

# Can Technological Combinations of Therapeutic Resources in Rehabilitation Act with Drug Synergy in the Treatment of Fibromyalgia Symptoms? - Pilot Study

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## Abstract

Fibromyalgia is a disease characterized by intense, diffuse musculoskeletal pain that lasts for more than 3 months. This disease can cause psychosomatic and psychosocial changes, impacting the lives of patients, most often women. There are several treatments, including pharmacological treatments, such as anxiolytics, antidepressants, analgesics, and anti-inflammatories, and non-pharmacological treatments, which include nutrition, physical therapy, and psychology. This study analyzed data from the medical records of patients aged 20 years and older who used photobiomodulation combined with therapeutic ultrasound in relation to the synergy of medications in patients affected by the syndrome. The assessment and questionnaire found in the medical records at both the beginning and end of treatment were examined. The evaluation mechanisms identified were the Visual Analog Scale and the International Fibromyalgia Questionnaire. Through the results obtained by this study, a significant improvement was observed in both drug and non-drug treatments, with emphasis on the evolution in older patients, concluding, therefore, that this strategy is ideal for fibromyalgia patients, restoring their quality of life.

**Keywords:** Fibromyalgia; drugs; Ultrasound; Low-level laser therapy; Fotobiomodulation; Pain

## Introduction

Fibromyalgia (FM) is a complex syndrome of chronic nociceptive pain and hyperalgesia that involves abnormalities in the neuroendocrine and autonomic nervous systems, genetic, psychosocial and environmental factors. It is characterized by intense and diffuse musculoskeletal pain lasting more than 3 months. In addition, symptoms such as intense fatigue, irritable bowel syndrome, mood and sleep disorders, paresthesias, headache, among others [1-4]. This disease leads to psychosomatic and psychosocial changes, directly impacting the patient's routine, drastically reducing the quality of life and increasing the time away from activities, generating economic losses for members and their families [2].

The prevalence in the general population is around 2.5% to 5%, being predominant in women (10 women to one man), with a peak incidence between 30 and 50 years of age [5,6].

The pathophysiology of fibromyalgia has not yet been fully elucidated. It is currently known that the onset of the syndrome may be associated with genetic and environmental factors [7,8]. The main pathophysiological phenomenon of FM is central sensitization, characterized by the attenuation of descending inhibitory nociceptive pathways and favoring of ascending pro-nociceptive pathways, thus presenting an imbalance, a decrease in inhibitory synapses and an increase in excitatory synapses, manifesting allodynia (pain when lightly touching the skin) and hyperalgesia (amplified pain) [9].

According to the American College of Rheumatology (ACR), there is no laboratory marker or imaging test that proves the existence of the syndrome; the diagnosis is predominantly clinical, made based on the assessment of the presence of pain and sensitivity in 11 or more of the 18 tender points, associated with the clinical judgment of the signs and symptoms reported by the individuals [10,11].

There are several treatments to improve symptoms due to the complexity of the symptoms, and they are divided into two aspects: pharmacological and non-pharmacological. Pharmacological treatments can treat each symptom with a specific medication, such as analgesics, muscle relaxants and anti-inflammatories, which can reduce pain and inflammation. In the case of antidepressants, anxiolytics and anticonvulsants, these are used to reduce the action of excitatory neurotransmitters or increase the activity of inhibitory neurotransmitters, enhancing the analgesic effects, sleep, mood, fatigue, among others [12,13].

Non-drug treatment is just as important as pharmacological treatment. Alternative treatments such as physiotherapy, acupuncture, nutrition and psychological rehabilitation can bring benefits in controlling fibromyalgia [14].

Physiotherapy emerges as a non-drug therapeutic approach offering a variety of techniques that play an important role in chronic pain [15], and currently new research and technologies have been improving and providing improvement and quality of life for fibromyalgia patients.

A new device developed by the Physics Institute of São Carlos of

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the University of São Paulo (IFSC-USP) and produced by the company MMOptics, Brazil. RECUPERO® allows a synergistic action of Laser and Ultrasound, overlapping the therapeutic fields, and thus enhancing the effects, reducing pain and consequently improving quality of life [16-20]. Ultrasound waves propagate causing agitation in molecules, generating vibrations in their equilibrium positions. They can propagate continuously or in pulses. It is already widely used, allowing the reduction of muscle pain, and, due to its thermal loop, it causes vasodilation and increases the speed of signaling, promoting analgesia and anti-inflammatory action [21].

Another technological resource is photobiomodulation, which consists of emitting light radiation in tissues with appropriate wavelengths, promoting specific chemical and physical reactions, altering cellular physiology, modulating mitochondrial enzymes and promoting greater ATP production [22].

With this innovation, the synergism of the resources when applied to the palms of the hands through a systemic approach, conduct afferent nerve stimuli to the brain, allowing the modulation of intracranial compliance, promoting homeostasis and the production of neurotransmitters, affecting the pain center, normalizing the amplified response of the condition imposed by fibromyalgia. In addition, these changes promote relaxation, favorable for sleep, gradually reducing anxiety and depression [20, 23,24].

Thus, the present study aimed to analyze retrospective observational data through intervention records on the combined effects of ultrasound and laser in relation to drug synergy in patients affected by fibromyalgia.

## Materials and Methods

### Approval and location

This study was approved by the Human Research Ethics Committee of the Santa Casa de Misericórdia de São Carlos and by the National Research Ethics Committee, through CAAE 58039522.8.0000.8148, following resolution 466/2012, with data searches carried out at the Photodynamic Therapy Unit, a research unit of the Physics Institute of São Carlos, University of São Paulo, São Carlos, São Paulo, Brazil.

### Patient and protocol

For the research, retrospective observational data were analyzed through intervention records on the combined effects of therapeutic ultrasound and photobiomodulation in relation to drug synergy in patients affected by fibromyalgia.

Thirty-eight medical records of patients diagnosed with fibromyalgia were analyzed. Of these 38 records, all were female, between 20 and 60+ years old, some were using drug treatments to control the symptoms caused by fibromyalgia, among the medications were antidepressants, anxiolytics, analgesics, anti-inflammatories and a combination of these.

All patients participated in non-drug treatment using equipment that synergistically combines photobiomodulation and therapeutic ultrasound. The parameters used for photobiomodulation were low-power laser with a wavelength of 660nm, power of 100mW, and therapeutic ultrasound, pulsed mode, 1MHZ, frequency of 100Hz, with an application time of 12 minutes, 6 minutes in each palm of the hand. There were 10 sessions, twice a week, for 5 weeks.

### Equipment and Patent

The equipment used during the research was developed by the Institute of Physics of São Carlos, University of São Paulo, and produced

by the company MMOptics, patent number BR102014007397-3 A2, certified by the National Health Regulatory Agency (ANVISA) nº80051420029, called RECUPERO®. The equipment is capable of synergistically emitting two resources, such as low-power laser and therapeutic ultrasound, allowing the overlapping of the fields at the same time.

### Questionnaires and scales

The assessment and questionnaire found in the medical records at both the beginning and end of treatment were examined. These assessment mechanisms identified were the Visual Analogue Scale (VAS) and the International Fibromyalgia Questionnaire (FIQ). Pain assessment is performed using the Visual Analogue Scale (VAS), where the patient is asked to indicate the degree of pain at the time of assessment, on a scale of 0 to 10. The International Fibromyalgia Questionnaire allows the patient's quality of life to be numerically quantified, inferring daily life issues and actions, establishing the degrees of difficulty in carrying out these actions.

### Statistical methodology

The data were subjected to the Kolmogorov Smirnov normality test and subsequently to Anova Two Away analysis, using the Student "t" test to analyze the evolution and between groups, considering  $p < 0.05$ . The software used was Instat 3.0 for Windows.

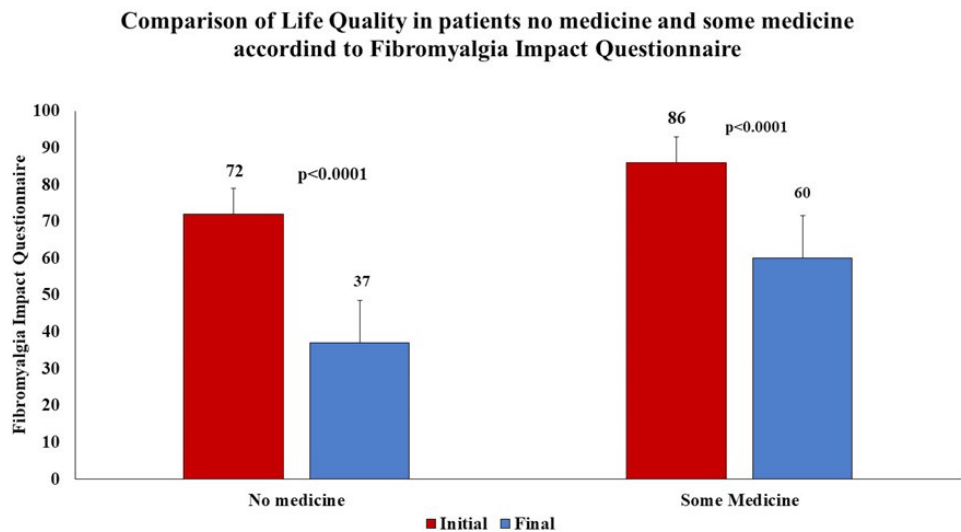
## Results

Figure 1 shows the monitoring of treatment using the therapeutic resource of photobiomodulation associated with therapeutic ultrasound, illustrating the values of the comparison of quality of life, measured through the Fibromyalgia Impact Questionnaire in patients with or without drug treatment in the pre- and post-treatment moments. It is possible to observe that without medication, before treatment a value of 72 was measured and after treatment 37 ( $p < 0.0001$ ). In relation to patients who used medication and associated the technology, a pre-treatment value of 86 was observed and after treatment 60 ( $p < 0.0001$ ).

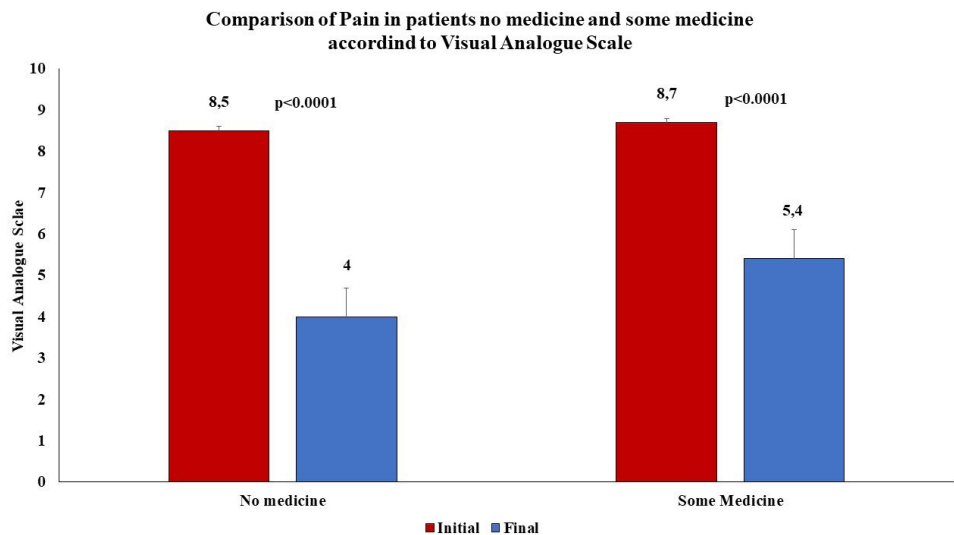
Figure 2 shows the monitoring of the treatment using photobiomodulation and therapeutic ultrasound, illustrating the comparison of pain values in patients with or without drug treatment according to the Visual Analog Scale (VAS) in the pre- and post-treatment moments. It was observed that, among the patients not using medication, a value of 8.5 was obtained before treatment and 4 after treatment, generating a significant difference ( $p < 0.0001$ ). In relation to the patients who used medication, a value of 8.7 was observed before treatment and 5.4 after treatment. In this context, there was a significant difference in the pre- and post-treatment comparison with  $p < 0.0001$ .

Figure 3 shows the treatment follow-up using photobiomodulation and therapeutic ultrasound, illustrating the values of the comparison of quality of life in patients in relation to different types of medications, according to the Fibromyalgia Impact Questionnaire. The pre-treatment and post-treatment comparisons show respectively 75.6 and 34.3 (antidepressants), 88.25 and 69.5 (anxiolytics), 88.5 and 65 (antidepressants and anxiolytics), 85.6 and 53.15 (antidepressants and others), 87 and 62.5 (anxiolytics and others). No patient was found using muscle relaxants, analgesics or anti-inflammatories.

Table 1 shows the mean of the patients correlated with their respective ages, initial and final Fibromyalgia Impact Questionnaire, initial and final visual analogue scale. Patients aged between 20 and 30 ( $n=0$ ) were not found in this age group. Patients aged between 31 and 40 ( $n=4$ ), between 41 and 50 ( $n=9$ ), between 51 and 60 ( $n=10$ )



**Figure 1:** Comparison of quality of life in patients without (n=11) and with (n=27) drug intervention, according to the Fibromyalgia Impact Questionnaire in the pre- and post-treatment moments. The Kolmogorov-Smirnov normality test was used, followed by the Student “t” test.



**Figure 2:** Comparison of pain in patients with or without drug treatment according to the Visual Analogue Scale (VAS) in the pre- and post-treatment moments. The Kolmogorov-Smirnov normality test was used, followed by the Student’s t-test analysis.

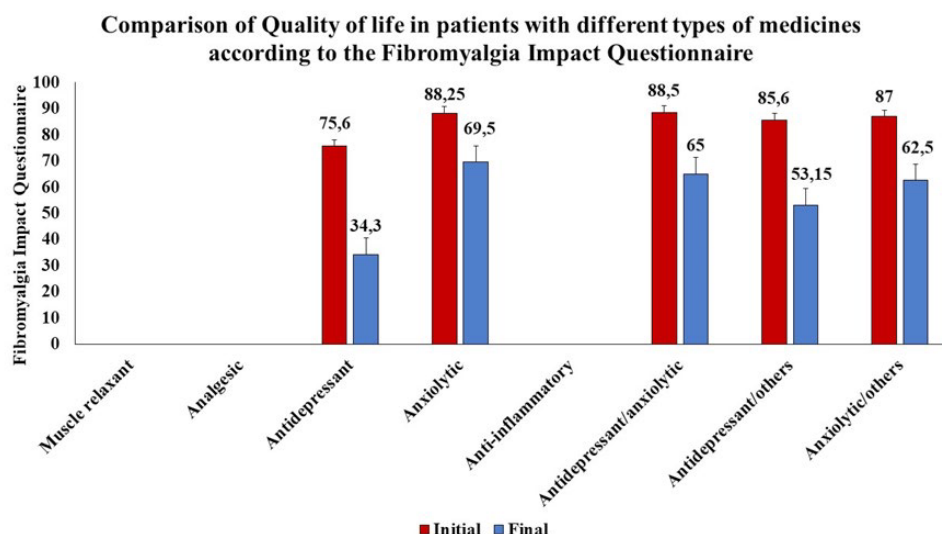
Ranges	MEDIUM Age	FIQ Initial	FIQ Final	VAS Initial	VAS Final
31 a 40 (n=4)	37.2	84	54	8.5	4.5
41 a 50 (n=9)	46.4	82.4	54.6	8.8	4.9
51 a 60 (n=10)	56.2	85.9	53.6	8.8	5.1
61+ (n=15)	67.6	78.8	53.6	8.5	5.2

**Table 1:** Illustrates the average of patients correlated with their respective ages, initial and final Fibromyalgia Impact Questionnaire, initial and final visual analogue scale.

and over 61 (n=15) are presented. When evaluating the Fibromyalgia Impact Questionnaire, relating initial and final intervention values, we observed ages between 31 and 40 (84 to 54), between 41 and 50 (82.4 to 54.2), between 51 and 60 (85.9 to 53.6) and over 61 (78.8 to 53.6). Regarding the Visual Analogue Scale, relating Initial and Final intervention values, we observed ages between 31 and 40 (8.5 to 4.5), between 41 and 50 (8.8 to 4.9), between 51 and 60 (8.8 to 5.1) and over 61 (8.5 to 5.2).

**Discussion**

Through knowledge of the nociceptive pathways in central sensitization, the use of assistive medications, which include antidepressants, anxiolytics, neuromodulators, among others, which are used for the metabolism and reuptake of serotonin and norepinephrine, decreasing the action of excitatory neurotransmitters or increasing the action of inhibitory neurotransmitters, enhancing the analgesic



**Figure 3:** Comparison of quality of life in patients with different types of medications. No statistical analysis was performed due to the sample being divided by medication. The comparison performed is a percentage.

effects, sleep, mood, fatigue, promoting well-being in the fibromyalgia patient [25]. However, the responses are sometimes unsatisfactory or present side effects associated with the long-term use of such drugs. Therefore, most patients seek other non-pharmacological therapies to complement the treatment [26].

Some studies have scientifically demonstrated the homeostasis of the syndrome through the synergistic association of photobiomodulation and therapeutic ultrasound [18,20,23]. Therapeutic laser is based on non-thermal effects, such as photochemical, photophysical and photobiological effects, promoting photobiomodulatory effects in cells. Radiation generates photochemical changes in the photoreceptor biomolecule, such as cytochrome C oxidase, present in mitochondria, increasing ATP synthesis, transmitting photobiological effects to other parts of the cell. Photophysical effects promote activation of the sodium/potassium pump, leading to ionic balance and maintenance of cell membrane polarity, modulating cellular processes resulting in analgesic, anti-inflammatory, immunomodulatory and tissue repair effects [27].

Therapeutic ultrasound is a type of sound energy generated by a transducer composed of piezoelectric crystals that transform the initial electrical energy into mechanical energy, and when transmitted to biological tissues, it is capable of producing cellular changes. For these ultrasonic waves to propagate, the medium must have elastic properties. The movement of a vibrating body is transmitted to adjacent molecules, which, before returning to the equilibrium position, transmit this movement to the surrounding molecules, resulting in the production of heat, promoting an increase in the metabolic rate of the tissue, temporary extensibility of collagen fibers, circulation, pain, muscle spasm and tissue healing, inducing biological responses such as muscle relaxation, tissue regeneration and reduction of inflammation [28-30].

Low-level laser therapy together with therapeutic ultrasound, when performed synergistically, allow the overlapping of these resources, enhancing their effects, promoting cellular homeostasis, relieving pain, accelerating the inflammatory response and cellular regeneration [24]. This application of the combined action occurs in the palms of the hands, enabling a systemic action, as it is a region that presents a differentiation in the number of nerve endings close to the blood vessels [30,31].

These photonic and ultrasonic stimuli are conducted by sensory nerves through afferent pathways leading to the brain, modulating and reducing intracranial compliance, allowing the normalization of the amplified response resulting from the central sensitization process [13]. In addition, the conduction stimulates one of the main neural pathways, the vagus nerve, which is responsible for modulation in order to provide adaptations and maintain the body's homeostasis, through the parasympathetic system, influencing processes such as bradycardia, sleep, reduction of stomach pain and irritable bowel syndrome [32-34].

With the absence of comorbidities between these nosological conditions, especially those of sensory interference, sleep quality is largely restored, thus allowing greater action of neuronal reverberation and expression of plasticity genes, favoring better acquisition of memory, concentration and learning [35-39], and reducing anxiety and depression [26,40].

However, due to the complexity imposed by fibromyalgia, there is no single intervention model, often requiring a multidisciplinary intervention. One of the multidisciplinary approaches is the combination of pharmacological and non-pharmacological treatment, which appears to be the ideal strategy for the treatment of fibromyalgia [9].

In this study, Figure 1 shows a comparison of the quality of life in patients with or without drug treatment according to the Fibromyalgia Impact Questionnaire in the pre- and post-treatment moments, and Figure 2 shows a comparison of pain in patients with or without drug treatment according to the Visual Analogue Scale in the pre- and post-treatment moments. In the figures, we observed a significant response for both treatments. With the illustration in Figure 3, which compares the quality of life in patients with different types of medication, we found that the best results were obtained with antidepressants and antidepressants and others. And in relation to the average of patients correlated with their respective ages, as shown in Table 1, it was found that the older the patient, the greater the number of patients. And the older the patient, the greater the reduction value found, whether in the Fibromyalgia Impact Questionnaire or in the Visual Analogue Scale.

This trend may be related to several factors, such as the aging



process, which contributes to greater sensitivity to pain, reduced muscle and joint functional capacity, in addition to an accumulation of comorbidities over the years [41,42].

## Conclusion

The study demonstrated that both drug and non-drug treatments contributed significantly to pain and all the complexity imposed by the syndrome, especially in older age groups, providing improvements in functional and emotional capacity, positively impacting overall quality of life.

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