

## Research Article

## Open Access

## Systemic Effects of Photobiomodulation and Ultrasound as a Potentiating Tool in the Treatment of Sleep Disorders - Pilot Study

Vanderlei Salvador Bagnato<sup>2,3,4</sup>, Tiago Zuccolotto Rodrigues<sup>1,2</sup>, Vanessa Garcia<sup>1,2</sup>, Heloisa Giangrossi Machado Vidotti<sup>1</sup> and Antonio Eduardo de Aquino Junior<sup>2,3\*</sup><sup>1</sup>Universidade Central Paulista, Brazil<sup>2</sup>Instituto de Física de São Carlos, Universidade de São Paulo, Brazil<sup>3</sup>Programa de Pós-Graduação em Biotecnologia, Universidade Federal de São Carlos, Brazil<sup>4</sup>Department of Biomedical Engineering, Texas A&M University, Texas, USA

## Abstract

Sleep is a fundamental physiological state in memory consolidation, allowing the brain to process a wide range of information obtained during the day. The absence of quality sleep produces deficits in memory consolidation. This type of characteristic can also occur in syndromes that are combined with non-restorative sleep, involving mood changes, anxiety, and depression among others. Thus, the present study aimed to evaluate patients with sleep disorders, with or without the use of controlled medications and who do not have fibromyalgia as a characteristic, with an intervention model of synergistic use of physiotherapeutic resources, applied to the palms of the hands. For the intervention, 10 application sessions were carried out, lasting 6 minutes on each palm, using laser and ultrasound at the same time. The evaluation of standardized questionnaire instruments, such as the Pittsburgh Sleep Quality Index, Hospital Anxiety and Depression Scale and Beck Depression Inventory-II, made it possible to observe significant changes, especially when analyzing patients who use controlled medication combined with laser and ultrasound intervention in the hands. Therefore, physiotherapy resources are potential in enhancing the effects of medication in the treatment of sleep disorders.

**Keywords:** Photobiomodulation; Ultrasound; Sleep disorders

## Introduction

Sleep is a fundamental physiological state in memory consolidation, where the brain is very busy processing all the information we acquire throughout the day. The lack of quality sleep produces deficits in memory consolidation, preventing important actions in brain development from occurring properly. Sleep acts on thermoregulation, energy conservation and restoration of metabolism, affecting memory, learning, mood, behavior, immune responses, hormone levels, digestive process, among other physiological actions [1,2].

The structure of sleep, when observed under normal conditions, begins with the so-called nocturnal sleep in stage I NREM sleep, which occurs after a brief latency period of about 10 minutes. Sleep deprivation can promote a very low latency period for NREM sleep onset. This type of characteristic can also occur in syndromes that combine with non-restorative sleep [3].

When properly evaluated, it is possible to identify the presence of psychic changes linked to depression and anxiety, in addition to physical changes such as pain, sleep-disordered breathing, urinary problems, as well as neurological conditions that can cause sleep fragmentation [1,2]. The characterization of depression as one of the mental disorders that is characterized as a disease with a high degree of overload, in an insidious way, destroys the hopes and brightness of the lives of its sufferers, having devastating consequences on their quality of life [4]. Anxiety, a disorder characterized by excessive anxiety and concern related to various events or activities, promotes symptoms such as agitation, fatigue, difficulty concentrating, mood disorder or irritability and muscle tension. In both cases, they act negatively in relation to sleep [5]. Thus, adequate homeostasis in the body depends on good sleep quality, directly influencing everyday life.

These alterations in the sleep pattern, psychic and sleep disorders, tend to increase the use of medications, such as benzodiazepines, as they act on the Central Nervous System and promote sleep induction,

causing a satisfactory effect in relation to sleep disorders. However, excessive and long-term use causes numerous consequences to the human organism, such as dependence, memory loss, wrong judgment, moments of lack of attention and brutal changes in the emotional state [6].

The association of issues related to sleep disturbance was also observed in patients who had post-COVID 19 sequelae [7]. In a study carried out, the synergistic action of photobiomodulation and ultrasound therapies, used through systemic action, promoted the improvement of sleep, being a disturbing factor for these individuals [7]. Sleep disturbance is reported in several cases in patients infected with COVID 19, and can be explained by the decrease in the production of neurotransmitters, such as serotonin, and the increase in pro-inflammatory mediators, such as histamines. In the same sense, the increase in pro-inflammatory cytokines is directly correlated with the pathogenesis of depression and anxiety, as well as the concentration/production of neurotransmitters, mainly serotonin [7].

Still in the same therapeutic model [8], the treatment of fibromyalgia, painful, chronic and generalized syndrome of the musculoskeletal system, which causes disabling pain, intense fatigue, non-restorative sleep, anxiety and depression, obtained positive feedback in a case study followed for 42 years months [9]. In addition, the synergistic

**\*Corresponding author:** Antonio Eduardo de Aquino Junior, Instituto de Física de São Carlos, Universidade de São Paulo, Brazil, E-mail: antonioaquino@ifsc.usp.br

**Received:** 04-May-2024, Manuscript No: jnp-24-135458; **Editor assigned:** 06-May-2024, Pre-QC No: jnp-24-135458(PQ); **Reviewed:** 20-May-2024, QC No: jnp-24-135458; **Revised:** 24-May-2024, Manuscript No: jnp-24-135458(R); **Published:** 31-May-2024, DOI: 10.4172/2165-7025.1000703

**Citation:** Aquino Junior AE (2024) Systemic Effects of Photobiomodulation and Ultrasound as a Potentiating Tool in the Treatment of Sleep Disorders - Pilot Study. J Nov Physiother 14: 703.

**Copyright:** © 2024 Aquino Junior AE. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

therapeutic action of photobiomodulation and ultrasound promoted a report of improved sleep in the evaluation of a fibromyalgia patient. This study evaluated intracranial compliance, noting modulation during treatment, resulting in improvement of hyperalgesic condition and other symptoms [10].

For Aquino Jr, et al. [7], the key to memory formation is adequate sleep, since neural reverberation takes place in REM sleep, and it is in the REM stage that changes in neuronal activities occur with the neuroinflammation caused by sleep. Sars-CoV-2, such as increases in acetylcholine levels Neuroinflammation caused by Sars-CoV-2 is responsible for sleep disorders, which affects memory formation because there is no neural reverberation in the REM stage. Regarding fibromyalgia, factors such as pain, anxiety and depression are, in addition to symptoms, direct causes of sleep disturbance.

Non-invasive and non-pharmacological synergistic therapy used in studies [7-10] uses laser for photobiomodulation and therapeutic ultrasound. The therapeutic laser between 650nm and 830nm acts by being absorbed by structures sensitive to light, such as cytochrome C oxidase, a unit of the mitochondrial respiratory chain, altering electron transport, mitochondrial membrane potential and thus ATP production. In addition, through photosensitivity of ion channels, photon absorption occurs, increasing the concentration of intracellular calcium ions, resulting in stimulation of anti-inflammatory, immunomodulatory, analgesic and tissue repair effects [11]. Ultrasound is a non-invasive therapeutic method in which the device is composed of piezoelectric crystals, which transform electrical energy into oscillatory mechanical energy. The deformation promoted by the waves, in a mechanical way, on the molecules of the tissues, results from the production of heat, to the induction of biological responses, such as muscle relaxation, tissue regeneration and reduction of inflammation [8].

When synergistically laser and ultrasound promote homeostasis and neurotransmitter production, cell regeneration and inflammatory modulation [7-10]. Still, through the application in the palms of the hands, there is an increase in ionic permeability as a result of ultrasound, high ATP production via photobiomodulation, in addition to the anti-inflammatory action of both resources. The hypothesis of conduction of stimuli through afferent pathways to the brain, allows modulation of intracranial compliance and homeostasis of the pain center next to the prefrontal cortex [10]. These changes are followed by relaxation promoted by ultrasonic and photonic stimuli, acting as a facilitator for sleep, enabling the REM phase, in addition to gradually reducing anxiety and depression [7-9].

Thus, the present study aimed to evaluate patients with sleep disorders, with or without the use of controlled drugs and who do not have fibromyalgia as a characteristic. The planned intervention made synergistic use of physical therapy resources, applied to the palms of the hands, where pain, anxiety, depression and quality of sleep, daytime sleepiness, as well as quality of life were evaluated, before and after the planned intervention.

## Materials and Methods

### Approval and location

The present study was approved by the Ethics Committee in Research for Human Beings of the Santa Casa de Misericórdia de São Carlos and by the National Committee of Ethics in Research, obtaining approval number CAAE 65030922.5.0000.8148, on 03/12/2022, following the resolution 466/2012, The research was conducted on the

premises of the clinical research unit of the Physics Institute of São Carlos, University of São Paulo, São Carlos, São Paulo, Brazil.

### Equipment and patent

The research used Laser and Ultrasound as a sinergic emission equipment, which allows the overlapping of therapeutic fields, providing synergism between them. The equipment was developed by the Institute of Physics of São Carlos, University of São Paulo, at the Technical Support Laboratory (LAT) and produced by the company MMOptics, patent number BR102014007397-3 A2, certified by the Brazilian Health Regulatory Agency (ANVISA) nº 80051420029 called RECUPERO®.

### Patients and protocol

The present study aimed to evaluate the quality of sleep, through the combined action of laser and ultrasound, focusing on patients with sleep disorders. For this purpose, 20 female patients aged between 30 and 50 years were selected, 50% of whom do not use medication to sleep and 50% use medication to sleep (use of medication controlled by the physician), composing 2 groups of N=10. The drugs used by patients belong to the class of benzodiazepines [6]. As exclusion criteria, it was established that pregnant women, pacemaker carriers and oncological history did not participate in the study. The performed protocol made use of Laser and Ultrasound therapies synergistically and concomitantly. There were 10 sessions, twice a week, for 5 weeks. The parameters used: Laser, wavelength 660nm, 100mW, application performed by scanning; o Ultrasound, pulsed mode, 1MHZ, 100Hz frequency. Application time of 12 minutes 6 on each palm. The application will be carried out in the entire extension of the palms of the hands. The intervention model was the same for both groups, differing in relation to the use of medication and non-use of medication.

### Questionnaires and scales

Assessments were performed at the beginning and end of the study. Visual Analog Scale (VAS), Pittsburgh Sleep Quality Index [12], Hospital Anxiety and Depression Scale (HADS) [13], Beck Depression Inventory – II (BDI -II) [14], Epworth Sleepiness Scale [15], Medical Outcomes Study Short Form 36-Item (SF-36) [16] questionnaire were used to assess quality of life and a subjective assessment of sleep difficulty.

Visual Analogue Scale (VAS), pain assessment, asking the patient to indicate the degree of her pain at the time of the assessment. The scale performs the appointment in values from 0 to 10.

The Pittsburgh Sleep Quality Index (PSQI) is an assessment instrument in the form of a questionnaire, which allows assessing the quality of sleep as well as its disturbances. The questionnaire has a total score of up to 21 points, where the highest value indicates greater sleep disturbance and the lowest, and the least sleep disturbance. The data is displayed in its entirety.

The Hospital Anxiety and Depression Scale (HADS) have two distinct scales, for anxiety and depression, consisting of 7 questions in each scale. The general score of each scale is distributed between 0 and 21 points. The higher is the score, the greater the questions involving anxiety and depression. The data is displayed in its entirety.

The Beck Depression Inventory Scale (BDI-II) is self-reported to quantify the intensity of depressive symptoms. It consists of 21 questions, the highest being the score, a greater indication of depression symptoms. The data is displayed in its entirety.

The Epworth Sleepiness Scale is a scale developed to measure daytime sleepiness in the clinical context of sleep disorders.

The Medical Outcomes Study 36-Item Short-Form Health Survey is a generic quality of life assessment questionnaire that is easy to administer and understand. It is composed of 8 distinct components: functional capacity, physical aspects, pain, general health status, vitality, social aspects, emotional aspects and mental health. It presents a score from 0 to 100, where zero corresponds to a worse state and 100 to a better state of health.

### Statistical treatment

In this study, the statistical analysis was performed using Instat 3.0 software for Windows (Graph Pad, San Diego, CA, USA, 1998). The data, in its totality, were expressed as mean and standard deviation. The level of significance was set at  $p < 0.05$ . To analyze the normality of data, the Kolmogorov-Smirnov test was used. Afterwards a one-way ANOVA with a t test and Student-Newman-Keuls for comparison between before and after treatment.

### Results

Figure 1 shows the comparison of the combined application between Laser and Therapeutic Ultrasound in relation to Visual Analogue Scale (VAS), when observing patients who do not use medications and who use medications in the moments before treatment and after treatment. It is possible to observe an improvement in pain scores from 4.4 to 2.4 in patients who do not use medication, which provides a significant difference of  $p < 0.009$ . In relation to patients who use medication, an improvement in pain was noted from 6 to 3.8, generating a significant difference of  $p < 0.008$ . It is important to highlight that the patient's pain report was questioned without specifying the location of pain, intensity or chronicity, only excluding the possibility of fibromyalgia (Figure 1).

Figure 2 shows the subjective assessment of sleep quality, where patients were spontaneously asked about their difficulty sleeping, with 10 being the greatest difficulty and 0 being no difficulty. A reduction in the value from 6 to 3.1 was observed in the comparison between patients who do not use medication, showing a significant difference at  $p < 0.001$ . In relation to patients who use medication, a reduction in the value from 6.6 to 2.8 was noted, showing a significant difference at

$p < 0.001$  (Figure 2).

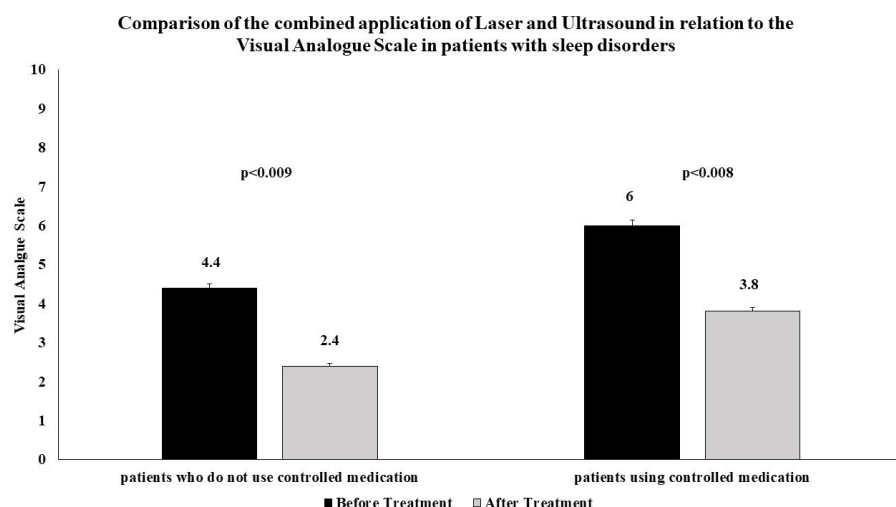
In Figure 3, it is possible to observe the comparison of the combined application of Laser and ultrasound resources when evaluating the Beck Depression Inventory (BDI-II), which was used with patients who do not use medication and who do use medication. A reduction in the value from 13.7 to 8.5 was observed in relation to patients who do not use medication, but with no statistical difference observed. However, when observing patients who use medication, the reduction presented was from 15.9 to 10.3, showing a significant difference at  $p < 0.01$  (Figure 3).

The comparison observed in Figure 4 shows the HAD Scale for Anxiety and Depression. The evaluation, aimed at patients who do not use medication, shows a reduction in the values obtained for anxiety, from 9.4 to 8 and for depression, from 8.5 to 7.3. However, there was no significant difference. When observing patients who use medication, a reduction in values from 12.4 to 9.8 in relation to anxiety and from 9.4 to 7.4 in relation to depression is shown, indicating a significant difference for  $p < 0.01$  and  $p < 0.003$ , respectively for anxiety and depression (Figure 4).

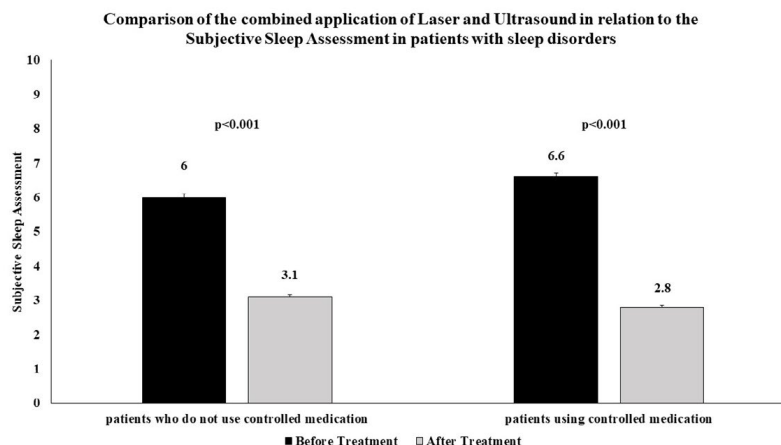
Figure 5, which represents the Epworth Sleepiness Scale, shows changes in sleepiness during the day. We observed that in both patient situations, without the use of medication and with the use of medication, they were not significantly different, with minimal or no change in their total observed values, being 5.4 and 5.5 for patients who do not use medication and 6.4 and 6.4 for patients who use drugs (Figure 5).

Figure 6, which represents the Pittsburgh Sleep Quality Index, is a questionnaire that numerically demonstrates sleep quality. The evaluation in relation to patients who do not use medication shows a reduction in values from 9.1 to 6.3, indicating a significant difference at  $p < 0.003$ . The evaluation that shows the evolution of patients who use medication shows a reduction from 13.8 to 9, which represents a significant difference at  $p < 0.01$  (Figure 6).

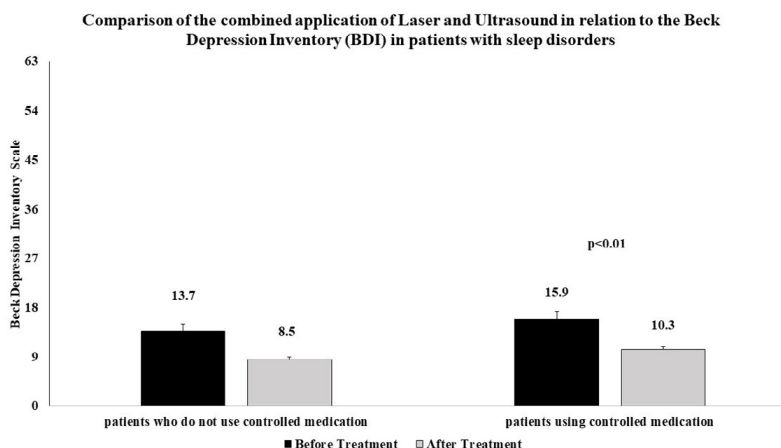
Table 1 shows the analysis of the SF-36 questionnaire, a questionnaire that numerically illustrates several variables on quality of life, where the higher the observed value, the better the patient's status in the given variable. When observing patients who do not use



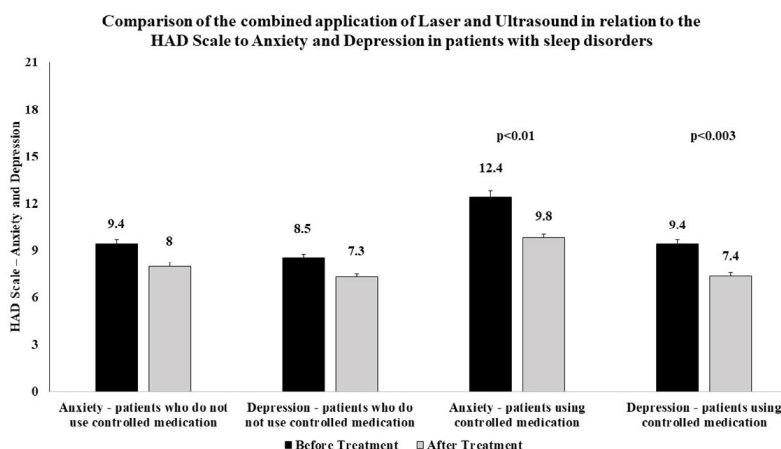
**Figure 1:** which represents the visual analogue scale, shows the moments before treatment versus after treatment in patients who do not use medication and who use medication. Kolmogorov-Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls "t" test for  $p < 0.05$ . Significant differences were observed when comparing patients not using medication for  $p < 0.009$  and comparing patients using medication for  $p < 0.008$ .



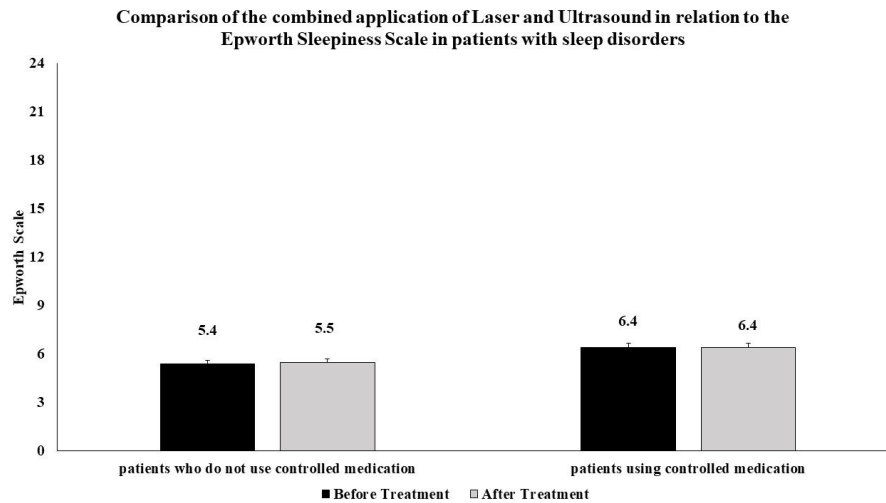
**Figure 2:** Represents the subjective evaluation of Sleep Quality, showing the moments before treatment versus after treatment. Kolmogorov-Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls “t” test for  $p < 0.05$ . Significant differences were observed when comparing patients not using medication for  $p < 0.001$  and comparing patients using medication for  $p < 0.001$ .



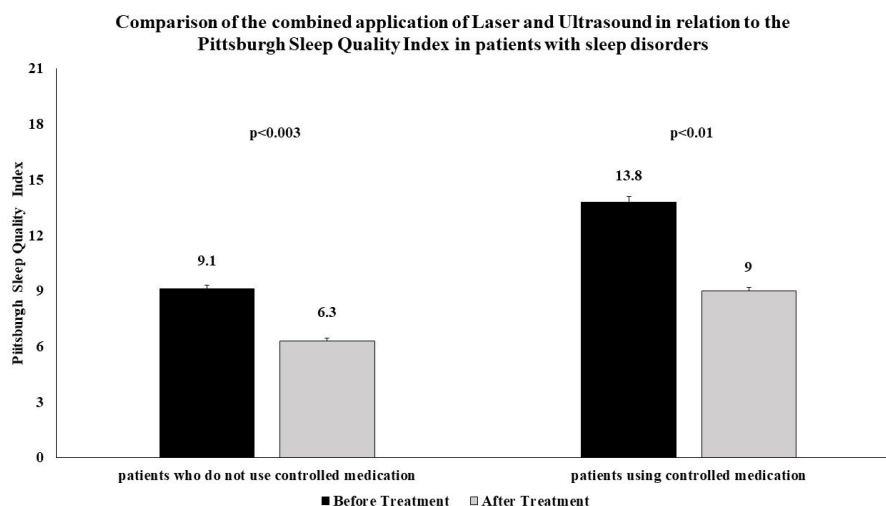
**Figure 3:** Shows the Beck Depression Inventory -BDI, showing the moments before treatment versus after treatment. Kolmogorov-Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls “t” test, for  $p < 0.05$ . No significant difference was observed in relation to patients who do not use medication. In the condition of patients who use medication, a significant difference of  $p < 0.01$  was observed.



**Figure 4:** Shows the HAD Anxiety and Depression Scale, showing pre-treatment versus post-treatment times. Kolmogorov-Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls “t” test for  $p < 0.05$ . No significant difference was observed in the condition of non-use of medication, both for Anxiety and Depression. In the condition of patients who use medication, a significant difference of  $p < 0.01$  for Anxiety and  $p < 0.003$  for Depression was observed.



**Figure 5:** Shows the Epworth Sleepiness Scale, showing pre-treatment versus post-treatment times. Kolmogorov Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls “t” test, for  $p < 0.05$ . No significant differences were observed in either comparison group.



**Figure 6:** Shows the Pittsburgh Sleep Quality Index, showing the moments before treatment versus after treatment. Kolmogorov-Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls “t” test for  $p < 0.05$ . Significant differences were observed when comparing patients not using medication for  $p < 0.003$  and comparing patients using medication for  $p < 0.01$ .

medication, it is possible to observe that all variables show positive evolution in relation to the moments before treatment in relation to after treatment. However, the Vitality and Mental Health variables show a significant difference at  $p < 0.02$  and  $p < 0.05$ , respectively. In relation to patients who use medication, we observed an improvement in the condition before and after treatment for all variables, being statistically different for  $p < 0.02$  and  $p < 0.002$ , the functional capacity and mental health variables respectively (Table 1).

Table 1 shows the SF-36 Quality of Life Questionnaire, showing the times before treatment versus after treatment in relation to total values, percentage difference and statistical difference. Kolmogorov-Smirnov normality test was used and later comparison between moments using Student-Newman-Keuls “t” test, for  $p < 0.05$ . In the condition of patients who do not use medication, a significant difference of  $p < 0.02$  for Vitality and  $p < 0.05$  for Mental Health was observed. In the condition of patients who use medication, a significant difference of  $p < 0.02$  for Functional Capacity and  $p < 0.002$  for Mental Health was observed.

Table 2 points to the Pearson correlation values in relation to the Visual Analogue Scale (VAS), Beck Depression Inventory (BDI-II), Hospital Anxiety and Depression Scale (HAD) and Pittsburgh Sleep Index Questionnaire (Pittsburgh) questionnaires, where they are only values above 0.70 are considered as strong values. Shown are: A correlation of 0.84 was observed in the comparison Beck x HAD Anxiety, a correlation of 0.83 in the comparison Beck x Pittsburgh, a correlation of 0.79 in the comparison HAD Anxiety x HAD Depression and a correlation of 0.79 in the comparison HAD Anxiety vs. Pittsburgh (Table 2).

Table 2 shows the Pearson Correlation, performed between the variables Visual Analog Scale (VAS), Beck Depression Inventory – BDI (Beck), Anxiety Scale – HAD (HAD – Anxiety), HAD Depression Scale – Depression (HAD) and the Pittsburgh Sleep Quality Index (Pittsburgh). The correlation of 0.84 was observed in the comparison Beck x HAD Anxiety, the correlation of 0.83 in the comparison Beck x Pittsburgh, the correlation of 0.79 in the comparison HAD Anxiety x



**Table 1:** Analysis of the SF-36 Questionnaire considering patients who do not use medication and patients who use medication.

Variable	No Use Controlled Medication				Use Controlled Medication			
	Before Treatment		%	p	After Treatment		%	p
Functional Capacity	74.4	79.4	6.3	-	81.4	87.1	6.5	0.02
Limitations due to Physical Aspects	61.1	63.8	4.2	-	57.1	67.8	15.8	-
Pain	44.2	45.6	3.07	-	57.3	65.9	13	-
General State of Health	62.6	67.3	6.98	-	56.7	62	8.5	-
Vitality	45	57	21	0.02	40	46.4	13.8	-
Social Aspects	54	55.5	2.7	-	51.8	58.9	12	-
Limitations due to Emotional Aspects	40.7	55.5	26.7	-	23.8	38	37.4	-
Mental Health	51.1	56.4	9.4	0.05	46.8	52	10	0.002

**Table 2:** Analysis of the different assessment instruments used in patients who do not use medication in relation to Pearson's correlation.

Assessment Instruments	VAS	Beck	HAD Anxiety	HAD Depression	Pittsburgh
VAS	1	0.34	0.68	0.36	0.35
Beck		1	0.84	0.67	0.83
HAD Anxiety			1	0.79	0.79
HAD Depression				1	0.51
Pittsburgh					1

**Table 3:** Analysis of the different assessment instruments used in patients who use medication in relation to Pearson's correlation.

Assessment Instruments	VAS	Beck	HAD Anxiety	HAD Depression	Pittsburgh
VAS	1	0.05	0.31	0.42	0.14
Beck		1	0.86	0.70	0.35
HAD Anxiety			1	0.27	0.70
HAD Depression				1	-0.30
Pittsburgh					1

HAD Depression and the correlation of 0.79 in the comparison HAD Anxiety x Pittsburgh. Correlations above 0.70 were considered.

Table 3 points to the Pearson correlation values in relation to the Visual Analogue Scale (VAS), Beck Depression Inventory (BDI-II), Hospital Anxiety and Depression Scale (HAD) and Pittsburgh Sleep Index Questionnaire (Pittsburgh) questionnaires, where they are only values above 0.70 are considered as strong values. Shown are: A correlation of 0.86 was observed in the comparison Beck x HAD Anxiety, a correlation of 0.70 in the comparison Beck x HAD depression, a correlation of 0.70 in the comparison HAD Anxiety x Pittsburgh (Table 3).

Table 3 shows the Pearson Correlation, performed between the variables Visual Analog Scale (VAS), Beck Depression Inventory-BDI (Beck), Anxiety Scale-HAD (HAD-Anxiety), HAD Depression Scale-Depression (HAD) and the Pittsburgh Sleep Quality Index (Pittsburgh). A correlation of 0.86 was observed in the comparison Beck x HAD Anxiety, a correlation of 0.70 in the comparison Beck x HAD depression, a correlation of 0.70 in the comparison HAD Anxiety x Pittsburgh. Correlations above 0.70 were considered.

**Discussion**

Sleep is an essential physiological process for the proper functioning of the human body [17]. Therefore, it is of great importance for the physiology of the body as it is a biological process, in which the repair and maintenance of biopsychosocial balance, occurs [17]. Therefore, poor sleep quality is the gateway to several consequences in an individual's daily life, leading to health problems, one of which is sleep disorders.

In this context, the concern with the development of new forms of non-drug treatment using physiotherapeutic resources such as intervention, laser and ultrasound, are of paramount importance. However, it differs in the application condition, which is synergistic and systemic, in which the resources are emitted simultaneously through the equipment, RECUPERO®, which allows the overlapping of therapeutic fields, resulting in greater effectiveness in treatments [7-10].

When the Laser is applied specifically, to the palms of the hands, it is possible to have the difference between a systemic action and a local application in photobiomodulation. In a way, photobiomodulation occurs through the action of low-power lasers, produced by wavelengths between 660nm and 808nm, in the red and infrared range, (being absorbed by photosensitive structures, present in Cytochrome C Oxidase), promoting reduction of edema and inflammatory processes, analgesic effects, production of ATP, that is, restoring homeostasis [18,19]. These effects occur due to the photosensitivity of ion channels, with an increase in the concentration of Ca2+, Na+ and K ions. Through this methodology, we have the stimulation of inflammatory, immunomodulatory, analgesic and tissue processing effects [11].

Ultrasound, widely used in physiotherapy, emits high-frequency mechanical waves, radiating energy through the ultrasonic waves, resulting in thermal or non-thermal action [20]. Therefore, there is an increase in tissue temperature, increasing membrane permeability, favoring vascularization, modulation of cytokines and nerve conduction speed, improving the nociceptive threshold, contributing to analgesic and anti-inflammatory effects [21].

Taking the base context, one of the factors that can influence the

quality of sleep is pain, which, as observed in previous studies, in which resources were applied to the palms of the hands, for the treatment of fibromyalgia, with success [7-10], showing a promising systemic therapy model for the treatment of pain.

Furthermore, poor sleep quality can generate other disorders, such as anxiety and depression. Anxiety or anxiety disorders are seen as pathological when exaggerated, disproportionate to the stimulus, and associated with emotional discomfort. Intensely present reactions develop in individuals with genetic predisposition, as well as external factors such as stress [22]. Depression is a chronic and recurrent psychiatric disorder, leading to mood changes and deep sadness, being related to feelings of pain, bitterness, disenchantment, hopelessness, low self-esteem and guilt, and may be linked to sleep disorders [23].

As a hypothesis made in a previous study in relation to the synergy effects of Photobiomodulation and Ultrasound associated in the palms of the hands, it is suggested that these resources are conducted and absorbed by the nerve endings and peripheral circulation [7-10], through the afferent pathways towards the central nervous system, having direct action through conduction in the vagus nerve (parasympathetic system). Through a study by Aquino Jr. et al [7-10] on fibromyalgia, the hypothesis emerges that instead of having the degradation of acetylcholine, due to the increase in the enzymatic production of acetylcholinesterase, modulation of the acetylcholinesterase itself occurs, reducing the degradation of the acetylcholine molecule, causing stimuli, both sonic and photonic, to reach the desired point (prefrontal cortex), linked to the central nervous system, reducing pain and enabling gradual improvement in sleep. Thus, it is observed that the systemic action has an effect on sleep (as observed in the present study). These observations are in line with studies of treatments for post-Covid 19 and Fibromyalgia sequelae, with neural reverberation and the REM sleep phase occurring [7-10].

By observing the patients' quality of sleep and life, the SF-36, a quality of life questionnaire, was applied, which mainly quantified the improvement in mental health (Table 1), a result of the improvement observed in the questionnaires carried out, presented below.

According to this concept, the results obtained using the visual analogue pain scale Figure 1, it was possible to observe an improvement in pain reporting in patients who do not use medication. In relation to patients who use medication, a significant improvement in pain was noted. It is important to highlight that the patient's pain report was questioned without specifying the location of pain, intensity or chronicity, only excluding the possibility of fibromyalgia.

It is possible to observe a certain convalescence when we observe the HAD Scale, being indicated among patients who do not use medication, showing a reduction in the values obtained for anxiety, without a significant difference. When observing patients who use medication, a reduction in values in relation to anxiety and depression is shown, showing a large difference Figure 4. Regarding the BECK Inventory, a reduction in the values analyzed was observed in relation to patients who do not use medications. However, when observing patients who use medication, the reduction presented was significant Figure 3.

Based on this point, the subjective perception of sleep quality was evaluated Figure 2, where patients were spontaneously asked about their difficulty sleeping, with 10 being the greatest difficulty and 0 being no difficulty, in which there was an improvement seen in Figure 2, A reduction in final values compared to initial values was observed, reducing in both groups.

When observing the values obtained using the Pittsburgh questionnaire, which assesses the severity and nature of the sleep disorder, both groups are significant, with the group using medication being more significant Figure 6.

Observation of the results of patients who do not use controlled medications, through Table 2, seen by the Pearson correlation in relation to the Visual Analogue Scale (VAS), Beck Depression Inventory (BDI-II), Hospital Anxiety and Depression Scale questionnaires (HAD) and Pittsburgh Sleep Index Questionnaire (Pittsburgh), where only values above 0.70 are considered as strong values. Strong correlations are shown when comparing Beck x HAD Anxiety, Beck x Pittsburgh, HAD Anxiety x HAD Depression, as well as HAD Anxiety x Pittsburgh. In the same way as in Table 3, of patients who use controlled medications, it was seen by the Pearson correlation values in relation to the Visual Analogue Scale (VAS), Beck Depression Inventory (BDI-II), Hospital Anxiety and Depression Scale (HAD) and Pittsburgh Sleep Index Questionnaire (Pittsburgh), where only values above 0.70 are considered strong values. Strong correlations are presented in Beck x HAD Anxiety, Beck x HAD depression and finally HAD Anxiety x Pittsburgh.

Thus, the use of physiotherapeutic resources with systemic action showed the enhancement of the medication effect, allowing the condition measured on various scales and questionnaires to show a significant improvement that is more pronounced in patients who use medications compared to those who do not use medications, pointing out the enhancement of medications through the use of photobiomodulation.

## Conclusion

We conclude that systemic therapy using photobiomodulation as a technological and non-drug tool can be a medication-enhancing and associative mechanism in the treatment of sleep, and consequently, a better quality of life.

## Acknowledgment

This work was supported by São Paulo Research Foundation (FAPESP – grants n°2013/07276-1 and 2014/50857-8) and by National Council for Scientific and Technological Development (CNPq – grant no 465360/2014-9).

## References

1. Payne JD, Stickgold R, Swanberg K, Kensinger EA (2008) Sleep preferentially enhances memory for emotional components of scenes. *Psychol Sci* 19: 781-788.
2. Li W, Ma L, Yang G, Gan WB (2017) REM sleep selectively prunes and maintains new synapses in development and learning. *Nat Neurosci* 20: 427-437.
3. Le Bon O (2020) Relationships between REM and NREM in the NREM-REM sleep cycle: a review on competing concepts. *Sleep Medicine* 70: 6-16.
4. Roberts RE, Duong HT (2014) The Prospective Association between Sleep Deprivation and Depression among Adolescents. *Sleep* 37: 239-244.
5. Sejbuk M, Mironczuk-Chodakowska I, Witkowska AM (2022) Sleep Quality: A Narrative Review on Nutrition, Stimulants, and Physical Activity as Important Factors. *Nutrients* 14: 1912.
6. de Mendonça FMR, de Mendonça GPRR, Souza LC, Galvão LP, Paiva HS, et al. (2023) Benzodiazepines and Sleep Architecture: A Systematic Review. *CNS Neurol Disord Drug Targets* 22: 172-179.
7. de Aquino Junior AE, Rodrigues TZ, Garcia V, Simão G, Carbinatto FM, et al. (2022) Conjugated and Synergistic Therapies in the treatment of Covid 19 Dysfunction - Pain, Weakness, Paresthesia, Respiratory Condition, Memory, Olfactory and Taste: Case Series. *J Nov Physiother* 12: 545.

8. de Aquino Junior AE, Carbinatto FM, Franco DM, Silva JD, Bruno A, et al. (2021) The Laser and Ultrasound: The Ultra Laser like Efficient Treatment to Fibromyalgia by Palms of Hands: Comparative Study. *J Nov Physiotherapies* 11: 447.
9. de 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: 2.
10. de Aquino Junior AE, Carbinatto FM, Tomaz CDSR, Bagnato VS (2022) Photosonic treatment and Fibromyalgia: The Effect on Brain Compliance-Case Report. *J Nov Physiother* 12: 510.
11. 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.
12. Fatemeh G, Sajjad M, Niloufar R, Neda S, Leila S, et al. (2022) Effect of melatonin supplementation on sleep quality: a systematic review and meta-analysis of randomized controlled trials. *J Neurol* 269: 205-216.
13. Nyer M, Farabaugh A, Fehling K, Soskin D, Holt D, et al. (2013) Relationship between sleep disturbance and depression, anxiety, and functioning in college students. *Depress Anxiety* 30: 1-14.
14. Gorenstein C, Andrade L (1996) Validation of a Portuguese version of the Beck Depression Inventory and the State Trait Anxiety Inventory in Brazilian Subjects. *Brazilian J Med Bio Res* 29: 453-457.
15. Johns MW (1992) Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 15: 376-381.
16. Busija L, Pausenberger E, Haines TP, Haymes S, Buchbinder R, et al. (2011) Adult measures of general health and health-related quality of life: Medical Outcomes Study Short Form 36-Item (SF-36) and Short Form 12-Item (SF-12) Health Surveys, Nottingham Health Profile (NHP), Sickness Impact Profile (SIP), Medical Outcomes Study Short Form 6D (SF-6D), Health Utilities Index Mark 3 (HUI3), Quality of Well-Being Scale (QWB), and Assessment of Quality of Life (AQoL). *Arthritis Care Res (Hoboken)* 63: S383-412.
17. Zielinski MR, McKenna JT, McCarley RW (2016) Functions and Mechanisms of Sleep. *Neuroscience* 3: 67-104.
18. Enwemeka CS, Parker JC, Dowdy DS, Harkness EE, Harkness LE, et al. (2004) Efficacy of low-power lasers in tissue repair and pain control: a meta analysis study. *Photomed Laser Surg* 22: 323-329.
19. Karu TI (2006) Mitochondrial mechanisms of photobiomodulation in context of new data about multiple roles of ATP. *Photomed Laser Surg* 28: 159-160.
20. Zhou S, Schmlz A, Seufferlein T, Li Y, Zhao J, et al. (2004) Molecular mechanisms of low intensity pulsed ultrasound in human skin fibroblasts *J Biol Chem* 279: 54463-54469.
21. Panhóca VH, Tamae PE, Aquino Jr AE, Bagnato VS (2021) Comparison of the Synergistic Effect of Vacuum Therapy or Ultrasound Associated with Low Power Laser Applied in Temporomandibular Disorders. *OHDM* 20.
22. Saradhadevi S, Hemavathy V (2022) Anxiety Disorders. *Cardiometry* 4: 1010-1012.
23. Stewart DE, Gucciardi E, Grace SL (2004) Depression. *BMC Women's Health* 4 Suppl 1: S19.