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Effects of Intravenous Laser Irradiation of Blood on Pain, Function and Depression of Fibromyalgia Patients

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Abstract

Objective: Fibromyalgia, labeled for an illness of wide spreading pain, fatigue, restless sleep, gastrointestinal disturbances, and mood disorders, is a complex and heterogeneous disease. Novel and improved treatments would allow healthcare professionals to improve the conditions of patients with fibromyalgia. For instance, photo biomodulation is a new treatment that minimizes heavy usage of drugs and side effects. This study investigated the clinical effects of intravenous laser irradiation of blood on pain, sleep, mood disorders, and quality of life in patients with fibromyalgia.

Methods: Fifteen patients diagnosed as having fibromyalgia based on the modified 2010 criteria of the American College of Rheumatology from an outpatient clinic were recruited. Before admission, all subjects were asked to submit visual analog scale (VAS), numbers of tender points, revised Fibromyalgia Impact Questionnaire (FIQR), revised Beck Depression Inventory (BDI) and Pittsburgh Sleep Quality Index (PSQI) according to their outcomes before/after drugs in a previous outpatient clinic. After admission, all participants received two courses of intravenous laser irradiation of blood, each course is composed of 10 intravenous laser irradiation of blood sessions, each session of the therapeutic duration lasted for 60 minutes. Two consecutive courses had a 7-day rest interval. The trial lasted for 4 weeks. Outcomes based on patient-reported symptoms of the aforementioned tests were evaluated on two separate occasions: baseline and within 24 hours after the last day of the protocol.

Results: The drugs resulted in significant reduction in pain intensity only. However, the before/after comparisons of intravenous laser irradiation of blood showed a significant improvement in VAS (p=0.001), number of tender points (p=0.002), FIQR (p=0.001), BDI (p=0.003) and PSQI (p=0.01). We also noted significantly positive effects of ILIB compared with drugs in all tests.

Conclusion: Intravenous laser irradiation of blood had a better effect on pain severity, sleep, mood disorder, and quality of life in patients with fibromyalgia. No unfavorable events were recorded; thus, intravenous laser irradiation of blood appears to be an effective treatment for patients with fibromyalgia.

Keywords: Fibromyalgia; Quality of life; Intravenous laser irradiation of blood; Photo biomodulation; Chronic pain syndrome; Laser; Pain

Introduction

Fibromyalgia, which is characterized by wide spreading pain, fatigue, restless sleep, gastrointestinal disturbances, and mood disorders, is a complex and heterogeneous disease [1-3]. However, its pathogenesis remains to be clearly established. Numerous professionals assume the role of central nervous system (CNS) pain processing abnormalities in fibromyalgia, including central sensitization and inadequate pain inhibition [4,5], and tonic peripheral nociceptive input associated with augmented windup and/or central sensitization in responses to neurotransmitters, genetic features, psychosocial changes, and environmental stress [4-6].

Clinicians and researchers have observed minimal progress in the treatments available for fibromyalgia within the last 20 years. Recent developments in the understanding of fibromyalgia would allow the identification of both pharmacological and non-pharmacological ways targeting specific active mechanisms of the disease, thereby enabling an effective management of the patients' conditions [7]. Moreover, new and improved treatments would allow healthcare professionals to improve the conditions of patients with fibromyalgia, which is often overlooked and grossly underfunded. For instance, photo biomodulation is a new treatment that minimizes heavy usage of drugs and side effects [8,9].

Low-level laser therapy (LLLT; topical laser) is one of the recent developments in the treatment of fibromyalgia [9-11]. LLLT can affect multiple signaling cascades and mechanisms associated with analgesia [12-14]. This therapeutic approach apparently increases β-endorphin levels, lymphatic flow, and blood supply. Moreover, researchers have

indicated that specific doses of LLLT could reduce blood lactate, oxidative stress, and inflammatory biomarker levels, which in turn limits inflammation, fatigue, and induces muscle relaxation [10,11,13,14].

However, because of the characteristic of pain and numerous tender points in patients with fibromyalgia, LLLT is typically performed for at least 20 minutes, moving from one tender point to another [9,11,15]. Intravenous laser irradiation of blood (ILIB), which is considered a safe therapeutic method, is more comfortable for patients. Another advantage of ILIB is that it requires less medical attention than the extracorporeal version [12,16,17]. In addition to the fundamental effects of LLLT, other integral influences of ILIB were also found, including positive effects on rheological properties of the blood, modulation of redox system in the mitochondria, and decreased oxidative stress makers [12,18]. Moreover, advantages of ILIB over LLLT can be expected as the former is more direct and less energy-consuming [16].

Currently, only two studies on "ILIB therapy patients with fibromyalgia are available": one is a non-randomized interventional study [17] and the other is a single descriptive study [12]. Although current treatment guidelines for fibromyalgia support the core concept of patient-tailored, multicomponent therapy [19,20], in this study ILIB was used to investigate its therapeutic effect on pain, sleep condition, mood, and health-related quality of life (QOL).

Materials and Methods

Participants

All patients with fibromyalgia according to the modified 2010 criteria of the American College of Rheumatology(ACR) were recruited from an outpatient clinic in the Department of Rehabilitation and Physical Medicine, Taipei Veterans General Hospital, Taiwan [21,22] Patients who had uncontrolled heart disease, who withdrew their participation because of personal reasons, and who were taking medications that caused sensitivity to light therapy (e.g. astemizole, estrogen, diclofenac, doxycycline) [23] were excluded.

Fifteen patients with fibromyalgia (all women) were included (mean age 53.77 years). Prior to hospital admission, all patients had been taking medications for at least 6 months and they were asked to provide pre-hospitalization data on pain intensity, depression and anxiety, sleep quality, and QOL. Most patients had tried one or more Food and Drug Administration-approved and/or off-label medications, such as pregabalin, duloxetine, and opioids. Most of the patients were advised to quit their medications if possible during admission; however, they were allowed to continue their current medications as they wish. This study was approved by our institution's human research committee and informed consent was obtained from all participants.

Protocol

All participants received two courses of ILIB; each course is composed of 10 ILIB sessions, and each therapeutic duration was 60 minutes. Two consecutive courses had a 7-day rest interval. During ILIB, each patient lay down in bed with supine position. A 24-gauge intravenous catheter was used for an elbow venous puncture (phlebotomy). The intravenous needle was subsequently replaced with a fiber-optic needle, which was inserted into the inner cannula of the intravenous catheter. The other side of the fiber optic needle was connected to a helium-neon laser illuminator (YJ-ILIB-5, Bio-ILIB Human Energy Ltd, Taiwan), which emits red-light laser in continuous wave mode with a wavelength of 632.8 nm and a power output of 2.5 mW.

Measurements

Pain assessment

A visual analogue scale (VAS) was used to evaluate pain (0=no pain and 10=as painful as imaginable) caused by fibromyalgia.

Depression and anxiety

The Revised Beck Depression Inventory (BDI) was employed for the assessment of depression. BDI is a widely used 21-item self-report inventory that measures the severity of depression in adolescents and adults [24].

Sleep quality

We used the Pittsburgh Sleep Quality Index (PSQI) to evaluate sleep conditions. It estimates sleep duration, sleep latency, and the frequency and severity of specific sleep-related problems during the past months. The index comprises 19 items which were grouped into 7 component scores, and weighted equally on a 4-point Likert scale, ranging from 0 (not during the past month) to 3 (≥ 3 times a week). The component scores are summed to yield a global PSQI score (ranges from 0–21), with higher scores indicating worse quality of sleep. Reliability estimates showed internal consistency of 0.83 for the 7 component scores, and test–retest reliability of 0.85 for the PSQI global scores [25].

Quality of life evaluation

The QOL of the patients with fibromyalgia was assessed using the Revised Fibromyalgia Impact Questionnaire (FIQR) [26], which contains three domains similar to those of the Fibromyalgia Impact Questionnaire (FIQ; function, overall impact, and symptoms). However, it differs from the FIQ as function questions were modified and questions on memory, tenderness, balance and environmental sensitivity were included. All questions are graded from 0 to 10. The FIQR is an updated version of the FIQ and has good psychometric properties, which could be easily scored and completed in 2 minutes.

The trial lasted for 4 weeks, and outcomes were evaluated on two separate occasions: baseline and within 24 hours after the last day of the protocol.

Statistical Analyses

Statistical analyses were performed with the SPSS 18.0 PC program. Results were expressed as mean ± S.D. Wilcoxon rank-sum test (featuring non-parametric statistics) was used to compare the measurements of therapeutic outcomes pre/ post treatments and the gain differences between the effects of drug and ILIB, including pain, tender point, quality of life, sleep quality, and depression. P values <0.05 were considered statistically significant.

Results

Table 1 showed the demographic characteristics of all the participants. Comorbidity, medication history and medication at admission were also shown in Table 1. All participants had received at least two types of drugs for fibromyalgia before admission. All the

participants were women with a mean age of 53.77 years (range: 31–64 years) and a mean body mass index of 24.30 (range: 17.9-32.65).

Subject	Sex	Age (year)	BMI	Fibromyalgia duration (year)	Comorbidity	Medication History	Medication at admission
1	F	31	17.9	3	Osteoarthrosis	Neurontin 7 months	Nil
						Anxiedin 9 months	
2	F	56	21.5	7.5	Poliomyelitis	Dormicum 1 year	Flurbiprofen 5 years
						Lorazepam 1 year	
						Celecoxib 2 years	
3	F	51	20.3	9	Sicca syndrome; L4/5 Herniated intervertebral disc	Pregabalin 2 years	Estazolam 9 years
						Estazolam 9 years	Sertraline 8 years
						Sertraline 8 years	
						Xanax 3 months	
						Amitriptyline 4v	
						Ultracet 5 months	
						Celecoxib 5 months	
4	F	51	22.9	5	Depressive disorder; Breast Fibroadenoma	Amitriptyline 1 year	Vytorin 4 years
						Pregabalin 6 months	Lipanthyl 4 years
						Alprazolam 6 months	
						Meitifen 5 months	
5	F	59	29	5	Chronic migraine; Prolactinonemia in left pituitary fossa; Major depression; L4/5 Spondylolisthesis	Remeron 4 years	Clonazepam 5 years
						Zopiclone 5 years	Flunarizine 4 years
						Flunarizine 4 years	Remeron 4 years
						Propranolol 4 years	Propranolol 4 years
6	F	63	24.8	8		Clonazepam 5 years	Zopiclone 5 years
					Rheumatoid arthritis; Osteoarthritis; Obstructive sleep apnea	Alprazolam 2 years	Salazine 6 years
						Salaxine 6 years	Eltroxin 6 years
						Zolpidem 8 years	Zolpidem 8 years
						Concor 1 year	Norvasc 3 years
						Clonazepam 1 year	
						Eltroxin 6 years	
7	F	62	30.4	4	Failed back surgery syndrome; L4/5 herniated intervertebral disc	Pregabalin 2 years	Ultracet 3 years
						Ultracet 3 years	Celecoxib 1 year
						Celecoxib 1 year	Crestor 3 years
						Crestor 3 years	Isosorbide
						Isosorbide mononitrate 3 years	mononitrate 3 years
8	F	64	30.5	4	Sicca syndrome; L4/5/S1 spinal stenosis	Trazodone 7 months	Aspirin 1 year

					mitral, aortic, and tricuspid regurgitation; hypertension; cataract	Clonazepam 2 years	Crestor 1 year
						Diclofenac 7 months	Prednisolone 2 years
						Pregabalin 1 year	
						Prednisolone 2 years	
9	F	54	22.3	1	Systemic lupus erythematosus; ankylosing spondylitis	Pregabalin 4 months	Propranolol 6 months
						Propranolol 6 months	
10	F	51	22.7	7	Left breast mixed invasive ductal carcinoma, s/p modified radical mastectomy, s/p CCRT; L-spine spondylosis	Clonazepam 2 years	Estazolam 7 years
						Zolpidem 4 years	
						Estazolam 7 years	
						Lorazepam 6 months	
						Pregabalin 2 years	
						Imipramine 1 year	
						Amitriptyline 3 years	
11	F	63	32.7	7	Type 2 Diabetes Mellitus; metabolic syndrome; stress urinary incontinence; L4/5 Spondylolisthesis	Glucophage 5 years	Copidogre 8 years
						Simvastatin 6 years	Insulin 2 years
						Flunarizine 4 months	Olmetec 4 years
						Glimepiride 4 years	Plaquenil 1 year
						Lorazepam 2 years;	Prednisolone 1 year
						Losartan 2 years	Simvastatin 6 years
						Copidogre 8 years	
12	F	50	19.7	4	Complex regional pain syndrome	Pregabalin 1 years	Ultracet 3 years
						Celecoxib 1 years	
						Ultracet 3 years	
						Tramadol 7 months	
						Baclofen 1 months	
						Etoricoxib 7 months	
13	F	50	20.7	15	Multiple sclerosis; Retractable migraine; Psoriasis vulgaris; bilateral optic neuropathy; major depression; Iron deficiency anemia	Meloxicam 6 months	Zolpidem 10 years
						Modipanol 4 years	Ultracet 5 years
						Zolpidem 10 years	Imigran 1 year
						Quetiapine 10 years	Quetiapine 10 years
						Duloxetine 9 years	Morphin 6 years
						Ultracet 5 years	Modipanol 4 years
						Topamax 8 months	Duloxetine 9 years
						Flunarizine 2 months	Amantadine 6 years
						Pregabalin 7 months	

						Morphine 6 years	
						Amantadine 6 years	
14	F	68	28		Rheumatoid arthritis; T-L spine degenerative joint disease with spur formation; hepatocellular carcinoma S3, pT2Nx, Stage II, s/p segmentectomy and transcatheter arterial chemoembolization	Lorazepam 2 years;	Alprazolam 5 years
						Alprazolam 5 years	Norvasc 4 years
						Prednisolone 2 months	Fludiazepam 1 year
						Sulfasalazine 2 months	Valsartan 3 years
						Etoricoxib 3 months;	
15	F	45	17.9	11	Sicca syndrome; peptic ulcer; iron deficiency anemia; Irritable bowel syndrome	Ultracet 8 years	Ultracet 8 years
						Amitriptyline 7 months	
						Pregabalin 3 months;	
						Clonazepam 2 years	

Table 1: Demographic and clinical characteristics of the study population.

Table 2 presented the measured outcomes before and after the treatment. The drugs therapy before admission achieved significance in VAS (p=0.006) only. However, all tests including VAS (p=0.001), numbers of tender points (p=0.002), FIQR (p=0.001), BDI (p=0.003) and PSQI (p=0.01) reached significance after the ILIB intervention. Moreover, comparing with drugs, the ILIB therapy demonstrated significantly positive effects on pain intensity, mood, sleep quality and QOL.

Measurements	Medication + exercise (Pre/Post)	ILIB + exercise (Pre/Post)	Difference (p-value)
VAS	8.00 ± 1.4/6.93 ± 1.8*	7.80 ± 2.0/4.73 ± 2.0**	0.006
Tender point	15.13 ± 3.7/14.53 ± 4.2	14.00 ± 4.0/10.73 ± 5.7**	0.038
FIQR	75.86 ± 20.5/69.17 ± 22.0	77.14 ± 17.0/49.93 ± 20.5**	0.005
BDI	20.40 ± 9.8/19.73 ± 10.0	19.93 ± 9.7/10.46 ± 7 .1**	0.016
PSQI	15.60 ± 3.5/15.26 ± 4.1	14.60 ± 3.4/11.46 ± 4.9*	0.027
Results are expressed as mean ± standard deviation (SD), *p<0.05, **p<0.005 Abbreviation: ILIB: Intravenous Laser Irradiation of Blood , VAS: Visual Analogue Scale, FIQR: Revised Fibromyalgia Impact Questionnaire, BDI: Revised Beck Depression Inventory, PSQI: Pittsburgh Sleep Quality Index			

Table 2: Wilcoxon tests for pre and post-intervention comparisons and the differences between the two treatments.

Figures 1-5 portrayed the distributions of all measurements before and after medication and intravenous laser irradiation, which also highlighted the significant results in Wilcoxon tests.

Figure 1 displayed the Wilcoxon tests of VAS scores, which reached significance in both the intra-group comparisons and the differences between the two treatments.

Figure 2 demonstrate the number of tender points before and after medication and intravenous laser irradiation, and the Wilcoxon test achieved significance in laser group and the differences between the two treatments.

Figures 3-5 possessed similar Wilcoxon result as Figure 2, and they showed the distributions of the FIQR scores, the BDI scores, and the PSQI scores, separately.

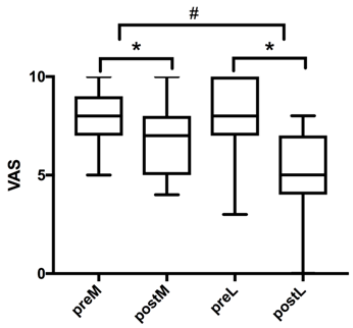

Figure 1: The distributions of VAS scores before and after medication and intravenous laser irradiation.
Abbreviation: M: medication; L: Intravenous Laser Irradiation of Blood (ILIB); VAS: Visual Analogue Scale

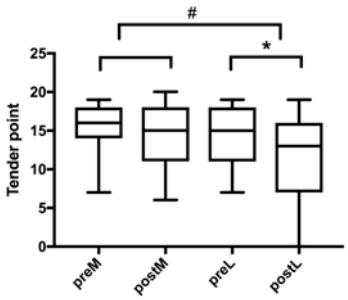

Figure 2: Number of tender points before and after medication and intravenous laser irradiation.
Abbreviation: M: Medication; L: Intravenous Laser Irradiation of Blood (ILIB)

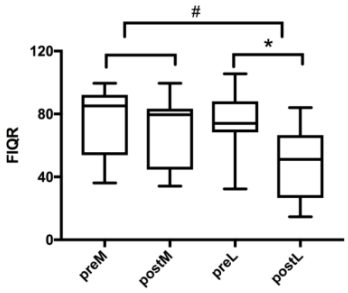

Figure 3: The distributions of FIQR scores before and after medication and intravenous laser irradiation.
Abbreviation: M: Medication; L: Intravenous Laser Irradiation of Blood (ILIB); FIQR: Revised Fibromyalgia Impact Questionnaire.

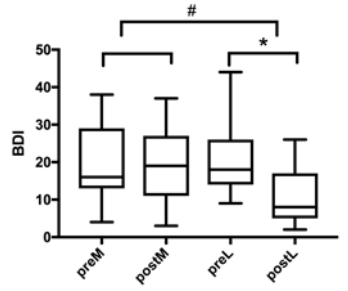

Figure 4: The distributions of BDI scores before and after medication and intravenous laser irradiation.
Abbreviation: M: Medication; L: Intravenous Laser Irradiation of Blood (ILIB); BDI: Revised Beck Depression Inventory.

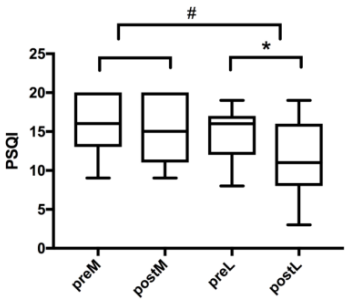

Figure 5: The distributions of PSQI scores before and after medication and intravenous laser irradiation.
Abbreviation: M: Medication; L: Intravenous Laser Irradiation of Blood (ILIB); PSQI: Pittsburgh Sleep Quality Index

Discussion

The etiology of fibromyalgia remains enigmatic and treatment results are often unsatisfactory. Currently, no cure for fibromyalgia exists. A multifaceted attempt tailored to the patients' needs is a crucial element in the treatment of pain, fatigue, and other diverse symptoms. Thus, ILIB has been widely used for its analgesic, spasmolytic, and sedative abilities [12,16].

Our findings showed that the maximum pain intensity significantly decreased after the ILIB therapy. Previous meta-analyses have shown that red laser phototherapy effectively relieves pain through several etiologies, thereby making it a valuable tool for pain management [27,28]. In addition, the ILIB therapy had effects on peripheral neural stimulation, the regulation of microcirculation, and interrupting persistent pain, and it promotes analgesia [12,29]. The hallmark of ILIB therapy encompasses concepts of physical, biochemical mechanisms, tissue photobiology, vasodilation via increasing localized nitric oxide production, and cell signaling [12,29-34].

Non-restorative sleep, fatigue, and depression are common among patients with fibromyalgia, which is possibly due to the pathophysiology of central sensitization [3,19,35,36]. We observed that patients treated with ILIB had marked improvement in quality of life, sleep, and mood disorders, which was possibly mediated by soluble mediators such as endorphins and serotonin [31,37-39]. The increase in total body serotonin, including CNS serotonin after red light laser [38,39], could have partially contributed to the improvement in pain, mood, and sleep improvements. In addition, research showed that mitochondrial impairment possibly has a significant effect causing the dysfunction of regulatory system cells, such as the nervous, endocrine, and lymphatic cells and their communicative network [40]. Hence, pain, mood disorders and sleep are prevalent in fibromyalgia. With ILIB, the redox system appears to be modulated resulting in ATP production and reduction in the generation of free radicals and super oxidants [12,18] which could be related to the antioxidant defenses in patients with fibromyalgia. Delayed skeletal muscle fatigue and better exercise performance may also be associated with the recovery from oxidative stress [15,41].

Moreover, the majority of patients in our study used a wide range of medications (e.g. pregabalin, duloxetine, tricyclic antidepressants, and non-steroidal anti-inflammatory drugs) for pain relief, fatigue, and

other symptoms. However, the relief felt from any single drug is minimal and most of the patients experienced side effects. By contrast, no complaints of discomfort were observed in all patients who had ILIB therapy.

Despite our efforts to reduce selection bias and to reduce confounding variables in our subjects by employing a vast collection of medical profiles, this study still has some limitations. No gold standard diagnostic biomarkers for fibromyalgia exist; thus, physicians only depend on patient-reported symptoms in understanding the complexities of this condition. Consequently, recall bias was not prevented in this study. Further studies may need prospective designs with randomized controls to limit recall bias.

Conclusion

This pilot study demonstrates that ILIB could lessen the effects of fibromyalgia, by improving pain severity, mood, sleep conditions, and quality of life. Hence, ILIB is a potential therapeutic regimen for patients with fibromyalgia.

Conflict of Interest

All authors declare that there is no conflict of interest.

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