalgia Unit, always by the same health professional trained for this task, with the purpose of reducing inter-examiner error. After completing the initial assessments, the patients that followed the LIMS protocol were taken to the room where the treatment was performed; they were familiarized with the equipment, and the protocol was explained. Each pa-

Table I. Mean, standard deviation, confidence intervals (95% CI) and level of significance for the WPI, SS Score and S-FIQ diagnostic variables analysed at the time of diagnosis (Pre) and at 2 (Post), 12 (3 M) and 24 weeks (6 M) after the last treatment session, for all patients.

Period	WPI (points)	SS score (points)	S-FIQ (points)
Pre w/o LIMS	14.1 $\pm$ 2.6 (10.8-13.1)	8.6 $\pm$ 2.1 (7.4-7.9)	74.3 $\pm$ 12.2 (66.8-71.9)
Post w/o LIMS (2 weeks)	12.9 $\pm$ 3.5 (9.2-13.0)	7.9 $\pm$ 2.7 (7.1-8.0)	69.9 $\pm$ 14.9 (56.5-62.3)
3 M w/o LIMS (12 weeks)	13.1 $\pm$ 3.9 (10.7-13.5)	8.1 $\pm$ 2.1 (7.3-7.9)	59.4 $\pm$ 10.6* (52.3-59.8)
6 M w/o LIMS (24 weeks)	13.7 $\pm$ 3.3 (10.9-13.8)	7.3 $\pm$ 3.5 (6.8-7.8)	57.9 $\pm$ 13.3* (50.8-58.1)
Pre with LIMS	12.2 $\pm$ 4.2 (11.7-12.7)	7.8 $\pm$ 2.0 (7.6-8.0)	69.9 $\pm$ 16.8 (67.5-71.4)
Post with LIMS (2 weeks)	5.7 $\pm$ 4.5** (5.2-6.2)	4.8 $\pm$ 2.3** (4.6-5.1)	40.1 $\pm$ 20.8** (37.7-42.5)
3 M with LIMS (12 weeks)	5.9 $\pm$ 4.4** (5.4-6.4)	4.9 $\pm$ 2.3** (4.7-5.2)	39.9 $\pm$ 19.7** (37.6-42.2)
6 M with LIMS (24 weeks)	6.4 $\pm$ 4.3* (5.9-6.9)	5.2 $\pm$ 2.4* (4.9-5.5)	41.1 $\pm$ 20.4** (38.7-43.5)

$p \leq 0.05$ *; $p \leq 0.001$ **; w/o: without.

tient was scheduled the following week for the first application, maintaining the same day and time throughout treatment. Eight sessions lasting 20 minutes each (1 session/week) were performed. Two, 12 and 24 weeks after completing treatment all patients (with and without LIMS) were assessed based on the 2010 ACR criteria (WPI; SS score) and the S-FIQ test. As the LIMS sessions progressed, drug doses decreased, a reflection of the improvement in the three variables analysed, and after the last session, medication became unnecessary, except antidepressants, but the dose was reduced to 25 mg/day.

LIMS was applied inside a cabin with a Faraday cage to eliminate electromagnetic interference. The equipment included a flexible cap with 33 coils that surrounded the head. The amplitude of the applied current was 545 μ A. Each coil produced a magnetic field of 43 nT at a distance of 1 cm and 0.9 nT at a distance of 4 cm. A square-pulse current with low frequency (8 Hz) was used. Signal fluctuations associated with noise were approximately 3%.

Statistics

The basic statistics (mean, standard deviation, CI_{95} and range) and data

normality (Kolmogorov test) were calculated for each analysed variable (S-FIQ, WPI and SS score). To verify the changes in and analyse the evolution of the variables studied (before treatment with LIMS and at weeks 2, 12 and 24 after LIMS treatment), ANOVA was used for repeated measurements when the series had a normal distribution, and Friedman's ANOVA, with Wilcoxon's matched pairs *post hoc* analysis, was used when the series did not show a normal distribution. In the pairwise comparison, Student's *t* test and the Wilcoxon test were applied. Differences with $p \leq 0.05$ were accepted as significant. Last, the *effect size* (moderate ≥ 0.5 ; high ≥ 0.8) was calculated. The data were analysed using IBM SPSS Statistics v24.0.

Results

Changes in the WPI (range: 0-19 points), SS score (range: 0-12 points) and S-FIQ (range: 0-100 points) for the entire sample are shown in Table I. Patients treated only with drugs did not show significant differences for WPI and SS score at any time after pharmacological treatment (Table I). However, this group of patients showed significantly lower values ($p \leq 0.05$) for S-FIQ

12 and 24 weeks after treatment (Table I). In the case of patients treated with drugs plus LIMS, the three variables were significantly lower ($p \leq 0.001$) 2 and 12 weeks after completing LIMS treatment. Twenty-four weeks after treatment, the reduction in the three variables remained significant, although to a lesser degree ($p \leq 0.05$).

Two weeks after completing LIMS treatment, the WPI decreased by 53.3% ($p \leq 0.001$), while the SS score decreased by 38.5% ($p \leq 0.001$). The S-FIQ reduced 42.6% ($p \leq 0.001$), remaining at similar values during the 24 subsequent weeks (Table I).

In a second analysis, the sample was reorganized based on age (patients older than 50 years ($n=70$) and those younger than 50 ($n=70$) and WPI score (the 70 highest scores versus the 70 lowest scores), at the time of diagnosis, to observe the variation in scores for the three questionnaires 2, 12 and 24 weeks after the completion of LIMS treatment.

According to the 19 pain areas included in the WPI (Fig. 1A), the mean initial score at the time of diagnosis was similar for both groups (older: 12.6 ± 4.4 ; 95% CI: 11.6-13.6; younger: 12.0 ± 4.5 ; 95% CI: 10.9-13.0). After LIMS, the reduction in the WPI score was significant ($p \leq 0.001$) and the same in the two groups of women and therefore independent of age. This reduction was already observed at 2 weeks after treatment and was maintained in the two groups of women during the 24 weeks of follow-up. However, in younger women, the decrease in WPI values was lower 24 weeks after treatment compared to that in older women. After LIMS, reductions in WPI values were significant throughout the follow-up period (Fig. 1A) in both age groups. For SS score, the results were similar (Fig. 1B). SS scores for patients from the two age groups showed a statistically significant decrease ($p \leq 0.001$) 2 weeks after treatment. This improvement was maintained in both groups throughout the 24 weeks of monitoring. However, in younger women, the decrease in SS score was lower 12 and 24 weeks after treatment than that in older women (Fig. 1B).

Fig. 1. Box-plot of the evolution of the WPI (A), SS score (B) and S-FIQ (C) values for the patients at the time of diagnosis (Pre) and 2 (Post), 12 (3 M) and 24 weeks (6 M) after the last treatment session. The evolution of patients older than 50 years ($n=70$) appears on the left (lighter bars). The evolution of patients younger than 50 years ($n=70$) is shown on the right (shaded bars).

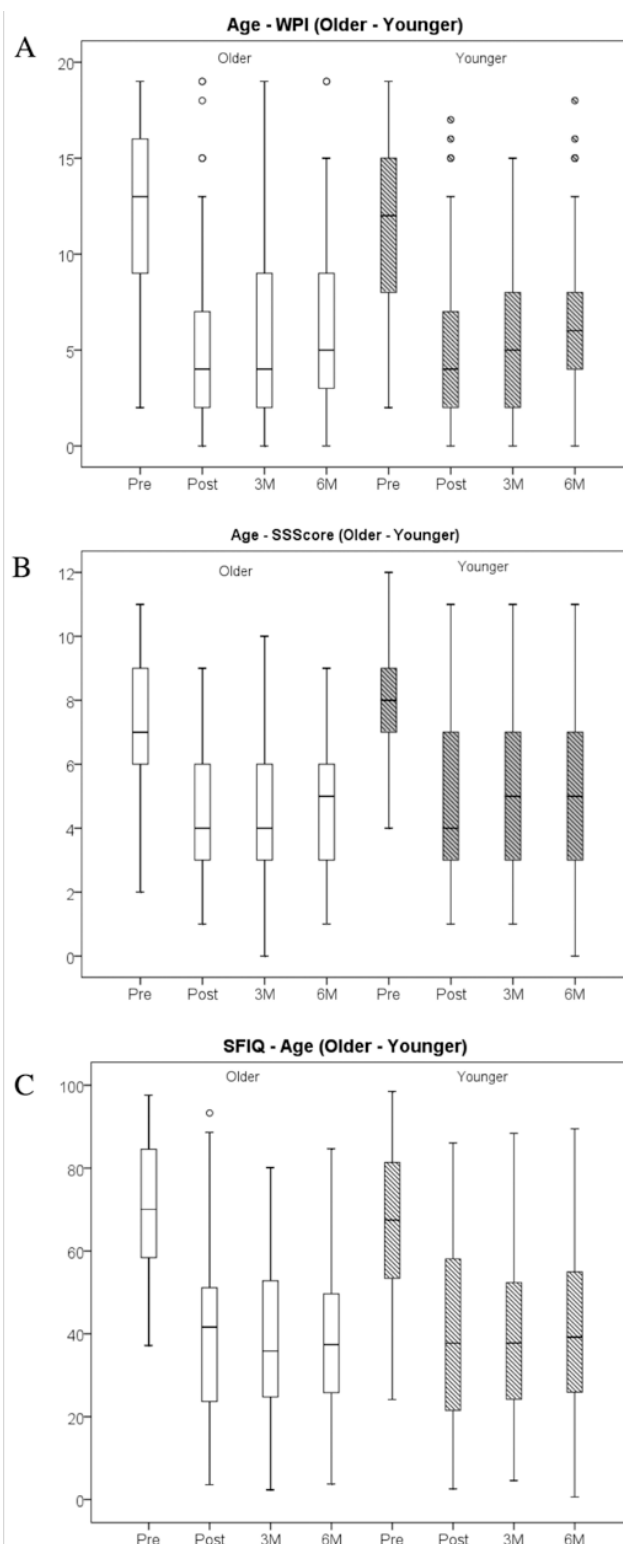


Figure 1C shows the variation in S-FIQ values in older and younger women. As observed for the previous variables, for both groups of women, a significant reduction in the values ($p \leq 0.001$) was observed starting two weeks after LIMS. The improvement remained

constant through 12 and 24 weeks of follow-up. In this case, unlike the WPI and the SS score, no differences were observed between the two groups in the degree of decrease in values throughout the follow-up period.

Figures 2A, 2B and 2C show the evo-

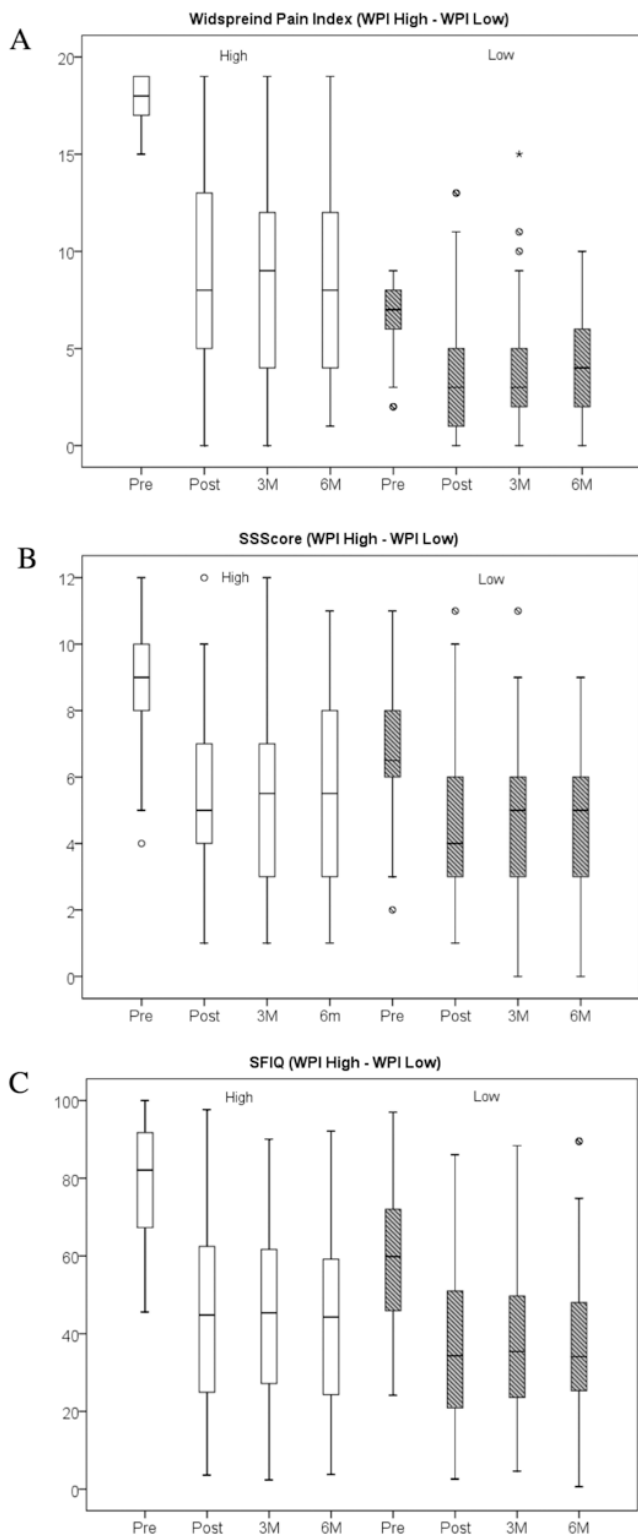


Fig. 2. Box-plot of the evolution of the WPI (A), SS score (B) and S-FIQ (C) values, grouping the patients according to pain severity (high level = WPIH and low level = WPIL) at the time of diagnosis (Pre) and 2 (Post), 12 (3 M) and 24 weeks (6 M) after the last treatment session. The evolution of the patients with the highest level of pain (WPIH; $n=70$) at the time of diagnosis is shown on the left (lighter bars). The evolution of patients with lower pain levels (WPIL; $n=70$) at the time of diagnosis is shown on the right (shaded bars).

WPIH group, the reduction remained stable throughout the 24-week follow-up, while in the WPIL group, the reduction was not observed 24 weeks after LIMS (Fig. 2B).

The second variable used to split the sample was SS score, and the same observation was made (Fig. 2B). There was a significant reduction in SS score in the two groups two weeks after the last treatment ($p \leq 0.001$). In the WPIH group, the reduction remained stable throughout the 24-week follow-up, while in the WPIL group, the reduction was progressively lost 12 weeks after the intervention ($p=0.067$).

For the S-FIQ (Fig. 2C), two weeks after treatment, significant improvement was observed in the two groups (WPIH and WPIL; $p \leq 0.001$), which was maintained throughout the 24-week follow-up, indicating 6 months of control.

As expected, for the three variables, the decrease in their values two weeks after completing LIMS treatment was always higher in the WPIH group than in the WPIL group.

Discussion

In this study, we analysed the impact of eight LIMS treatment sessions (one each week) on the WPI, SS score and S-FIQ for 24 weeks after the last treatment session. The data obtained show that LIMS is an effective intervention strategy for the treatment of FM, producing a decrease in WPI, SS score and S-FIQ. This decrease was independent of age and pain severity. Our finding confirms that LIMS is a valid tool for the treatment of this disease, confirming the conclusions of recent studies, who analysed (26) and performed (27) clinical trials that validated the use of rTMS for reducing pain, associated symptoms and improving the quality of life of patients with FM. To note that in the absence of LIMS, no significant decrease was observed for WPI and SS score values after the treatment and we only observed a significant decrease in S-FIQ values after 12 weeks of treatment. Yang and Chang (26) concluded that rTMS was effective reducing pain and could be a possible therapeutic option for controlling pain associated with FM. Moreover, Tanwar *et al.* (26)

lution of the same parameters (WPI and SS score and S-FIQ, respectively) when women were ranked based on the highest WPI score (WPIH; $n=70$) or lowest WPI score (WPIL; $n=70$).

The greatest initial differences between the two groups were found when ana-

lysing the WPI value at the time of diagnosis (Fig. 2A) (WPIH: 17.6 ± 1.4 ; 95% CI: 17.3-18.0; WPIL: 6.8 ± 1.8 ; 95% CI: 6.3-7.2; $p \leq 0.001$). Two weeks after treatment, there was a significant reduction ($p \leq 0.001$) in the WPI values in the two groups. However, in the

indicated that rTMS significantly reduced pain and associated symptoms of FM probably through targeting spinal pain circuits. To note, that LIMS, unlike rTMS, has not presented side effects (seizures and headaches after application) (28), which increases its safety and provides more comfort to patients. Notably, these types of therapies are not yet incorporated into the guidelines and clinical recommendations used to address this disease (29) because there is not sufficient availability of clinical trials to prove its effects on larger samples. The study by Sutbeyaz *et al.* (30) showed the clinical effectiveness of low-frequency pulsed electromagnetic field (PEMF) therapy. To do this, the authors compared two groups of women between 18 and 60 years diagnosed with FM according to the ACR. One group received full body applications of PEMF (40 μ T; 0.1 to 64 Hz) for three weeks at a rate of two daily applications. The same protocol was applied to the other group without PEMF. The FIQ was used to measure quality of life, and a visual analog scale (VAS) was used to measure pain. Both tests were performed before application at 4 and 12 weeks after treatment. Effectiveness 4 weeks after the completion of FIQ treatment increased 52% compared to baseline but reduced to 17% at 12 weeks posttreatment. This same trend was observed when the VAS was applied. Table I shows a 42% decrease in the FIQ average, when LIMS were used. In the absence of LIMS the decrease in the FIQ average was 20%. The fact that in the absence of LIMS we did not observe, after treatment, an improvement in WPI and SS score, but we do for S-FIQ could be due to the fact that WPI and SS score reflect issues more concrete and measurable. However, S-FIQ is more subjective and tends to underestimate function impairment.

A study by Maestú *et al.* (24) that used LIMS to treat patients with FM showed significant results regarding pain thresholds, performing activities of daily living, perception of chronic pain and quality of sleep, with no adverse effects. These were measured as acute responses with a small number of

participants (n=28). Our study complements these findings by extending the sample size 10x and monitoring up to 24 weeks after the last LIMS session. Similarly, it provides information associated with the increased functionality of patients, which is verified through the results obtained for the S-FIQ. Overall, 70% of the sample, 2 weeks after the last LIMS session, obtained scores below 50 points, which is the consensus value above which FM manifests. The improvement observed in the patients was independent of age and pain severity. Based on the data obtained and the evaluation instruments used, LIMS is an effective therapeutic tool for improving FM symptoms and the impact of this disease on the quality of life of patients, independent of age and degree of pain. The effect of LIMS is maintained for at least 24 weeks. As expected, these benefits are greater for more severe pain. In contrast, those patients who initially showed a lower level of pain benefit in a lesser degree in the short term and the loss of benefits over time is more accelerated. Given that starting at 24 weeks the benefits began to disappear, at least in the group with the lowest degree of pain, new LIMS sessions may be appropriate after this period of time.

Despite the data obtained in our study, the number of existing studies regarding the therapeutic usefulness of LIMS remains small. Therefore, it is necessary to continue investigating the use of LIMS for the treatment of FM. In this sense, it is important to establish the most appropriate treatment protocol (number of sessions, application time, rest period between sessions and frequency and intensity of stimulation). Like the study by Maestú *et al.* (24), this study does not address the physiological effects that underlie the improvement observed in patients. Therefore, it is necessary to carry out studies that explain the neurophysiological foundations that support the use of this therapy. Other limitations of the study are that anthropometric variables such as weight, fat mass, muscle mass and other behavioural changes or alternative therapies that patients performed

during the course of this study, such as physical activity, were not controlled.

To conclude, the data from our study indicate that in patients with FM, the use of LIMS induces a significant decrease in the diagnostic variables related to pain, symptoms severity and quality of life. This effect was significant two weeks after the last treatment session and was maintained for at least 24 weeks.

Acknowledgments

We are grateful to the patients that participated in this study.

References

1. YUNUS MB: Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. *Semin Arthritis Rheum* 2007; 36: 339-56.
2. DAVIS F, GOSTINE M, ROBERTS B, RISKO R, CAPPELLERI JC, SADOSKY A: Characterizing classes of fibromyalgia within the continuum of central sensitization syndrome. *J Pain Res* 2018; 23: 2551-60.
3. POMARES FB, FUNCK T, FEIER NA *et al.*: Histological Underpinnings of Grey Matter Changes in Fibromyalgia Investigated Using Multimodal Brain Imaging. *J Neurosci* 2017; 37: 1090-101.
4. BAIR MJ, KREBS EE: Fibromyalgia. *Ann Intern Med* 2020; 172: ITC33-ITC48.
5. CLAUW DJ: Fibromyalgia: a clinical review. *JAMA* 2014; 311: 1547-55.
6. YUNUS MB: Central sensitivity syndromes: a new paradigm and group nosology for fibromyalgia and overlapping conditions, and the related issue of disease versus illness. *Semin Arthritis Rheum* 2008; 37: 339-52.
7. THEOHARIDES TC, TSILIONI I, ARBETMAN L *et al.*: Fibromyalgia syndrome in need of effective treatments. *J Pharmacol Exp Ther* 2015; 355: 255-63.
8. WOLFE F, SMYTHE HA, YUNUS MB *et al.*: The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990; 33: 160-72.
9. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al.*: 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum* 2016; 46: 319-29.
10. HEIDARI F, AFSHARI M, MOOSAZADEH M: Prevalence of fibromyalgia in general population and patients, a systematic review and meta-analysis. *Rheumatol Int* 2017; 37: 1527-39.
11. D'AGNELLI S, ARENDT-NIELSEN L, GERRA MC *et al.*: Fibromyalgia: genetics and epigenetics insights may provide the basis for the development of diagnostic biomarkers. *Mol Pain* 2019; 15: 1744806918819944.
12. DOCAMPO E, ESCARAMIS G, GRATACOS M *et al.*: Genome-wide analysis of single nucleotide polymorphisms and copy number

- variants in fibromyalgia suggest a role for the central nervous system. *Pain* 2014; 155: 1102-09.
13. TALOTTA R, BAZZICHI L, DI FRANCO M *et al.*: One year in review 2017: fibromyalgia. *Clin Exp Rheumatol* 2017; 35 (Suppl. 105): S6-12.
 14. ANGEL-GARCIA D, MARTINEZ-NICOLAS I, SATURNO-HERNANDEZ PJ: Clinical approach to fibromyalgia: Synthesis of Evidence-based recommendations, a systematic review. *Reumatol Clin* 2016; 12: 65-71.
 15. GARCIA-HERMOSO A, SAAVEDRA JM, ESCALANTE Y: Effects of exercise on functional aerobic capacity in adults with fibromyalgia syndrome: A systematic review of randomized controlled trials. *J Back Musculoskelet Rehabil* 2015; 28: 609-19.
 16. EVCIK D, KETENCIA, SINDEL D: The Turkish Society of Physical Medicine and Rehabilitation (TSPMR) guideline recommendations for the management of fibromyalgia syndrome. *Turk J Phys Med Rehabil* 2019; 65: 111-23.
 17. BERNARDY K, KLOSE P, BUSCH AJ, CHOY EHS, HÄUSER W: Cognitive behavioural therapies for fibromyalgia. *Cochrane Database Syst Rev*, 2013; 9: CD009796.
 18. SILVA AR, BERNARDO A, COSTA J *et al.*: Dietary interventions in fibromyalgia: a systematic review. *Ann Med* 2019; 51(suppl. 1): 2-14.
 19. ABLIN J, FITZCHARLES MA, BUSKILA D, SHIR Y, SOMMER C, HÄUSER W: Treatment of fibromyalgia syndrome: recommendations of recent evidence-based interdisciplinary guidelines with special emphasis on complementary and alternative therapies. *Evid Based Complement Alternat Med* 2013; 2013: 485272.
 20. DA SILVA-COSTA I, GAMUNDI A, VIVAS-MIRANDA JG, SOUZA-FRANÇA LG, NOVAES DE SANTANA C, MONTTOYA P: Altered Functional Performance in Patients with Fibromyalgia. *Front Hum Neurosci* 2017; 11: 14.
 21. LEFAUCHER JP, ALEMAN A, BAEKEN C *et al.*: Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): an update (2014-2018). *Clin Neurophysiol* 2020; 131: 474-528.
 22. BAZZICHI L, GIACOMELLI C, CONSENSI A *et al.*: One year in review 2020: fibromyalgia. *Clin Exp Rheumatol* 2020; 38 (Suppl. 123): S3-8.
 23. CARRETERO B, MARTÍN MJ, JUAN A *et al.*: Low-frequency transcranial magnetic stimulation in patients with fibromyalgia and major depression. *Pain Med* 2009; 10: 748-53.
 24. MAESTÚ C, BLANCO M, NEVADO A *et al.*: Reduction of pain thresholds in fibromyalgia after very low-intensity magnetic stimulation: a double-blinded, randomized placebo-controlled clinical trial. *Pain Res Manag* 2013; 18: e101-6.
 25. SALGUEIRO M, GARCÍA-LEIVA JM, BALLESTEROS J, HIDALGO J, MOLINAR; CALANDRE EP: Validation of a Spanish version of the Revised Fibromyalgia Impact Questionnaire (FIQR). *Health Qual Life Outcomes* 2013; 11: 132.
 26. YANG S, CHANG MC: Effect of repetitive transcranial magnetic stimulation on pain management: a systematic narrative review. *Front Neurol* 2020; 18: 114.
 27. TANWAR S, MATTOO B, KUMAR U, BHATIA R: Repetitive transcranial magnetic stimulation of the prefrontal cortex for fibromyalgia syndrome: a randomised controlled trial with 6-months follow up. *Adv Rheumatol* 2020; 60: 34.
 28. O'CONNELL NE, MARSTON L, SPENCER S, DE SOUZA LH, WAND BM: Non-invasive brain stimulation techniques for chronic pain. *Cochrane Database Syst Rev*, 2018; 4: CD008208.
 29. MACFARLANE GJ, KRONISCH C, DEAN LE *et al.*: EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017; 76: 318-28.
 30. SUTBEYAZ ST, SEZER N, KOSEOGLU F, KIBAR S: Low-frequency pulsed electromagnetic field therapy in fibromyalgia: a randomized, double-blind, sham-controlled clinical study. *Clin J Pain* 2009; 25: 722-8.