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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 nociplastic 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 minuts 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)

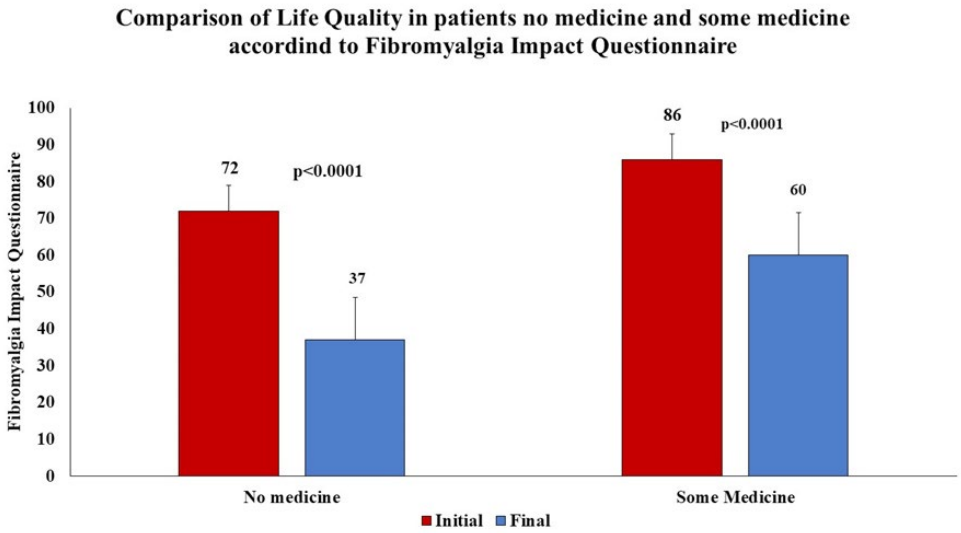

Figure 1: Comparison of quality of life in patients without (n=11) and with (n=27) drug intervention, according to the Fibromyalgia Impact Questionnaire in the pre- and post-treatment moments. The Kolmogorov-Smirnov normality test was used, followed by the Student "t" test.

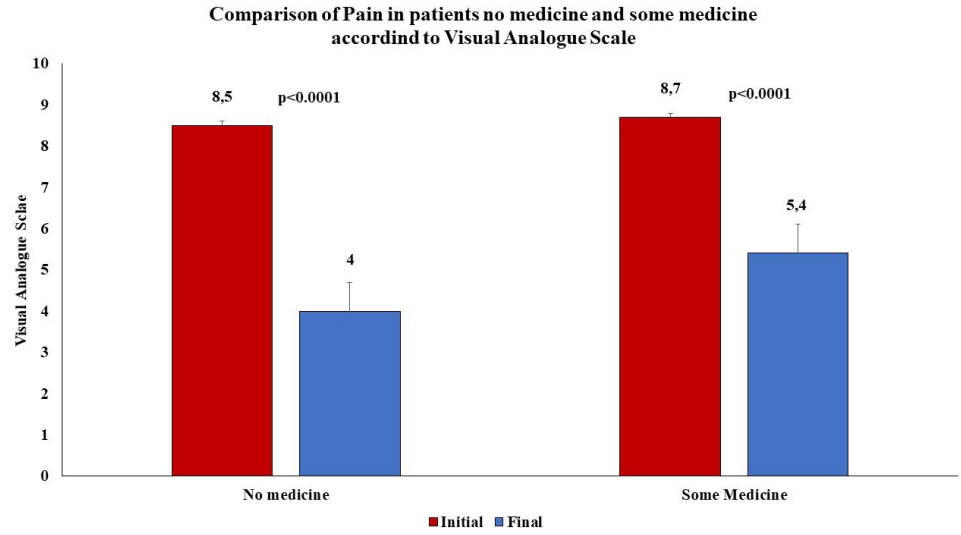

Figure 2: Comparison of pain in patients with or without drug treatment according to the Visual Analogue Scale (VAS) in the pre- and post-treatment moments. The Kolmogorov-Smirnov normality test was used, followed by the Student's t-test analysis.

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

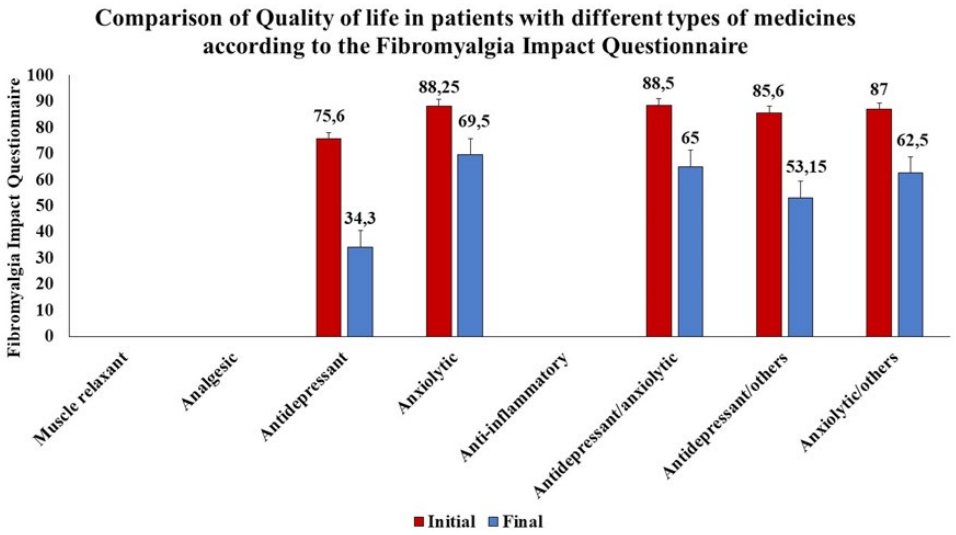

Figure 3: Comparison of quality of life in patients with different types of medications. No statistical analysis was performed due to the sample being divided by medication. The comparison performed is a percentage.

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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References

1. Hausteiner-Wiehle C, Henningsen P (2023) Nociplastic pain is functional pain. Lancet 339: 1603-1604.
2. Batista AS, Maia JB, Souza CG, Lins CA, Souza MC (2020) Depression, anxiety and kinesiophobia in women with fibromyalgia practitioners or not of dance. BrJP 3: 318-321.
3. Bradley LA (2009) Pathophysiology of fibromyalgia. Am J Med 122: 22-30.
4. Arnold LM, Crofford LJ, Mease PJ, Burgess SM, Palmer SC, et. al (2008) Patient perspectives on the impact of fibromyalgia. Patient Educ Couns 73: 114-120.
5. Assumpção A, Cavalcante AB, Capela CE, Sauer JF, Chalot SD, et al. (2009) Prevalence of fibromyalgia in a low socioeconomic status population. BMC Musculoskelet Disord 10: 64.
6. Carmona L, Ballina J, Gabriel R, Laffon A, EPISER Study Group (2001) The burden of musculoskeletal diseases in the general population of Spain: Results from a national survey. Ann Rheum Dis 60: 1040-1050.
7. Choi CJ, Knutsen R, Oda K, Fraser GE, Knutsen SF (2010) The association between incident self-reported fibromyalgia and nonpsychiatric factors: 25-years follow-up of the Adventist Health Study. J Pain 11: 994-1003.
8. Oliver JE, Silman AJ (2009) What epidemiology has told us about risk factors and aetiopathogenesis in rheumatic diseases. Arthritis Res Ther 11: 223.
9. Russell IJ, Larson AA (2009) Neurophysio Pathogenesis of fibromyalgia syndrome: A unified hypothesis. Rheum Dis Clin North Am 35: 421-435.
10. Santos MM, Ribeiro L (2020) Fibromyalgia: offering evidence based treatment. Psicosom Psiquiatr 12: 46-54.
11. Bentes RdS, Camargo C, da Silva BL, Andrade MCH, Junior EJPG, et al. (2020) Fibromyalgia Syndrome and Depressive Disorder: an analysis of cross-sectional and longitudinal studies. Brazilian J Health Rev 3: 10080-10094.
12. Sauer K, Kemper C, Glaeske G (2011) Fibromyalgia syndrome: Prevalence, pharmacological and non-pharmacological interventions in outpatient health care. An analysis of statutory health insurance data. Joint Bone Spine 78: 80-84.
13. Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, et al. (2017) EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 76: 318-328.
14. Kozasa EH, Tanaka LH, Monson C, Little S, Leao FC, et al. (2012) The effects of Meditation-based interventions on the treatment of fibromyalgia. Curr Pain Headache Rep 16: 383-387.
15. Offenbacher M, Stucki G (2000) Physical therapy in the treatment of fibromyalgia. Scand J Rheumatol Suppl 113: 78-85.
16. Amaral J, Franco DM, de Aquino AE Jr, Bagnato VS (2018) Fibromyalgia Treatment: A New and Efficient Proposal of Technology and Methodological-A Case Report. J Nov Physiother 8: 1-3.
17. Bruno JSA, Franco DM, Ciol H, Zanchin AL, Bagnato VS, et al. (2018) Could Hands be a New Treatment to Fibromyalgia? A Pilot Study. J Nov Physiother 8: 1-5.
18. De Aquino Junior AE, Carbinatto FM, Franco DM, Amaral Bruno JS, Souza Simão ML, et al. (2021) The Laser and Ultrasound: The Ultra Laser like Efficient Treatment to Fibromyalgia by Palms of Hands -Comparative Study. J Nov Physiother 11: 1-12.
19. De Aquino Junior AE, Carbinatto FM, Fernandes AC, Franco DM, Lara AA, et al. (2021) The Combined Photobiomodulation and Therapeutic Ultrasound: How does the Efficient Treatment of Fibromyalgia by the Palms Promote a Prolonged Effect?. J Nov Physiother 11: 1-5.
20. De Aquino Junior AE, Carbinatto FM, Rocha Tomaz CS, Bagnato VS (2022) Photosonic Treatment and Fibromyalgia: The Effect on Brain Compliance-Case Report. J Nov Physiother 12: 1-6.
21. Çitak-Karakaya I, Akbayrak T, Demirtürk F, Ekici G, Bakar Y (2006) Short and Long-Term results of Connective Tissue Manipulation and Combined Ultrasound Therapy in Patients with Fibromyalgia. J Manipulative Physiol Ther 29:524-528.
22. Karu TI (2006) Mitochondrial mechanisms of photobiomodulation in context of new data about multiple roles of ATP. Photomed Laser Surg 28:159-160.
23. Aquino Junior AE, Carbinatto FM, Rodrigues TZ, Garcia V, et al. (2023) The Regulatory Action of Fibro fog: Pain, Quality of Life, Sleep, Anxiety and Depression observed after 42 Months of Treatment: A Case Report. J Nov Physiother 13: 1-7.
24. Junior AEA, Rodrigues TZ, Garcia V, Simão G, Carbinatto FM, et al. (2022) Conjugated and Synergistic Therapies in the treatment of Covid 19 Dysfunction - Pain, Weakness, Parestheria, Respiratory Condition, Memory,Olfactory and Taste: Case Series. J Nov Physiother 12: 1-10.
25. Heymann RE, Paiva EdS, Helfenstein Jr M, Pollak DF, Martinez JE, et al. (2010) Brazilian consensus on the treatment of fibromyalgia. Rev Bras Reumatol 50: 56-66.
26. Crofford LJ, Appleton BE (2001) Complementary and alternative therapies for fibromyalgia. Curr Rheumatol Reports 3: 147-156.
27. Nejatifard M, Asefi S, Jamali R, Hamblin MR, Fekrazad R (2021) Probable positive effects of the photobiomodulation as an adjunctive treatment in COVID-19: A systematic review. Cytokine 137: 155312.
28. Speed CA (2001) Therapeutic ultrasound in soft tissue lesions. Rheumatology (Oxford) 40: 1331-1336.
29. Haar Gt, Daniels S, Eastaugh KC, Hill CR (1982) Ultrassonically induced cavitation in vivo. BR J Cancer 5: 151 -155.
30. Lin G, Reed-Maldonado AB, Lin M, Xin Z, Lue TF (2016) Effects and Mechanisms of Low-Intensity Pulsed Ultrasound for Chronic Prostatitis and Chronic Pelvic PainSyndrome. Int J Mol Sci 17: 1057.
31. Albrecht PJ, Hou Q, Argoff CE, Storey JR, Wymer JP, et al. (2013) Excessive peptidergic sensory innervation of cutaneous arteriolevenule shunts (AVS) in the palmar glabrous skin of fibromyalgia patients: implications for widespread deep tissue pain and fatigue. Pain Med 4: 895- 915.
32. Vanderlei LCM, Silva RA, Pastre CM, Azevedo FM, Godoy MF (2008) Comparison of the Polar S810i monitor and the ECG for the analysis of heart rate variability in the time and frequency domains. Braz J Med Biol Res 41: 854-859.
33. Porges SW (2009) The polyvagal theory: new insights into adaptive reactions of the autonomic nervous system. Cleve Clin J Med 76 Suppl 2: S86-S90.
34. Kim H, Jung HR, Kim JB, Kim DJ (2022) Autonomic Dysfunction in Sleep Disorders: From Neurobiological Basis to Potential Therapeutic Approaches. J Clin Neurol 18: 140-151.
35. Buysse, DJ, Reynolds CF3rd, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Res 28:193-213.
36. Ribeiro S, Nicolelis MAL (2004) Reverberation, storage, and post synaptic propagation of memories during sleep. Learn Mem 11: 686-696.
37. Peigneux P, Laureys S, Fuchs S, Destrebecqz A, Collette F, et al. (2003) Learned Material Content and Acquisition Level Modulate Cerebral Reactivation During Posttraining Rapid-eye-movements Sleep. Neuroimage 20: 125-134.
38. Datta S (2000) Avoidance Task Training Potentiates Phasic Pontine-wave

Density in the Rat: A Mechanism for Sleep-dependent Plasticity. J Neurosci 20: 8607-8613.

39. Maquet P, Schwartz S, Passingham R, Frith C (2003) Sleep-related Consolidation of a Visuomotor Skill: Brain Mechanisms as Assessed by Functional Magnetic Resonance Imaging. J Neurosci 23: 1432-1440.

40. Fitzcharles MA, Ste-Marie PA, Goldenberg DL, Pereira JX, Abbey S, et al. (2013) 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary. Pain Res Manag 18: 119-126.

41. Birse TM, Lander J (1998) Prevalence of chronic pain. Can J Public Health 89: 129-131.

42. Neumann L, Buskila D (2003) Epidemiology of fibromyalgia. Curr Pain Headache Rep 7: 362-368.