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Pulsed Laser Acupuncture in the Treatment of Pain and Heart Rate Variability in Fibromyalgia Patients: A Pilot Randomized Clinical Trial

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Abstract

Introduction: Laser acupuncture (LA) is a medically approved treatment for chronic pain, especially fibromyalgia. It is widely known that all pain is related to autonomic modulation, which may influence heart rate variability (HRV). There are robust studies in the literature on the effect of LA with continuous frequency on musculoskeletal pain and autonomic modulation. However, little is known about the effect of pulsed frequency on fibromyalgia. Therefore, this study aimed to evaluate whether an individualized intervention protocol applying pulsed LA would provide benefits related to pain symptoms and cardiac autonomic modulation in patients with fibromyalgia.

Methods: In this pilot randomized clinical controlled trial, the sample consisted of women with fibromyalgia between the ages of 40 and 80, randomized into two groups: a control group (CG; n = 10) and an experimental group (EG; n = 10). EG received the intervention twice per week for 3 weeks. Statistical analysis was conducted by delta (difference between post-intervention and pre-intervention) and the Shapiro-Wilk test (normality). For comparison between the groups, the Mann-Whitney test was used.

Results: The results showed a significant reduction in pain intensity as reported via the pain numerical scale (PNS; $P = 0.00$), generalized pain index (GPI; $P = 0.00$), and symptom severity scale (SSS; $P = 0.00$). There was no significant difference in any HRV variable ($P > 0.05$).

Conclusion: Pulsed LA, when applied in an individualized protocol, can reduce pain intensity, as reported on the PNS, GPI, and SSS. However, no therapeutic effect was observed for HRV.

Keywords: Acupuncture; Fibromyalgia; Lasers; Rehabilitation.

Introduction

Fibromyalgia (FM) is a chronic and painful disease characterized by widespread pain, fatigue, disturbed sleep, impaired cognition, and anxiety.[1] The disease may present with associated symptoms, such as migraine, limb paresthesia, and gastrointestinal complaints, among others. Its causes can be attributed to genetic history, autoimmune diseases, or a sedentary lifestyle.[2] Its worldwide prevalence is 3% to 6%[3]; in Brazil, the prevalence is between 2% and 2.5%, predominantly in 40- to 50-year-old women.[4]

Increased pain may contribute to the dysfunction of the autonomic nervous system (ANS), which is considered one of the pathophysiological mechanisms for FM.[5] This dysfunction has been investigated through the analysis of heart rate variability (HRV), and there is scientific evidence of a good prognosis for both health and disease. A change in autonomic activity has been found in FM with a reduction in HRV.[6]

FM treatment involves controlling pain and psychological symptoms, which are addressed with medications, combined therapies,[7] and acupuncture, and it has no side effects.[8–11] The physiological effect of acupuncture is known to modulate the peripheral

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and central action of pain,[12,13] qualifying the technique as adequate for treating chronic pain.[14,15] As a result, acupuncture is considered a systemically effective and safe intervention.[16] There are several ways of generating stimuli at these points, which include LA, a non-invasive method.[17,18]

Laser acupuncture (LA) continuous frequency exerts positive effects on musculoskeletal diseases and has additional effects on chronic pain, including inhibition of the synaptic activity of the vagal nerve, peripheral nerve block, neurotransmitter modulation, and reduction of muscle spasm.[12,19–21]

The high prevalence of FM in the global population and the associated suffering attributed to the condition have increased the need for research on its mitigation.[22] Specifically, studies with greater methodological rigor are needed to investigate the effectiveness of protocols involving acupuncture with pulsed frequency lasers.[12,16,23]

Chronic pain responds better to laser application than needles,[24] and individual protocols determined by Ryodoraku electrodiagnostics have also been found to have better responses.[25] To our knowledge, no studies have applied LA with Nogier's pulsed frequencies for the treatment of FM.

Here we aimed to evaluate whether an individualized intervention protocol applying pulsed LA would provide benefits related to pain symptoms, such as cardiac autonomic modulation in patients with FM. The study hypothesized that the individualized intervention protocol with pulsed LA would effectively reduce pain intensity and improve HRV in the studied sample.

Material and Methods

Trial Design

The study was characterized as a pilot controlled randomized clinical trial.

Sample Study

Eligibility criteria were 40-80-year-old females who were clinically diagnosed with FM.

Inclusion Criteria

The inclusion criterion was confirmation of diagnosis using the American College of Rheumatology Diagnostic Criteria for Fibromyalgia (ACR, 2010).

Exclusion Criteria

Exclusion criteria were as follows: bleeding diathesis; pregnancy or lactation; history of a heart transplant, complex arrhythmias, or pacemaker use; physical therapy treatment, massage, or acupuncture in the last 2 weeks before the intervention; use of muscle relaxants or anti-inflammatory drugs in the last 2 days before the intervention; cancer with acute infection or other associated chronic diseases (rheumatic or degenerative); the presence of tattoos, birthmarks, alteration of pigmentation at the site of laser application; dermatoses; and post-traumatic hematomas.

Sample Recruitment

The sample was recruited from the Family Health Units and the Physiotherapy Clinic of the university. The research team contacted the volunteers by telephone and scheduled the assessments at the Physiotherapy Clinic. Recruitment took place from December 2019 to January 2020, and interventions took place in February and early March 2020.

Interventions - Independent Variable

All procedures were performed at the Physiotherapy Clinic in a large, well-lit, ventilated room without environmental acclimatization. Team members were previously trained by a qualified professional in using all assessment and intervention instruments.

Control Group

The control group (CG) underwent an initial and final assessment. This group received a health education lecture about FM, covering its main aspects such as pathophysiology, signs and symptoms, treatments, and daily care. The lecture lasted 30 minutes and was held at the end of the study at the Physiotherapy Clinic at UNIFAL. After the end of the research, further treatment was to be offered, but this did not occur due to the COVID-19 pandemic.

Experimental Group (EG)

LA was applied to individual points that were evaluated before the beginning of each session. The determination of the individual points was made through the electrodiagnostic Ryodoraku (Ryodoscope RDC Ryodoraku® brand, Vera de Mattos Vanique Costa-ME, São Carlos-SP, Brazil – ANVISA series number: 03.18.071.01110). This instrument is designed to assess the profile of the meridians through the electrical resistance of the skin at certain points.[26,27] This equipment had two cables: a ground cable (which the subject was instructed to hold) and a point evaluation cable (where a piece of cotton soaked in saline solution was placed). Data were processed with KiMeter software. This equipment is validation for scientific.[28]

Assessment to determine the points for treatment consisted of the following steps. First, the individuals were instructed to remove jewelry and other metals from their bodies, socks, and shoes and remain in the supine position at rest for 15 minutes before the evaluation. Asepsis was then performed on the anterior and posterior sides of the wrists and the lateral, anterior, and medial sides of the ankles with 70% alcohol. The collection sequence was MMSS (left→right) → MMII (left→right).

The measurement was performed at the following points of the hand: Lung 9 (Lu9), Pericardium 6 (PC6), Heart 7 (HT7), Larger Intestine 5 (LI5), Triple Energizer 4 (TE4), and Small Intestine 5 (SI5), and on the foot, Spleen 3 (SP3), Liver 3 (LR3), Kidney 4 (Ki4), Bladder 65 (BL65), Gallbladder 40 (GB40), and Stomach 42 (ST42). The collection was bilateral, starting on the left upper limb and ending on the right lower limb. Points Lu9, PC6, and HT7 are located on the flexor crease of the lateral wrist, centrally and medially, respectively. Points LI5, TE4, and SI5 are located in the extensor fold of the lateral wrist, centrally and medially, respectively. The location of the Ki4 points is between the medial malleolus and the Achilles tendon; SP3 is located in the depression between the head and the diaphysis of the first metatarsal; LR3 is found in the metatarsal base; BL65 is located in the depression between the head and diaphysis of the fifth metatarsal; GB40 is in the depression in front of the lateral malleolus; ST42 can be found at the base of the third metatarsal.[29]

The profile of the acupuncture meridians is determined in μA, where values between 40 and 60 μA indicate a pattern of energy balance, values above indicate an excess (fullness), and values below indicate the deficiency (emptiness) of energy.[27] Through this analysis, the device determined the necessary points for the treatment. Then, the deficiency had to be treated with tonification (approximation); otherwise, sedation (dispersion) of the meridian had to be carried out. After determining the points with the Ryodoraku device, a low-power laser (Acupuncture – Ecco Fibras ópticas e dispositivos LTDA®, Campinas-SP, Brazil – ANVISA Registration 80323310001) was applied within the following predetermined parameters: infrared laser at a wavelength of 808 nm (deep), optical power of 120 mW, pulsed frequency (36.5 Hz - "E" - Nogier), and a dose of 5.0 J/cm^2 for sedation and 3.0 J/cm^2 for toning. The application time was determined by the device according to the dosage. According to the laser energy density determined by the Arndt-Schultz curve, values between 1.0 and 4.0 J/cm^2 induce activation (tonification), and values above induce inhibition (sedation).[30] The intervention protocol was performed twice per week for 3 weeks, with the duration of each session being determined based on the diagnosis of the device.[12,31]

Outcomes

The main outcome of this study was pain intensity, and the secondary outcome was HRV. The use of protocols for diagnosis and treatment elaboration is a strong recommendation for evidence-based practices.[32]

Clinical Parameters

Clinical parameters evaluated were age, body mass, height, body mass index, time of diagnosis, and medications in use.

Fibromyalgia Diagnostic Criteria – ACR 2010

The American College of Rheumatology (ACR) determined the diagnostic criteria.[33–35] These criteria have been validated[33] and shown to be 88.1% accurate in diagnosing FM.[1] The ACR combines the chronic pain assessments of the generalized pain index (GDI > 7) and the symptom severity scale (SSS > 5 or chronic pain of GDI 3–6 and ESS > 9) for the presence of diffuse pain.[35]

The GDI has a score from 0 to 19, and subjects must indicate feelings of pain or weakness in the last 7 days in each region of the body. Its cohort point is > 7.0 (positive diagnosis).

The SSS has a total score ranging from 0 to 12, which indicates the severity of the symptoms in the last week. A score of 0 to 3 indicates the presence of symptoms, such as fatigue, tired awakening, difficulty thinking or remembering, and somatic symptoms (in the last six months). A score of 0 indicates no symptoms, 1 indicates mild symptoms, 2 indicates moderate symptoms, and 3 indicates severe symptoms. The sum of the symptom scores generates a total score out of 12 points. This criterion was used in the pre-intervention (i.e. diagnosis and evaluation) and after six sessions in both groups for comparison.

Primary Outcome - Pain Numerical Scale

The pain numerical scale (PNS) is a unidimensional tool for pain assessment.[36] This pain intensity assessment scale has good validity and reliability and has an intraclass correlation coefficient (ICC) of 0.97.[37] It also has greater reliability, especially in elderly and less educated patients,[38,39] a greater reliability index for assessment of musculoskeletal pain intensity,[38] and greater responsiveness to chronic pain.[40] For general purposes, the PNS has good sensitivity and generates data that can be statistically analyzed for auditing purposes.[41]

The total PNS score is out of 11 points, ranging from 0 to 10, allowing the user to grade the intensity of their pain within this range. "0" means "no pain" and "10" means its opposite or extreme pain. Thus, higher values mean greater pain intensity. Easy to use and understand, this scale is considered the best for individuals with chronic pain.[17,42]

A decrease of two values or 30% on the PNS is considered a difference of minimal clinical importance for this instrument.[39]

This scale was applied at the initial assessment and at the end of the six sessions.

Secondary Outcome - RR Recording and Heart Rate Variability Analysis

The RR interval recording was performed with a heart rate monitor (Polar® V800 Heart Rate Monitor, Kempele, Finland), the validity and reliability of which have already been confirmed in the literature for this type of analysis.[43]

The device has a strap with electrodes to be placed on the person's chest, which captures the electrical impulses from the heart and transmits them via Bluetooth to the wristwatch, where the data is stored. In this equipment, the time units are fixed in milliseconds, and the samples of the RR intervals are collected at a frequency of 1000 Hz.[44] After capturing the data, the watch is connected to the computer by a USB cable, through which the data is synchronized to the Polar Flow Sync software, where it is stored.

To record HRV, the individuals were previously instructed not to ingest coffee, tea, and soft drinks during the day, not to practice physical activity 24 h before the evaluation, and to sleep at least 7 hours the night before. They remained in the supine position, at rest and in silence, for 15 minutes before recording. The collection was carried out in the morning, before and after the intervention period and at room temperature, for 5 minutes.[45]

Signal processing was performed using Kubios HRV Standard 3.5.0. For data analysis, sections containing the capture of 5 minutes of consecutive RR intervals were selected. A very low-intensity filter was used, when necessary, to remove noise or ectopic beats.

HRV was analyzed using linear statistical measures in the time and frequency domain and non-linear statistical measures. The mean of R-Ri (RR), the mean of HR, the standard deviation of the mean of all normal R-Ri (STDRR), the square root of the difference in the sum of the squares between R-Ri on the record divided by the determined time minus one (RMSSD), and the total number of R-Ri divided by the height of the histogram of all R-Ri (RRtri) and width of the R-Ri triangle distribution (TINN) were computed as time domain measures, with RMSSD representing the parasympathetic modulation and last two indices of global HRV. For the frequency domain analysis, the power spectral components were reported at low (LF; 0.04 to 0.15 Hz) and high (HF; 0.15 to 0.4 Hz) frequencies (obtained using the fast Fourier transform in ms^2 and normalized units -n.u) and the LF/HF ratio. Signals in the LF band have been predominately related to high sympathetic modulation and low parasympathetic modulation, and signals in the HF have been attributed only to parasympathetic activity; at the same time, LH/HF represents the sympathetic-vagal balance.[46]

Non-linear statistical measures were calculated by the standard deviation of the Poincaré plot perpendicular to the line-of-identity (SD1; representing the parasympathetic modulation), the standard deviation of the Poincaré plot along the line-of-identity (SD2; representing the parasympathetic and sympathetic modulation), and the SD2/SD1 ratio (representing the sympathetic-vagal balance).[47] The degree of complexity of the distribution of the iR-R series was obtained through the approximate entropy (ApEn) and sample entropy.[48] Higher values of these indices represent greater complexity of the series and, therefore, better cardiac autonomic modulation.[48]

Randomization

Randomization was performed by a researcher who did not participate in the study. On the Research Randomizer website (www.randomizer.org), two columns (A and B) were created, with column A representing the CG and column B the EG. The allocation was simple random (1:1) within these two columns. Ten individuals were allocated to each group.

Blinding

There was no blinding of the assessment and intervention team or the research volunteers.

Statistical Analysis

The data were tabulated in Excel 2010 and later analyzed with the Statistical Package for Social Sciences (SPSS version 20.0). It used the delta calculation (difference between post-intervention and pre-intervention). Data distribution was examined using the Shapiro-Wilk test, and for comparison between the groups, the Mann-Whitney U test was used for all study variables. Data were presented as a median and interquartile range, and the significance level adopted was $P<0.05$. The effect size, when comparing the variables, was calculated using software G*Power 3.1.9.2 with $\alpha=0.05$ and $\beta=0.95$, which were analyzed following Cohen's guidelines where <0.2 was considered small, 0.2–0.8 was considered moderate, and >0.8 was considered large.[49]

Results

Figure 1 shows the sample recruitment flowchart. Table 1 shows the baseline characteristics of the participants in both groups. The sample was homogeneous. Table 2 shows the intergroup comparisons (control and experimental) of the variables [PNS, Diagnostic Criteria in Fibromyalgia – ACR 2010 (GPI, SSS)]. There was a significant intergroup reduction in the PNS ($P=0.00$), GPI ($P=0.00$), and SSS ($P=0.00$) variables. Table 3 compares the control and experimental groups concerning HRV. There was no significant difference in any HRV variable.

Discussion

This manuscript has multiple innovative findings. To our knowledge, this is the first study to verify whether an intervention protocol with pulsed LA applied to individual points established by Ryodoraku would provide benefits related to pain and autonomic cardiac modulation. Our main findings showed that pain intensity assessed by the GPI, PNS, and SSS scales was significantly reduced after the intervention period. However, the applied protocol could not promote expressive changes in cardiac

Table 1. Baseline Characteristics of the GROUPS

Variable		Randomized (n = 20)		*P* Intergroup
		Control Group (n = 10)	Experimental Group (n = 10)	
Age (y), median (interquartile range – 10%-75%)		62.00 (45.10 to 63.25)	65.50 (43.20 to 69.00)	0.05
Height (m), median (interquartile range – 10%-75%)		1.57 (1.49 to 1.61)	1.56 (1.46 to 1.62)	0.87
Body mass (kg), median (interquartile range – 10%-75%)		74.00 (57.00 to 77.00)	72.00 (58.40 to 81.75)	0.62
Body Mass Index (kg/m²), median (interquartile range – 10%-75%)		22.44 (17.81 to 24.36)	23.06 (18.01to 27.02)	0.56
Diagnoses time *(y)*, median (interquartile range – 10%-75%)		10.00 (4.10 to 16.25)	10.00 (1.50 to 20.00)	0.40
Drug use - Atenolol - Atorvastation – Certracina – Losartana – anti-inflammatory – n (%)	Yes	3 (30%)	6 (60%)	0.36
	No	7 (70%)	4 (40%)	

Mann-Whitney test, *$P<0.05$.

Table 2. Data Presented by Calculating the Delta for the PNS, Fibromyalgia Diagnostic Criteria - ACR 2010

	Groups		*P* Intergroups	Effect Size	Power Data
	Control (n = 10)	Experimental (n = 10)			
PNS (points), median (Interquartile range – 10-75%)	0.00 -3.70 to 0.25	-4.00 -6.00 to -2.75	0.00*	2.00	0.98
ACR 2010 (Points), median (Interquartile range – 10-75%)					
GPI	0.00 -6.80 to 3.25	-7.00 -13.80 to -4.00	0.00*	1.82	0.96
SSS	0.00 -3.90 to 0.75	-6.00 -7.00 to -5.00	0.00*	2.34	0.99

Mann-Whitney test; *$P<0.05$.
PNS: Pain numerical scale; Fibromyalgia diagnostic criteria ACR 2010; GPI: Generalized pain index; SSS: Symptom severity scale.

autonomic modulation, assessed through HRV.

Red and infrared low-intensity laser therapy has been used therapeutically to relieve pain, reduce inflammation and edema, heal wounds, and prevent tissue damage.[50] There is strong evidence for its anti-inflammatory effect with wavelengths of 633 and 904 nm.[51]

Laser therapy studies [52] and LA have shown to be beneficial for reducing the intensity of chronic pain[12,53] and treating chronic musculoskeletal pain.[23] However, these studies have varied parameters, such as wavelength, continuous frequency, dosage, and potency. These studies differ the most from the present study in relation to frequency because, in the present study, the pulsed frequency was adopted.

It is widely known that low-frequency laser therapy with a wavelength of 632 nm inhibits the increase in nociceptor sensitization in the inflammatory process,[54] thus reducing the inflammatory signs of arthritis in an animal model with wavelengths of 685 nm and 830 nm.[55] There is strong evidence that laser therapy improves angiogenesis as it increases growth factor secretion and formation of collaterals in the injured region; this finding has been confirmed in cell and animal studies during the first 7 days after injury, with limited evidence of the increase in the level of endorphins responsible for pain reduction.[56]

The neurobiological effects of systemic acupuncture or auriculotherapy must also be considered. It has been noted that these effects interfere with neurotransmitters related to pain and depression and are thus suitable for treating chronic pain.[14] Vas et al[57] reported the effectiveness of acupuncture treatment in reducing pain intensity compared to placebo. The difference from the present study is that an individualized treatment was used here, without a defined protocol, for FM.[58]

In a recent review of the effects of acupuncture on patients with FM, positive effects of this treatment were shown for individuals with this syndrome.[59] Among these studies, one showed a better persistent effect of acupuncture associated with moxibustion on affected meridian points based on location differentiation than a group using tramadol and amitriptyline. To assess the intervention, the PNS and FIQ instruments were used.[60] Another meta-analysis showed that acupuncture has a greater effect than sham acupuncture in alleviating pain intensity and improving quality of life. Based on the presentation of low-to-moderate, short-term evidence, and long-term assessment, it has been found to have a superior effect over sham acupuncture.[61]

FM is a chronic pain condition, and most patients seek treatment with acupuncture for pain relief. Patients with greater pain intensity who received acupuncture in three blocks, one to three times a week, for 3 weeks had greater pain intensity reduction than the placebo group.[62] The present study showed an improvement in pain intensity, verified by the analysis of the PNS and GPI instruments, but in the pulsed LA modality.

Another variable investigated in this study was HRV.

Table 3. Data presented by calculating the delta for HRV parameters

HRV	Groups		*P* Intergroups	Effect Size	Power Data
	Control (n = 7)	Experimental (n = 9)			
RR (ms) - median (Interquartile range – 10-75%)	-70.00 (-216.00 to 6.00)	26.50 (-59.50 to 124.00)	0.05	1.18	0.59
HR (bpm) - median (Interquartile range – 10-75%)	7.00 (-5.00 to 13.00)	-1.5 (-17.50 to 3.00)	0.05	1.14	0.56
STDRR (ms) - median (Interquartile range – 10-75%)	4.00 (-8.30 to 18.30)	-2.40 (-32.20 to 4.65)	0.1	0.75	0.29
RMSSD (ms) - median (Interquartile range – 10-75%)	4.20 (-9.70 to 20.50)	-0.85 (-53.67 to 8.60)	0.38	0.71	0.26
NN50 (beats) - median (Interquartile range – 10-75%)	2.00 (-8.00 to 17.00)	-1.00 (-130.40 to 3.00)	0.17	0.69	0.25
pNN50 (%) - median (Interquartile range – 10-75%)	0.24 (-2.26 to 4.82)	-0.31 (-40.68 to 0.87)	0.28	0.59	0.19
RR triangular index - median (Interquartile range – 10-75%)	0.33 (-2.46 to 1.66)	0.76 (-6.78 to 1.68)	0.77	0.01	0.05
TINN (ms) - median (Interquartile range – 10-75%)	21.00 (-45.00 to 235.00)	-21.50 (-308.90 to 44.25)	0.14	0.76	0.29
LF (ms^2) - median (Interquartile range – 10-75%)	129.00 (-79.00 to 198.00)	- 70.00 (-618.00 to 146.50)	0.14	0.76	0.29
HF (ms^2) - median (Interquartile range – 10-75%)	116.00 (-127.00 to 233.00)	-130.00 (-1428.70 to 5.75)	0.55	0.94	0.41
LF/HF - median (Interquartile range – 10-75%)	0.07 (-1.12 to 1.79)	0.24 (-3.64 to 0.50)	0.62	0.52	0.16
LF (n.u) - median (Interquartile range – 10-75%)	1.00 (-37.43 to 14.10)	7.98 (-21.04 to 14.71)	0.77	0.32	0.09
HF (n.u) - median (Interquartile range – 10-75%)	-7.73 (-28.39 to -0.46)	-7.73 (-40.58 to 3.52)	0.77	0.05	0.05
SD1 - median (Interquartile range – 10-75%)	3.00 (-6.90 to 14.50)	-0.6 (-38.03 to 6.02)	0.38	0.64	0.22
SD2 - median (Interquartile range – 10-75%)	6.00 (-155.80 to 22.00)	-2.55 (-25.78 to 11.05)	0.62	0.27	0.07
SD2/SD1 - median (Interquartile range – 10-75%)	0.20 (-1.12 to 0.85)	0.01 (-0.82 to 0.28)	0.55	0.22	0.07
Approximate Entropy (ApEn) - median (Interquartile range – 10-75%)	0.06 (-0.42 to 0.14)	-0.02 (-0.17 to 0.00)	0.24	0.14	0.05
Sample Entropy (SampEn) - median (Interquartile range – 10-75%)	-0.14 (-1.17 to 0.25)	0.12 (-0.35 to 0.40)	0.24	0.67	0.24

Mann-Whitney test; *$P < 0.05$.

HRV: Heart Rate Variability; RR: Interval between heartbeats; HR: Heart Rate; STDRR: Standard deviation of RR intervals; RMSSD: Root mean square of the successive differences between heartbeats; NN50: Number of R-R intervals that differ by more than 50ms; pNN50 (%): Percentage of number of R-R intervals that are different from each other by more than 50ms; RR triangular index: Triangular index of normal RR intervals; TINN: Triangular interpolation of the R-R interval histogram; LF: Low Frequency (Low frequency spectral component); HF: High Frequency (High-frequency spectral component); LF/HF: – Relationship between the low frequency and high frequency component; LF (n.u): Low Frequency (standard units); HF (n.u): high Frequency (standard units); SD1: Index of instantaneous recording of beat-to-beat variability; SD2: Representation of HRV in long-term recordings; SD2/SD1: ratio between the short and long variations of the RR intervals; Entropy (ApEn): Approximate entropy; Sample Entropy (SampEn).

The results showed that the parameters did not change. Lee et al[63] reported that LA exerts an influence on HRV, increasing LF and LF/HF values when compared to manual acupuncture and electroacupuncture. This suggests a greater influence on the sympathetic system when applied to LA (wavelength of 660 nm) at the BL15 acupoint. Another study using 830-nm LA at the PC6 acupoint concluded that there is an increase in vagal activity and suppression of sympathetic activity.[64] It is well known that FM triggers ANS dysfunction, which may be due to sympathetic hyperactivity and hyporeactivity to stress.[65] The present study differed in its reliance on individual application (no protocol), pulse rate, and a heart rate monitor for HRV analysis, and these parameters did not trigger changes in the HRV parameters.

The literature also demonstrates that there is a decline in HRV with advancing age; that is, it varies less than an individual age. Concerning gender, there are reports that middle-aged men have lower HRV compared to women of the same age group.[66] Another study found greater vagal modulation and less sympathy in women compared to men of the same age.[67] The present study sample consisted of 40–78-year-old women. More acupuncture studies are using HRV as an analytical tool, but due to

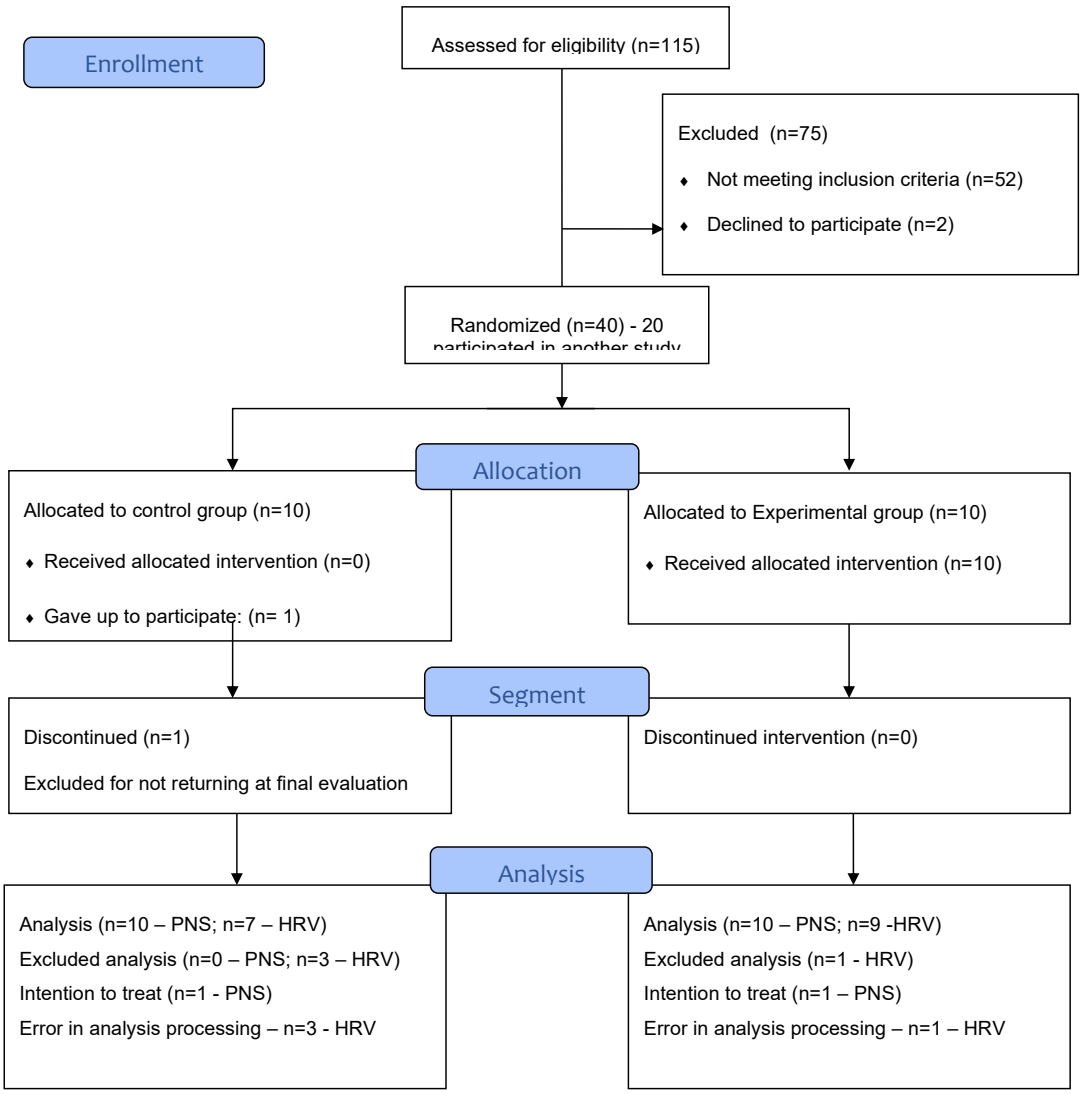

Figure 1. Flow Diagram Adapted to CONSORT

many interfering factors in HRV detection and various data analysis methods, the results are reported differently. The influence of LA on HRV in the present study cannot yet be fully established. However, we assume that some factors can be considered confounders in these findings. Despite being well distributed among the groups, patients who use drugs known to affect autonomic modulation (such as beta blockers) can interfere with these results. In addition, uncontrolled factors such as stress level and sleep quality can also influence the HRV measurement.

As the main outcome, the present study innovatively advanced the use of LA with pulsed frequency ("E" by Nogier) at the points of the Ryodoraku protocol, with individualized and effective treatment in reducing pain. The studies found in the literature on AT or laser therapy mostly present continuous frequency, and few studies include individual points. To date, no studies with this pulsed frequency have been reported in the literature to discuss the relevant data.

Regarding clinical applications, it is known that FM negatively affects the clinical outcomes of these patients. The results of the present study support the use of LA with pulsed frequency and individual points established by the Ryodoraku protocol, suggesting that it is an effective analgesic treatment without side effects for this population. In the framework of cardiac autonomic function, our research findings do not provide evidence of significant changes in autonomic modulation, not confirming our initial hypothesis regarding HRV improvement. Therefore, despite the established influence between pain and autonomic modulation, even with a significant reduction in pain intensity in the patients studied, it was not possible to show any perceptible influence on HRV responses with this protocol.

Possible limitations of this study are the non-blinding of researchers and volunteers and the absence of a placebo. In addition, the onset of the COVID-19 pandemic made it impossible to recruit a larger sample. We recommend

further research using a larger sample size and a greater number of intervention sessions to check possible changes in HRV besides including the Sham group and the analysis of other FM symptoms. A possible risk of bias could be the number of times the intervention group was in the clinic compared to the control group.

Conclusion

It is concluded that pulsed LA, applied via an individualized protocol, reduced pain intensity as measured through PNS, GPI, and SSS. However, no therapeutic effect was observed for HRV.

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Conflict of Interests

The authors declare that they have no conflict of interest

Ethical Considerations

The procedures followed the standards of good practice in clinical studies involving human beings (Helsinki Declaration) and were approved by the Research Ethics Committee of the University with approval number 3.759.306 and CAAE – 24769719.0.0000.5142 and registered by Brazilian Registry of Clinical Trials (REBec) (identifier: RBR-833mm2). Volunteers received all information related to the objectives, methodological procedures of the study, and possible risks before initiation. After agreeing to participate, they signed an informed consent form.

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