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Analgesic effects of high intensity laser therapy (HILT) for chronic hemophilic arthropathy: a pilot study on safety, tolerability and clinical outcomes.

Demartis F.¹, De Cristofaro R.², Fasulo M.R.³, Bocalandro E.⁴, Cobianco A.⁵, Santagostino E.⁶

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ABSTRACT

The aim of this study was to verify analgesic effects of High Intensity Laser Therapy (HILT) for the treatment of chronic arthropathy in adult hemophilic patients and to verify its safety and tolerability.

Eleven adult hemophilic patients of any degree with or without inhibitors, diagnosed with chronic arthropathy, were enrolled in this pilot open-label study by three Hemophilia Treatment Centers. All patients were treated with 3 High Intensity Laser applications/week in the symptomatic joint for 3 consecutive weeks. Clinical evaluations assessed reactions at application site and skin

reactions. Outcomes were defined as variations in the Nieschl's and VAS Scores and Hemophilia Joint Health Score 2.0, compared to the baseline, as well as documented adverse events (AEs) and serious adverse events (SAEs).

At the end of the study, after 3 weeks of therapy, we recorded a statistically significant decrease of Nieschl's score (-1.9 ± 2.47) and VAS score (-27.1 ± 30.66) (both at $P < 0.05$), while no statistical difference was observed between the basal and last visit with regard to HJH-2.0 scores. Three local reactions at the site of therapy were reported, two of which were non-severe and one (paresthesia) was of moderate intensity. Three adverse

events were experienced, such as transient gonalgia of the right knee that was considered to be possibly related to the study treatment. No bleeding at the site of therapy application was reported. In this pilot study, HILT demonstrated a statistically significant analgesic effect for chronic arthropathy in hemophilic adult patients; the analgesic effect was evident even after few treatment sessions and it was well tolerated with rare adverse events. Further studies have to be carried out to clarify if different doses and schedule applications could improve the clinical outcomes.

INTRODUCTION

Hemophilia is a hereditary bleeding disorder caused by mutations in the gene for factor VIII (Hemophilia A) or factor IX (Hemophilia B) [1]. Progressive joint destruction resulting from intra-articular bleeding is the major morbidity and disability affecting patients with hemophilia. This process starts in the joints when affected children begin to walk and just few recurrent bleeding episodes in a single joint can determine the onset of a progressive degenerative process that eventually leads to hemophilic arthropathy [2]. The joints most commonly affected are the ankles, knees and elbows. The progressive functional incapacity and chronic pain that requires pain killer medications and surgical intervention, together with manifestations of acute hemarthrosis, are the cause of frequent clinical visits and hospitalization associated with a poor quality of life (QoL) and loss of self-confidence. Disability is directly correlated with pain level [3-4].

High power lasers application in physiotherapy is quite recent; High Intensity Laser Therapy (HILT) performs a pulsed Nd: YAG laser beam that principally induces photomechanical and photo thermal effects at a sufficient depth to irradiate human joints (Figure 1). The

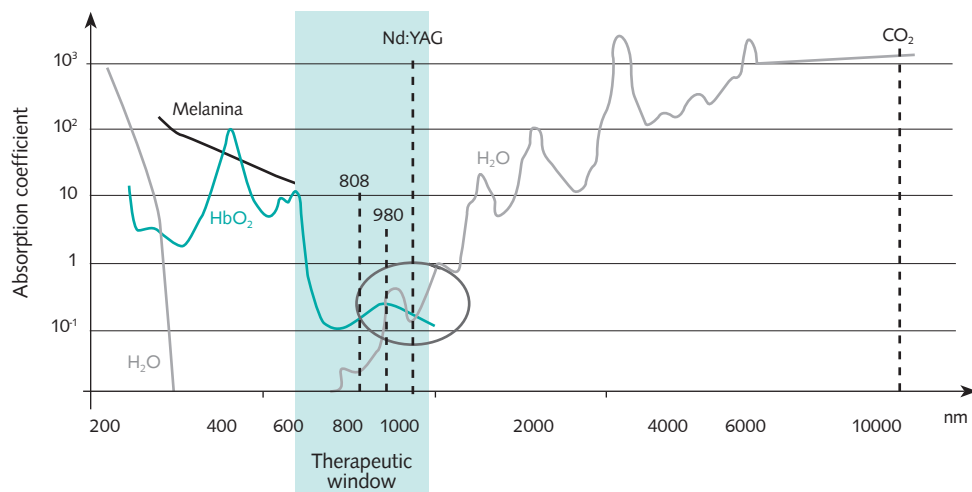


Figure 1: Laser Nd: YAG 1064 λ therapeutic window.

AGE, YEARS (SD)	40.6 (13.4)	
SEVERITY OF HEMOFILIA		
	Moderate	1 (9%)
	Severe	10 (91%)
BLEEDING HISTORY		
	Target joints	11
	Sport Activities	7 (64%)
	Recurrent hemarthrosis	10 (91%)
	Recurrent bleeding	3 (27%)
	Bleeding in the last 7 days	2 (18%)
REASON FOR TREATMENT		
	Back pain	1 (9%)
	Bilateral ankle pain	1 (9%)
	Joint pain	3 (27%)
	Joint pain and stiffness	1 (9%)
	Pain at rest	1 (9%)
	Pain affecting left ankle	1 (9%)
	Pain right ankle	1 (9%)
	Pain right elbow	1 (9%)
	Right shoulder pain	1 (9%)

Table I: Patients characteristics

duty cycle of pulsed Nd: YAG laser used for HILT allows to have photothermal effects without tissue denaturation or extravascular cell membrane lesions

[5]. High Intensity Laser Therapy (HILT) peculiarity is its ability to transfer highly energetic photonic packages in deep tissues in a completely non-invasive way,

helping to rebalance the homeostasis in the course of chronic-degenerative phenomena [6-8]. Since 1960 Low Level Laser Therapy (LLL) has been used clinically to stimulate several biological tissues, targeting cell metabolism, reducing post injury inflammatory processes, accelerating soft tissue healing and stimulating new blood vessels growth [9-13].

HILT demonstrated to be more effective than LLLT in pain and disability management showing good results in osteoarthritic disease as well as in osteoarthritis [5-7] with consequent QoL improvement [14,15].

Although the pathogenesis of hemophilic arthropathy has not been fully elucidated, it appears to have similarities with the degenerative joint damage that occurs in osteoarthritis and the inflammatory processes associated with rheumatoid arthritis [16]. The purpose of this pilot study is to verify the safety, tolerability and clinical outcomes of high-intensity laser applications for the treatment of chronic arthropathy in adult hemophilic patients.

MATERIALS AND METHODS

Eleven hemophilic patients older than 18 years of age, with a mean age of 41, diagnosed with chronic arthropathy were enrolled in 3 Haemophilia Treatment Centers. Ten patients were affected by severe hemophilia, one by moderate hemophilia (Table I). All patients were not infused by replacement therapy before laser exposure, or had taken cortison therapy during or after laser exposure. They were treated with the equipment ASA-SH1, (ASA s.r.l. El.En.Group Italy) laser type Nd:YAG, Class 2a, λ 1064 nm, that emits infrared light. Three non-invasive, transcutaneous HILT applications per week in the target joints for three consecutive weeks were provided keeping within the following parameters: Fluence: 360 to 760 mJ/cm²; Frequency range: 10 - 35 Hz; Total energy: from 500 to 1500 J; Application time: 6

Mean ± S.D.	Nieschl's score	VAS score	HJH Global Gait score	HJH Total score
Baseline	4.27±1.95	62.82±22.84	1.18±2.00	27.45±15.05
After 1 week	3.00±1.48	45.64±20.11	1.36±2.00	27.45±15.31
After 2 weeks	2.60±1.51	39.00±19.69	1.40±2.00	26.00±15.78
After 3 weeks	2.50±1.90	38.00±25.41	1.40±2.00	26.00±15.78
Difference vs basal visit				
N. Mean ± S.D.	Nieschl's score	Signed Rank Test Significance	VAS score	Signed Rank Test Significance
After 1 week	11 1.27±2.00	N.S.	11 17.18±18.69	P<0.01
After 2 weeks	10 1.80±2.25	P<0.05	10 26.10±28.85	P<0.05
After 3 weeks	10 1.90±2.47	P<0.05	10 27.10±30.66	P<0.05

Table II: Clinical outcomes

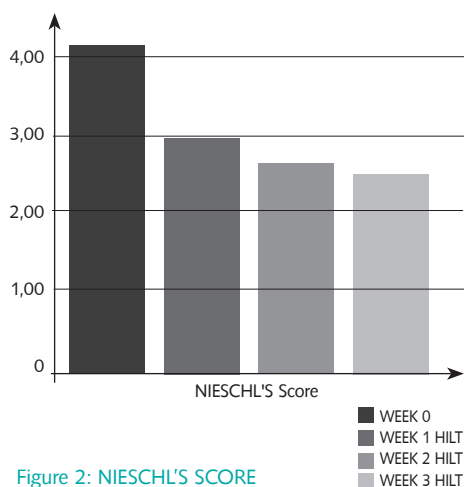


Figure 2: NIESCHL'S SCORE

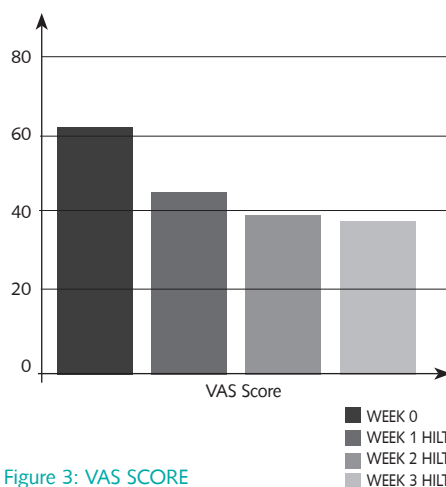


Figure 3: VAS SCORE

- 11 minutes. Treatment time was related with the skin area to be treated, according to the general rule: 50 J/cm². Before treatment all patients underwent clinical evaluations with regards to medical history, presence of antibody to FVIII, frequency of previous total and joint bleedings (average frequency), evaluation of joint damage (hemarthrosis), presence of a target joint, initial assessment of subjective pain evaluated by Nieschl's Score and Visual Analogue Scale - "VAS", initial assessment of the joint status ("Hemophilia Joint Health

Score 2.0"), and concomitant medications [17]. All patients signed the Study informed consent form. Patients were monitored during and after the HILT treatment to assess reactions at application site (heat, numbness, loss of feeling and tingling) identified as mild, moderate or severe by the Investigators. Outcomes were defined as variations in subjective pain at baseline, during treatment and at last visit using the Visual Analogue Scale (VAS) score (0 = no pain, 100 = maximum pain) and the Nieschl's Score; joints were evaluated by

the "Hemophilia Joint Health Score 2.0", with the same schedule. All bleeding episodes occurred since the previous visit were recorded, as well as documented adverse events (AEs) and serious adverse events (SAEs). The Trial was approved by the local Ethical Committee.

STATISTICAL ANALYSIS

A statistical evaluation of HILT efficacy was performed based on Nieschl's score, VAS score and Haemophilia Joint Health 2.0 scores (HJH-2.0). Non-parametric Signed Rank Test was used in order to evaluate the difference between basal value (Visit 1) and the values after 1 (Visit 4), 2 (Visit 7) and 3 (Visit 10) weeks of therapy at a level of 5% significance. Statistical analysis was performed using SAS software (Ver. 9.2), by SAS Institute Inc., Cary, North Carolina, USA. Descriptive statistics for continuous demographic and clinical parameters were described in mean, standard deviation, median, range and frequency. Nominal or discrete parameters were reported as contingency tables (Table II).

RESULTS

At the end of the study after 3 weeks of therapy, the decrease of Nieschl's score was: -1.9±2.47 (Figure 2) the decrease of VAS score was -27.1±30.66 (Figure 3) both statistically significant (P<0.05) (Table II).

Both scores showed a statistically significant (P<0.05) difference also just after 2 weeks of therapy as compared to basal values.

A statistically significant (P<0.01) pain relief, measured as VAS score, was also observed after a single week of therapy (-17.18±18.69).

No statistical significant differences were observed in term of HJH Global Gate score and HJH Total score (Table II) with respect to baseline values. Regarding tolerability and safety, two patients experienced mild heat at the site of application therapy and one patient suffered moderate local paresthesia. No

bleeding at application site was reported. Three adverse events were reported: a mild episode of esophageal reflux, a mild episode of cough and a moderate episode of gonalgia of the right knee. Only the last event was considered to be possibly related to the study treatment.

DISCUSSION

The well known dose-response relationships between non-steroidal anti-inflammatory drugs (NSAIDs) and serious upper gastrointestinal bleeding is a caveat for pain therapy in hemophilia [17,18]. This is the reason that induced our team to look for an alternative therapy, as laser therapy for chronic joint pain in hemophilic patients.

Laser therapy seems to be a promising approach [5,6]. In this pilot study we investigated the role of an innovative treatment called High Intensity Laser Therapy (HILT). HILT should overcome some limitations of traditional laser therapy, as it can achieve good tissue penetration, possibly enabling the repair/regeneration of chronic articular lesions. Recent studies in osteoarthritis confirm that HILT can improve pain control. Under physiological conditions a complex homeostatic mechanism regulates all processes of the chondrocyte.

Such rigid control seems to be the result of a balanced production of anabolic and catabolic cytokines: the production of the constituents of the matrix is in equilibrium with its degradation. HILT seems able to promote the anabolic cytokines which can be able to re-balance the ongoing catabolic process, exerting their effect on the activation of the intrinsic tyrosine kinase which triggers a series of intracellular and extracellular phenomena affecting the homeostasis itself [5,6].

The functional impact and disability of chronic articular inflammatory disease in adult hemophilic patients is well

known. The pathogenesis starts early in childhood and the recurrence of intra-articular bleedings causes the common reported symptoms of itching and heat followed by pain, swelling and decreased range of motion [2]. The pathogenesis of the subsequent arthropathy is not fully understood, especially in its early stages, but can be seen as a multi factorial process: inflammation in the synovium and degeneration of articular cartilage. During an episode of acute hemarthrosis, within a few hours the synovium is infiltrated by polymorphonuclear cells and subsequently by lymphocytes and monocytes.

Macrophages remove the blood from the joint cavity, however the recurrence of acute bleedings can reduce their depletion capacity. This gives rise to the formation of substantial hemosiderin deposits that induce synovial proliferation, determine the formation of villi and induce a process of neo-vascularization in the below layer which in turn facilitates the inflammation. The inflamed synovium is highly vascularized and fragile and bleeds easily, even for minimal stress, giving rise to the establishment of a vicious circle that is difficult to stop. Inflammatory cells infiltrating the synovium release cytokines and enzymes which cause the destruction of the cartilage, without allowing any possibility of repair, giving rise to the typical clinical manifestations of debilitating arthritis and complete disruption of the joint architecture. Iron plays a fundamental role in the establishment of the process as it is responsible for the activation of genes involved in cell proliferation [2]. The final result of these mechanisms is represented by the abnormal synovial hypertrophy. Experimental studies seem to support the hypothesis that even a single episode of bleeding can cause irreversible changes in cartilage coating in mice and in human beings. How many repeated bleedings in the joint itself that are required to determine irreversible damage to the articular cartilage is still unknown,

however it is common to observe that a few are sufficient to trigger a chain reaction in which the hemarthrosis begins to occur with considerable frequency. Since the amount of blood in the joint cavity affects the magnitude of inflammation and consequently the proliferation and degeneration of synovial and cartilage structures, an early treatment should to be established at any onset of hemarthrosis. Controlling the pain together with maintaining or improving joint functions are considered the principal aims of the therapy [17-19].

We have therefore assessed the safety, tolerability and efficacy of HILT in this pilot treatment of 11 hemophilic patients with chronic arthropathy. HILT treatment demonstrated to have a significant analgesic effect and was able to obtain a fast pain control after only few applications: Nieschl's score improved after 2 weeks of treatment and 9 HILT sessions, while VAS score was already significant after 1 week of therapy and 3 sessions.

This confirms that HILT can be a useful tool in the management of pain in these patients allowing an ultimate result of a better quality of life. These results confirmed the positive findings obtained in osteoarthritis [14]. Unfortunately it was not possible to assess if these benefits were long lasting, as the protocol was designed to evaluate only the acute effects and no follow up was scheduled. The overall tolerability was good, with one paresthesia of moderate intensity at the application site and three adverse events, none of which were serious. No changes were reported in the Hemophilia Joint Health Scores: different HILT parameters and changes in the duration of the treatment should be further investigated to assess if a longer or more intense application could ameliorate the HJHS.

CONCLUSIONS

The results of this pilot study support

the hypothesis that laser medicine offers potential benefits in treating chronic hemophilic arthropathy. Our results suggest that High Level Laser Therapy is a safe and well tolerated treatment, working quickly and efficiently in the management of pain, even after few treatment sessions. It may be considered as a possible alternative to pain killer medications, due to its analgesic effect. Further studies should be carried out to clarify if different doses and schedule applications can improve or modify the articular status.

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Achilles tendinopathy treatment with Triple Therapy.

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ABSTRACT

Achilles tendinopathy is a painful and inflammatory condition which can be acute or chronic and is common in both active and inactive individuals. In literature it has been shown the effectiveness of laser therapy in increasing blood flow from capillary and arteriolar vasodilatation, stimulating electrolyte exchange, modulating fibroblast metabolism and collagen deposition, decreasing inflammation through reduction of PGE2 concentrations and inhibition of cyclooxygenase 2, raising the threshold of perception of sensory nerve endings and accordingly less painful sensitivity.

Between February 2012 and July 2012 we collected and evaluated 45 patients, age between 42 and 55 years, with chronic Achilles tendinopathy. The patients were treated with Triple Therapy, a scanning laser. Triple Therapy was used with an amperage of 8 W (21 J) for the diode of 808 nm and 12 W (31 J) for the diode of 1064 nm in continuous mode, for a total 52 J for each session. The patients were treated with a frequency of 3 session every 7 days for 3 weeks. The study protocol provided for an initial, a control and a

follow up, after 6 months, ultrasound evaluation associated with VISA-A score; thermographic evaluation, pain level by VAS and Fischer algometer were assessed before and after each treatment session. Before treatment ultrasonography found hypoechogenicity of the Achilles tendon and of the peritendinous part, an average value at the thermography equal to 30.1°C, a pre-treatment average value of the VISA-A score equal to 32% and an average value of the VAS pain scale equal to 8.2 (range 6-9) and an average value of the Fischer algometer equal to 5 kg/cm² (range 3-7).

At the end of the treatment protocol the ultrasound hypoechogenicity was significantly decreased, and there was an average value of temperature equal to 28.1°C, an increased average value of the VISA-A score equal to 78% and a reduction of pain on VAS scale by 83% and an increased average value of the Fischer algometer equal to 18 kg/cm² (range 16-20). None of patients experienced adverse reactions to treatment.

In conclusion, we can affirm that Triple Therapy can be able to act on

Achilles tendinopathy, promoting the tissue trophism and the reduction of inflammatory response in a shorter time, if compared with other treatments, reducing the operating costs and the need for more complex interventions.

INTRODUCTION

Achilles tendinopathy (AT) is the generic descriptor used to describe the clinical presentation of activity related Achilles tendon pain, focal tendon tenderness and intratendinous imaging changes. It is a common condition causing considerable morbidity in athletes and non-athletes alike (1). Symptoms can occur at the midportion or insertion of the tendon, with the underlying pathology reflecting a failed healing response, where both inflammatory and degenerative pathologies exist. Histology studies indicate that the pathology is predominantly of tendon degeneration ('tendinosis') as opposed to the historically hypothesized inflammation ('tendinitis') and can develop long before the onset of symptoms (2). This may result in advanced underlying pathology prior to clinical presentation, which has repercussions for management, as well as outcome expectations of both the clinician and patient. It also may partly explain why some individuals develop recalcitrant AT (3) and may progress to full tendon rupture (4).

One of the most frequent pain diseases; especially from the amateur sport; 11% from the runners; average onset age: between 28 and 55 years old; can be acute or chronic (3 weeks) (5).

Conservative or physical therapies are generally accepted as the first line approach for managing AT, and can be used in isolation or in conjunction with pharmacological and injectable agents. Surgical approaches are usually reserved for the most recalcitrant cases. Physical therapies for AT include exercise,

electrotherapeutic modalities, soft tissue therapies, braces and splints. These are often used in a multimodal approach for the purpose of alleviating symptoms and promoting functional recovery (1, 6-8). There is moderate evidence in literature for low-level laser therapy efficacy in the conservative management of midportion Achilles tendinopathy (8-11). The aim of our study was to investigate the effects at short and medium term of therapy with a combined double source scanning diode laser in subjects with chronic Achilles tendinopathy.

MATERIALS AND METHODS

The study was approved by the local ethics committee, and was performed in accordance with the 1964 Declaration of Helsinki. Subjects were informed about the procedures and purposes of the research and gave their written informed consent before participating.

INCLUSION CRITERIA were as follows:

- Chronic tendinopathy present at least 3 months
- Clinical and ultrasonography diagnosis
- Between 28 and 55 years
- Usual non competitive sport activities
- No pharmacological treatment

EXCLUSION CRITERIA:

- Pregnancy
- Cancer
- Bleeding diathesis area

Between February 2012 and July 2012 55 subjects, aged between 42 and 55 years (mean age 49 years), with chronic Achilles tendinopathy, were divided into 2 groups, evaluated and treated with different modalities.

Subjects underwent the protocol with Triple Therapy with a frequency of 3 sessions a week for 3 weeks; each session lasted 15 minutes. In the treatment group (Group A-45 subjects), Triple Therapy was used with an amperage of 8 W (21J) for

the diode of 808 nm and 12 W (31J) for the diode of 1064 nm in continuous mode for a total of 52 J for each session; in the control group (Group B-10 subjects) Triple Therapy was used without laser dispensing, but only with guiding light.

Ultrasound and VISA-A score evaluation were performed before T0, at the end of the protocol T1 and at follow up after 6 months of specific motor activity recovery. Pain assessment by VAS and Fischer algometer and thermographic evaluation were performed before and after each treatment session. In Group A, before treatment at ultrasonography it was found hypoechogenicity of the Achilles tendon and of the peritendineous part, an average value at the thermography equal to 30.1°C, a pre-treatment average value of the VISA-A score equal to 32%, an average value of the VAS pain scale equal to 8.2 (range 6-9) and an average value of the Fischer algometer equal to 5 kg/cm² (range 3-7). In Group B, before treatment at ultrasonography it was found hypoechogenicity of the Achilles tendon and of the peritendineous part, an average value at the thermography equal to 29.9°C, a pre-treatment average value of the VISA-A score equal to 36%, an average value of the VAS pain scale equal to 7.6 (range 4-10) and an average value of the Fischer algometer equal to 4.4 kg/cm² (range 3-8).

RESULTS

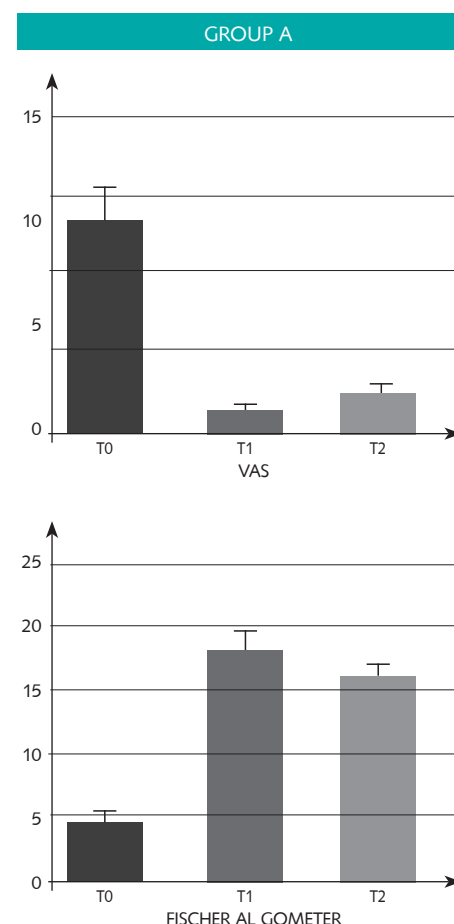
At the end of the treatment protocol, in Group A, the ultrasound hypoechogenicity was significantly decreased, and there was an average reduction of pain on VAS scale of 83% (T1 1.4) and an increased average value of the Fischer algometer equal to 18 kg/cm² (range 16-20). There was an average value of temperature equal to 28.1°C and, an increased average value of the VISA-A score equal to 78%. None of the treated patients experienced adverse reactions to treatment. In Group B, there

were no significant modifications of the evaluated parameters.

At the follow up after 6 months 3 of the 45 subjects of Group A showed recurrence of symptoms with pain score of 4.4 on VAS scale, average value of VISA-A score equal to 74% and an average value of the Fischer algometer equal to 12 kg/cm², they needed new treatment and were not included in the final evaluation.

The other 42 subjects of the Group A showed an average VAS score of 1.8 (range 0-3) and an average value of the Fischer algometer equal to 17 kg/cm² (range 14 - 20), with an average value of VISA-A score equal to 95%.

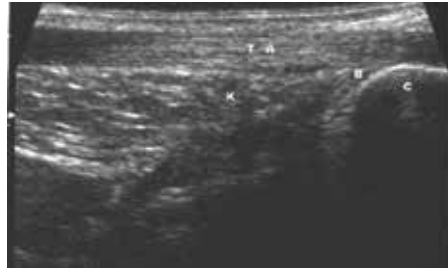
In Group B, there were no significant modifications of the evaluated parameters. At the follow up after 6 months, in the Group B, it was observed no significant modifications of the average values of the considered parameters.



ULTRASONOGRAPHY – GROUP A

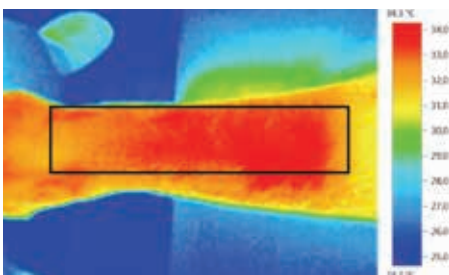


T0: accentuation of hypoechogenicity Achilles tendon and peritendineous components

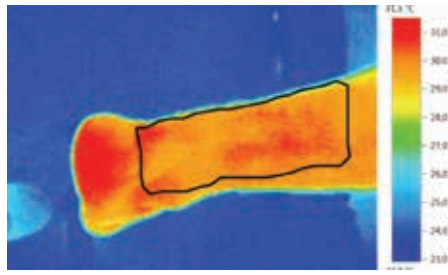


T1: significant reduction of ultrasonographic hypoechogenicity of evaluated structures

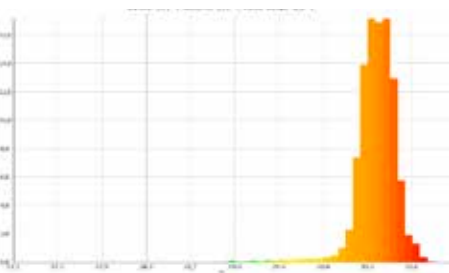
SINGLE REPORT



Before-treatment T0= 30.1° C



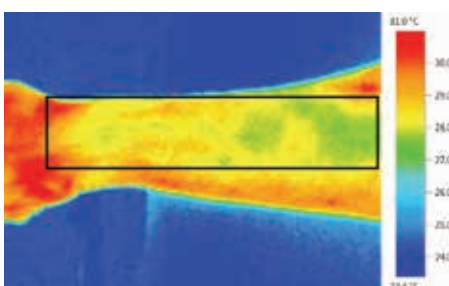
After-treatment T0= 34.4° C



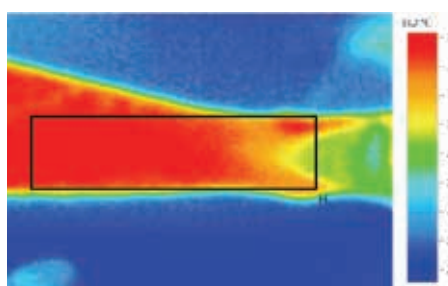
Before-treatment T0= 27.1°C<30°C<31°C



After-treatment T0= 27.7°C<33.1°C<34.3°C

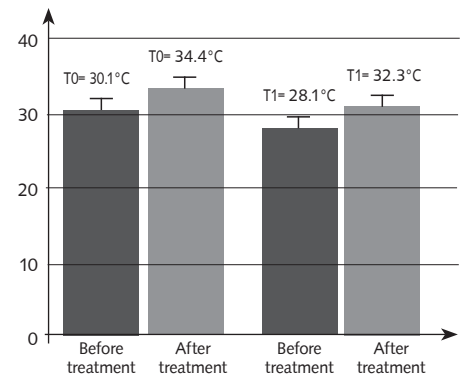


Before-treatment T1= 28.1° C

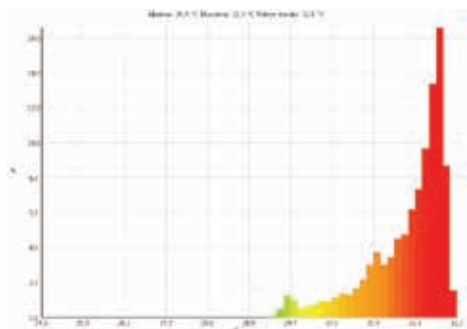


After-treatment T1= 32.3° C

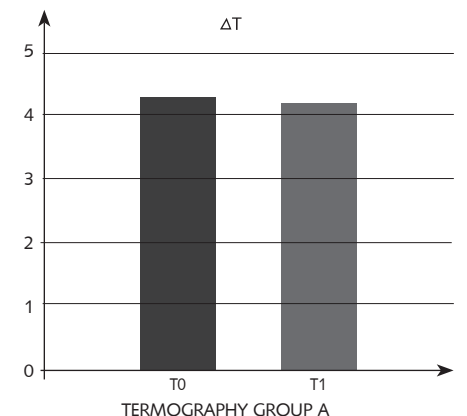
THERMOGRAPHY – GROUP A

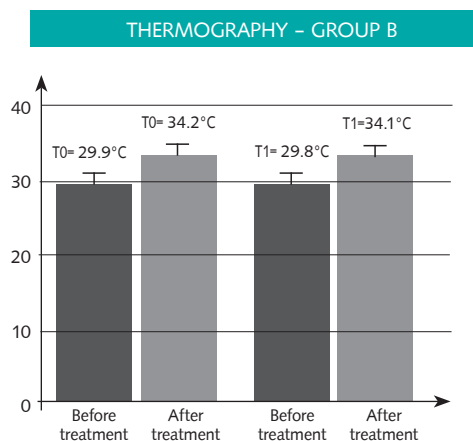


Before-treatment T1= 27.1°C<28.7°C<30.8°C



Post-treatment T1= 29.4°C<32.3°C<33.2°C





DISCUSSION AND CONCLUSION

A recently published clinical practice guideline on Achilles tendinitis of the American Physical Therapy Association reported, on the evidence of 2 trials (12), that clinicians consider low-level laser therapy (LLLT) as a treatment option for this condition. There have been 5 randomized controlled trials (RCTs) on human subjects during the last 2 decades exploring the use of LLLT for the treatment of Achilles tendinopathy, and these have delivered contrasting results (13, 14). Reviews on the effectiveness of treatment modalities for different tendinopathies does not support, on the whole, the use of LLLT and give weak or negative recommendations. However, a recent review on the use of LLLT for tendinopathy, although confirming this trend of contrasting results from RCTs, reported a dose-response relationship from a subset analysis of 12 positive studies supported by the World Association of Laser Therapy (WALT). Important effects of LLLT in the treatment of tendinopathy are decrease in inflammation, increase in angiogenesis and fibroblast activity, leading to an increase in collagen production and tensile strength, and decrease in pain (11). Literature still describes few evidences in the use of high power laser therapy, because of little case series, however our results demonstrate that Triple Therapy can act positively on Achilles tendinopathy, promoting the tissue trophism and the reduction of inflammatory response in a shorter time, if compared with other treatments, thus reducing the operating costs and the need for more complex interventions (12, 15). Eccentric exercise is known to induce a

statistically significant increase in collagen synthesis in the patellar tendon by 1% to 3%, as we have seen in our experience, and the rate remains elevated for 2 to 3 days after exercise. During the last 10 years, eccentric exercises was confirmed to be an effective exercise choice for the treatment of tendinopathies (9).

At the end of 9 sessions of treatment, carried out over a period of 3 weeks, a significant reduction of the inflammatory Achilles framework has been highlighted, resulting in reduction of pain symptoms (assessed by VISA-A score, VAS and Fischer algometer) and improvement of the ultrasound and thermographic framework. None of the 45 patients experienced adverse reactions.

Data allowed to identify significant results even at a distance with recovery and functional maintenance and absence of pain. Literature encourages us to propose the use of high-power laser therapy as best practice in the multimodal approach of the Achilles tendinopathy, with eccentric exercise and normalization of the ground-foot reaction, with specific viscoelastic insoles (16, 17).

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Efficacy of low frequency pulsed electromagnetic field therapy on physical fitness in juvenile rheumatoid arthritis: a randomized, placebo-controlled study.

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ABSTRACT

Juvenile rheumatoid arthritis (JRA) is the most common rheumatic disease of childhood. This study was conducted to examine the effects of low frequency pulsed magnetic field therapy on physical fitness in children with polyarticular JRA. Thirty children, with polyarticular JRA, aged 8 to 12 years were included. Children were randomized for treatment in two groups. In the group A (study) received low frequency pulsed magnetic field therapy 3 times per week for successive 12 weeks. In the group B (control) received a placebo treatment. Evaluation of knee joint pain using the Visual Analogue Scale (VAS) and physical fitness using 6 Minute Walk Test (6MWT) were performed

before and after the treatment. The result of this study revealed that there was a statistically significant improvement in physical fitness in children with JRA. Therefore, low frequency pulsed magnetic field is effective, innovative, non-invasive, non-expensive and can be used as a new trend physical therapy modality in the treatment of fatigue in JRA.

INTRODUCTION

Juvenile rheumatoid arthritis (JRA) is a disease that occurs in children beginning before sixteen years of age [1]. Although JRA is a chronic disease of childhood, the actual cause of the disease is unknown [2]. Some common signs and symptoms of JRA are morning stiffness, joint

guardian, fatigue, sleep disturbances and irritability [3, 4].

Fatigue in JRA is being increasingly recognized within pediatric practice. As in adult patients, it is characterized by longstanding, medically unexplained tiredness, functional disability and accompanied by a variety of physical and psychological complaints [5].

Functional impairment is a key aspect of the condition and it affects most areas in children's lives. Rangel et al., [6], reported that when the illness was at its worst, most children with chronic fatigue syndrome (CFS) had stopped socializing with their friends and family relationships had become strained in many instances. Half had been bedridden for prolonged periods and some were in wheelchairs. Most striking was the impairment caused in school attendance: two-thirds had been totally unable to attend school, with a mean time out of school for one year.

While juvenile arthritis is markedly different from adult rheumatoid arthritis, goals of management are similar, including reduction of joint inflammation, pain relief, prevention of disability and maintenance of function, the provision of education and attention to psychosocial, growth and development needs. A multi-disciplinary approach is required to deliver a comprehensive and effective program [7]. In the short term, decreased physical fitness and activity levels can lead to further functional deterioration. In the longer term, decreased physical fitness and activity levels can lead to an increased risk for cardiovascular disease [8].

Pulsed electromagnetic field (PEMF) exposure is approved by the United States Food and Drug Administration for the treatment of problems associated with musculoskeletal disorders, including delayed union or non-union fractures, failed joint fusions, and congenital pseudoarthroses [9]. Specific joint disorders that have been investigated using this treatment modality include

rheumatoid arthritis (RA) [10], osteoarthritis and rotator cuff tendonitis [11, 12].

Pulsed electromagnetic field induces time-varying ionic currents in tissues, which stimulate changes in cellular calcium and cyclic adenosine monophosphate levels [13], as well as in the synthesis of collagen, proteoglycans, DNA, and RNA [14]. In addition, some of the enzymes and hormones involved in skeletal homeostasis are affected by PEMF and it increases nitric oxide production and levels of reactive oxygen species [15].

There is growing evidence in the literature of the beneficial effects of magnetic fields on different multiple sclerosis symptoms [16], and there have been reports that the technique can alleviate symptoms such as fatigue, bladder control, and spasticity, as well as improve quality of life. The aim of this study was to investigate the efficacy of PEMF on physical fitness in children with juvenile rheumatoid arthritis.

MATERIALS AND METHODS

Study design

This was a randomized, placebo therapy controlled trial assessing the effects of low frequency magnetic fields versus placebo therapy on physical fitness in JRA children.

Subjects

Thirty children had polyarticular participated in the study ranged in age from 8 to 12 years. They were recruited for the study from an outpatient clinic of "Abo El-Rish pediatric Hospital-Cairo University Hospitals" according to the following criteria:

Inclusion criteria:

All patients should have fulfilled the American College of Rheumatology (ACR) criteria for polyarticular JRA: presence of arthritis in five or more joints during first 6 months of disease. Symmetry of arthritis however, the degree of involvement was varied. Cardinal hallmark signs and symptoms of joint involvement in JRA that generally were marked by pain,

swelling and morning stiffness.

Exclusion criteria:

- 1 - The use of drugs that could potentially interfere with fatigue.
- 2 - Possible secondary causes of fatigue.
- 3 - Psychiatric disorders, epilepsy and other chronic diseases that could cause fatigue.
- 4 - Patients who had advanced radiographic changes as bone destruction, bony ankylosis, knee joint subluxation, epiphyseal fractures, and growth abnormalities related to marked skeletal changes seen in JRA. All subjects gave written informed consent.

Randomization

After the baseline assessment and data collection, a computer-generated random number list was used to randomize patients into two equal groups, the PEMF and placebo group. Randomization was performed using sequential sealed envelopes prepared by an independent therapist before enrollment. The sealed envelopes contained a record of the allocation. The researchers and participants were all blind to the group allocation throughout the study.

Materials

The ASA magnetic field is a device for magneto-therapy, its model is (Automatic PMT Quattro pro). It consists of an appliance, motorized bed and solenoids. The appliance was connected to electrical mains supplying 230V \pm 10% at a frequency of 50 or 60 Hz with earth connection. The intensity and spatial layout of the generated magnetic field depend on the type of solenoid used.

Assessment

All children (control and study) received the standard physical therapy treatment for JRA, regardless of treatment allocation. The standard physical therapy program consisted of muscle stretching, strengthening exercises, proprioceptive training, gait and balance training for (one hour /day, 3 sessions/week) for

successive 12 weeks. The study group underwent additional PEMF with the standard physical therapy treatment.

All patients were assessed at baseline and at the end of therapy (after 12 weeks) by the same assessor who was blinded to treatment.

1 - Visual analogue scale (VAS) was used to assess levels of pain and anxiety, both before (pre) and after (post) magnetic field or placebo exposure. The pain scale ranged from no pain to worst (from no pain=0 to unbearable pain=10) [17].

2 - The six minute walk test (6MWT) was performed individually with standardized encouragements during the test. An indoor quiet corridor distance of 20 meters between turning points was used. Each child was instructed to cover as many laps of the course as possible in 6 minutes without running. The test was performed with no 'pacer' (a therapist who walks behind the patient) except when there is a high risk of falling [18].

Magnetic field application:

The child was asked to remove metal objects or anything sensitive to magnetic field such as chains, belts, watches, etc....before lying on the bed. Then the child was placed in a comfortable supine lying position over the motorized bed. During application, the child was asked not to move and remain stable as much as possible. The appliance was connected to electrical mains supplying 230V \pm 10%.The solenoids were adjusted to be over both knee joints. The options of the appliance were adjusted with very low frequency (15 Hz), very low intensity (20 G) for 20 minutes, 3 sessions/week for successive 12 weeks [19].

Statistical analysis

Statistical analysis was performed using SPSS version 16.0. Descriptive statistics of mean and standard deviation presented the child's age, weight, height and body mass index. Pain and physical fitness results pre- and post-treatment values were assessed using the ANOVA test. The significance level was set at (0.05).

Character	Study group (A)	Placebo control group (B)	F-Value	P-Value
	Mean \pm SD	Mean \pm SD		
Age (years)	12.22 \pm 2.33	11.90 \pm 2.74	0.145	**0.707
Height (Cm)	145.9 \pm 10.76	146.03 \pm 11.38	0.001	**0.974
Weight (Kg)	44.03 \pm 10.2	44.47 \pm 9.87	0.014	**0.907
BMI (kg/m ²)	20.16 \pm 2.24	20.55 \pm 1.65	0.285	**0.598
Right Knee joint Pain	5.53 \pm 0.83	5.53 \pm 0.64	0.000	**1.000
Left Knee joint Pain	5.6 \pm 0.83	5.67 \pm 0.62	0.063	**0.804
Functional Capacity (6MWT)(m)	543.93 \pm 18.65	544.87 \pm 24.04	0.014	**0.906

Table 1: The pre-test values of both groups

Level of significance at P<0.05. *= significant **= non-significant

Character	Study group (A)		T-Value	P-Value	Placebo control group (B)		T-Value	P-Value
	Mean \pm SD	Mean \pm SD			Pre	Post		
Right Knee joint Pain	5.53 \pm 0.83	2.87 \pm 0.64	16.73	0.00	5.53 \pm 0.64	3.67 \pm 0.82	14.00	*0.00
Left Knee joint Pain	5.6 \pm 0.83	2.93 \pm 0.59	16.73	0.00	5.67 \pm 0.62	3.60 \pm 0.63	31.00	*0.00
Functional Capacity (6MWT) (m)	543.93 \pm 18.65	570.00 \pm 21.29	- 23.67	0.00	544.87 \pm 24.04	552.33 \pm 24.09	- 13.35	*0.00

Table 2: Comparison between pre and post-test values of both groups

Level of significance at P<0.05. *= significant **= non-significant

RESULTS

Thirty children with juvenile arthritis (22 boys and 8 girls) commenced the 12-week low frequency pulsed electromagnetic therapy and underwent final analysis at the end of the 12-week period. In the baseline evaluation, the results of this study revealed that there were non-significant differences between the two groups (study group A and placebo control group B) before treatment (pre-test values) in the demographic characteristics including age, height, weight and body mass index. Also; results of this study revealed that there were non-significant differences between the two groups before treatment (pre-test values) in the measured variables including right knee joint pain, left knee joint pain evaluated via visual analogue scale (VAS) and functional exercise capacity evaluated via 6 minute walk test (6MWT) (Table 1).

When comparing the mean changes in levels of right knee pain, left knee pain between the two groups. Results revealed that there was significant reduction in levels of right and left knee pain. Furthermore, there are significant differences between both groups in levels of knee pain reduction in favor of group A. (P-value < 0.05) (Table 2). Also when comparing the mean changes in the levels of functional exercise capacity between the two groups; this revealed that there was a significant increase in levels of functional exercise capacity in both groups. Furthermore, there is a significant difference between both groups in functional exercise capacity improvement in favor of group A. (P-value < 0.05) (Table 2).

The result of this study also revealed that after 3 months of pulsed electromagnetic field treatment; the percentages of change in right & left knee pain levels

and functional exercise capacity for study group A were more than those in group B (Table 3).

DISCUSSION

This study was done to determine the efficacy of pulsed electromagnetic field treatment on physical fitness in children with JRA. PEMF therapy has been found to be effective in reducing pain and improving physical fitness in children with JRA.

Juvenile rheumatoid arthritis is the most common chronic rheumatic disease in childhood and one of the leading causes of pediatric acquired disability [20]. JRA persists into adulthood in up to 55% of patients, and may have a major impact on physical or psychosocial function. Children with JRA have reduced vigorous physical activity levels, sports participation and decreased fitness. Muscle atrophy,

Character	Study group (A)	Placebo control group (B)	F-Value	P-Value
Right Knee joint Pain	48.191 + 8.27	34.13 + 9.77	18.114	*0.00
Left Knee joint Pain	47.56 + 7.97	36.79 + 5.26	19.036	*0.00
Functional Capacity (6MWT) (m)	47.84 + 0.704	13.73 + 0.401	265.98	*0.00

Table 3: Comparison between the percentages of change in each variable of both groups

Level of significance at $P < 0.05$. *= significant **= non-significant

weakness and anemia contribute to reduced fitness, but deconditioning from reduced physical activity is likely the greatest cause. Reduced participation because of disease symptom severity, treatment-related side effects or worries that exercise may aggravate disease is problematic [21]. So it was the cause to conduct our study on those children with JRA.

The 6MWT is an inexpensive instrument for measuring functional exercise capacity in pediatric populations. The 6-min walk test is easier to administer, a better reflection of daily activities and better tolerated than other walk tests. Reproducibility testing has shown good reliability (ICC 0.96 in 0.98) for children with or without chronic disease [22].

The results of our study revealed a reduction in pain at the end of the treatment program. The results of this study come in agreement with Jacobson et al. [23] and Hinman [24]; they revealed that there was a significant pain relief due to the application of magnetic field for patients with RA. Magnetic field-related pain relief may be contributed to the analgesic effect of low frequency and low intensity pulsed magnetic field therapy that could be attributed to one of the following mechanisms:

First, the physiological mechanism for pain relief due to the application of magnetic field may be due to presynaptic inhibition or decreased excitability of pain fibers [24]. Others postulated that

magnetic field influences the small C fibers [25]. Also, Holcomb et al. [26], found that exposure to magnetic field produces a reversible blockade of sodium-dependent action potential firing and calcium-dependent responses to the irritant.

Second, the molecular mechanism of the effect of magnetic field may involve conformational changes in the ion channels or neuronal membrane. Considering the time required for the effect on action potentials, multiple mechanisms must be acting simultaneously, possible including indirect effects, such as reduction in activity of channel phosphorylating enzymes [27].

Third, evidence exists that pulsed magnetic fields can modulate the actions of hormones, anti-bodies and neurotransmitters at surface receptor sites of a variety of cell types [28].

The PEMF has been shown to increase upregulation of gene expression for aggrecan, type II collagen synthesis [29] and TGF β [30]. TGF β stimulates the aggrecan and collagen synthesis, suppresses the pro-enzyme forms of collagenase and interleukin-1 [31], which may result with pain reduction. The optimal frequency, intensity and duration required for the completion of these biological effects and for total recovery in human tissues, are unknown.

In the present study, the improvements in functional level in the PEMF group have been found superior to those of the placebo group. Improvement in the

stiffness level of the PEMF group can be due to enhanced blood circulation in the periarticular compartment. PEMF has been shown to activate the synthesis of nitric oxide which may enhance blood flow [32].

Scientific data on the mechanism of the effect of pulsed magnetic field therapy on fatigue are still unknown but some studies showed that short term exposure to pulsed electromagnetic fields can influence a variety of cellular and neurological processes, such as patterns of cortical activation and inhibition [33] and activity of various neurotransmitters [34-36]. However, most of these studies are based on small sample groups and used extreme different treatment protocols which could lead to different results between studies.

A possible and may be the most reasonable- explanation for the improved mobility of the PEMF treated joints that were reflected by the increased covered distances during the 6 minutes' walk could be an enhanced blood flow. Support for this idea could be found in the observation that PEMF activates synthesis of nitric oxide (NO) [37] and synthesis of NO in endothelial cells could be involved in enhancing blood flow. Furthermore, it was recently shown that PEMF increases in vivo and in vitro angiogenesis through the endothelial release of fibroblast growth factor 2, an important angiogenic factor [38]. Thus, there are data indicating that improved blood circulation in the periarticular compartment could occur following treatment. Recent data

from several laboratories have suggested that PEMF activates cellular signaling processes rapidly within 5-10 min [39-42] and signaling is largely blunted after 30 min. Thus, future studies could benefit from applying a shorter duration of PEMF-stimulation, that is, less than one hour but several times a day.

CONCLUSION

The results of the current study confirm past findings in humans exposed to chronic pain that exposure to a specific PEMF has a modest pain reducing effect in children with JRA. For these patients, exposure to a low frequency PEMF produced decreases in pain and an increase in physical fitness beyond those found in a placebo treatment control group. Future research using possibly more optimal PEMF parameters should be conducted to better understand how and when PEMF produce improvement in physical fitness.

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Burned wound healing response to helium neon versus gallium arsenide laser irradiation.

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ABSTRACT

Low Level Laser Therapy (LLLT) is widely used in many medical fields, and its effects are reported by several studies in literature. This study aimed at evaluating the effect of photostimulation to promote wound healing using laser irradiation (Helium Neon with wavelength: 632.8 nm and Gallium Arsenide at Wavelength: 904 nm). This study was an open, randomized, controlled trial. Forty-five (45) patients of both sexes and with dermal burn injuries on the upper limbs were randomly divided into three groups: two studies (laser irradiation groups) and one control (placebo) group. Wound surface area (WSA) was measured and pictures were taken for all the patients 72 hours after burn injury (Pre), after 10 days (Post I), and 21 days (Post II) from the beginning of treatment in all the groups. Results showed that there was a significant decrease in WSA ($P < 0.05$) and improvement in the status of the wounds in the two laser groups compared to the control, placebo group. There were no significant differences between the means

of WSA in GaAs and HeNe groups ($P > 0.05$) before, after the 10th and 21st days of treatment. These findings demonstrate that both Helium Neon and Gallium Arsenide were effective in accelerating wound healing.

INTRODUCTION

Burn is a coagulative necrosis of the skin that is caused by chemical, thermal and electrical agents; it exerts a catastrophic influence on people in terms of human life, suffering, disability and financial loss [1]. Most burns are not life threatening, but each burn causes a significant amount of pain for the patient, and some degree of Physical and psychological trauma to all those involved [2].

Tremendous efforts have been made to substantiate the use of physiotherapy to stimulate wound healing. Several putative therapeutic approaches have been proposed, including the use of antiseptics, growth factors, pressurized oxygen, and physical therapy modalities [3].

Laser is an acronym for Light Amplification

by the stimulated emission of radiation; it is a form of phototherapy which involves the application of monochromatic light over biological tissue to elicit a biomodulative effect within that tissue [4,5]. Photostimulation promotes tissue repair by accelerating the production of collagen and promote overall connective tissue stability in wound healing [6].

The action of low level laser therapy (LLLT) is based on the absorption of laser light by tissues, which will generate a series of modifications in cell metabolism. When the LLLT is applied to tissues, the light is absorbed by photoreceptors located in the cells, called chromophores. Once absorbed, the light can modulate chemical reactions in the cell and stimulate mitochondrial respiration, the production of molecular oxygen and ATP synthesis [7].

LLLT results in respiratory chain activation and subsequently, changes in the both mitochondria and cytoplasm. This may affect membrane permeability with a subsequent change in the Na^+/H^+ ratio and an increase in Na^+ and K^+/ATP -ase activity, which influences the Ca^{2+} flux. This is involved in the production of cyclic nucleotides that modulate DNA and RNA synthesis and, eventually, cell proliferation [8].

Wound healing of burn injury and its effects on elongation of hospitalization period are major economic problems that face physical therapists and other team members. The importance of this study arised from the severity of burn injury which leads to serious complications such as: delayed wound healing, risk of infection, limitation of range of motion, mal positioning, reduction of muscle power, and impairment of daily living activities. Based on the analgesic, anti-inflammatory, and anti-edema effects of laser therapy, as well as the stimulating action on tissue repair processes. This study was designed to evaluate the effects of

Laser	Mode	Wavelength (nm)	Power density (mW/ cm ²)	Time (s)	Energydensity (J/cm ²)
HeNe	Continuous	632.8	44.4	45	4
GaAs	Pulsed	904	31.7	63	4

Table I: The parameters of the two laser devices.

HeNe laser and GaAs laser on healing of burned wound as a new physical therapy method for promoting healing process of burn injury and also comparing effect of both types of laser on wound healing in burned patients.

MATERIAL AND METHODS

Subjects

This study was an open, randomized, controlled trial. 45 patients (22 male and 23 female) from the Department of Burn in OM El-Massrien hospital was engaged in this study; all participants were informed about the nature and the purpose of the study; patients were examined by physician before the study to determine inclusive and exclusive criteria. Demographic information was obtained from patient's file including age, sex, cause of burn, and total body surface area. Patients had thermal partial thickness burn injury of second degree with total burned surface area (TBSA%) 25- 40% . Their ages ranged from 20 to 40 years. All patients received equivalent nursing care. Patients were excluded if they had any disease that can affect healing process (diabetes, skin malignancy in the treated area, severe anemia, associated or inhalation injury, or post skin grafting). Patients were randomly divided into three equal groups:

Group A (HeNe) Group (First study group): This group was composed of 15 patients (7 males and 8 females) who received HeNe (manufactured by Melles Griot company LHX1) with the following technical specifications; model number :

25LHR121-230, wavelength: 632.8nm, power range: 2 mW, irradiance: E = 44.4 mW/cm².

Group B (GaAs) Group (second study group): This group was composed of 15 patients (8 males and 7 females) who received GaAs laser, obtained from the National Institute of Laser Enhanced Sciences Cairo University, model number: LS-90, wavelength: 904 nm, power range: 25 mW, irradiance: E = 31.7 mW/cm². Both laser groups received routine medical care and nursing care, as well as physical therapy program through the treatment period (laser therapy). Regardless of the two different power laser sources, the same energy density, 4 J/cm², was considered. Unification of the energy density was performed by varying irradiation times, 45s and 63s respectively for HeNe and GaAs lasers. The parameters of the two devices are shown in Table I.

Group C (control group): This group was composed of 15 patients (7 males and 8 females) who received only the same routine medical, nursing care and traditional physical therapy program.

The treatment procedure with laser was started 72 hours post-burn injury for all study groups and repeated 3 times/ week for 3 weeks. The wound surface area (WSA) was measured and pictures by digital camera were taken 72 hours after burn injury (Pre), after 10 days (Post I), and 21 days (Post II) from the beginning of treatment for all the groups of the study.

Ethical consideration

The study protocol was explained in details for each patient before the initial assessment and signed informed consent was obtained from each patient before enrollment in the study (or their families). This study was approved by the Scientific Committee of the Surgery Department and the Ethical Committee of the Faculty of Physical Therapy, Cairo University.

WSA measurement

This measurement was conducted by tracing burn surface area using the graph paper technique as reported by [9,10] in the following steps: the patient was positioned in a comfortable position with exposure of the affected limb, double sterilized transparent plastic films were placed directly (after rinsed it with antiseptic solution), flat and attached to the skin around the burn wound area with avoiding any movement and distortion of the limb margins were traced by the same investigator to establish reliability of measurements [11]. The burn wound perimeter was traced by using the film-tipped transparency marker. Three tracing of each burn wound was made at each measurement session by the same investigator to establish measurement reliability through obtaining the mean of these three measurements. After tracing, the side of the transparency film facing the ulcer was cleaned with a piece of cotton and alcohol. Carbon paper was placed over the 1-mm-squared metric graph paper. Then the traced transparency film was placed over carbon paper with a white paper in-between and transcribed the tracings onto metric graph paper.

WSA was calculated by counting the number of square millimeters on the metric graph within the wound tracing and the area was converted into cm^2 .

Photography by Using Digital Camera

Sony cyber shot S40, 4.1 mega pixels, zoom 3X optical zoom and a ruler (10cm). The light of the room was good enough to obtain clear photos in follow up. The position of the patient, the distance of photographs, the illumination, the magnification and the backgrounds were fixed for every patient in all steps of evaluation. A 10 cm ruler was included in each photograph field to allow calibration during subsequent measurement procedures.

Treatment procedures

The treatment procedure had been started 72 hours after admission for all groups, in the form of emergency and medical care support. All patients received equivalent nursing care. Cleaning of the burn was performed three times per week by nursing staff, using betadine, followed by an application of topical antimicrobial agents, and then dry dressing. Burn wound was mechanically debrided as necessary. Regular diet planned for all patients was sufficient to meet caloric, protein and vitamin requirements. Therapeutic intervention for the study was started at third day post burn for all groups.

Designed protocol for laser applications

Each patient was placed into a comfortable supported position to allow the vision of the treated area. The treatment procedure was started 72 hours post-burn. The therapist wore protective eye glasses. The probe of the HeNe and GaAs lasers was stabilized in horizontal alignment opposite to the

patient, but the beam of laser was in perpendicular direction to the burn.

The distance between the laser probe and burn was 1 cm length (non-contact) [12]. The treated area was divided into zones of equal squares ($1\text{cm}\times 1\text{cm}$). The tip of the laser source was directed perpendicularly to the target tissue for the designated time at the center of each square (grid technique) [21].

The treatment was applied 3 days per week for 21 days using the grid technique and finally the burned area was covered by sterile dressing after each application. Group (C) received only traditional physical therapy and placebo laser therapy.

All subjects received the same traditional physical therapy which included range of motion exercise (passive, active, active assisted), according to the patient need of splints followed by positioning of the affected part in the most suitable position for function and then the positions maintained by splints if needed.

Statistical analysis

Statistical analysis was performed using The Statistical Package for Social Science (SPSS). Paired T test was used to compare the dependent variable (WSA), within each group to detect level of significant. Unpaired T-test was applied to compare the dependent variable (WSA), and independent (age, sex, TBSA, causes of burn) variables between three groups to detect level of significant. P-values less than 0.05 were considered to be statistically significant.

RESULTS

Data concerning the patient demographic data (age, sex, TBSA, causes of burn) as well as WSA were collected at the beginning of the study. Follow up

evaluation of the WSA was performed after 10 days and 21 days of treatment.

Demographic and clinical characteristic of the patients:

As shown in (Table II), there were no statistical significant differences among the groups concerning general characteristics (age, sex, TBSA, or cause of burn). As well as clinical characteristics WSA (cm^2) at the beginning of the study. ($P>0.05$).

As shown in (Table III): Mean value, standard deviation and P value of WSA for group (A), group (B) and group (C) before initiation of treatment (Pre), after 10 days (Post I) and after 21 days (Post II).

Results for group (A): The mean value and standard deviation of WSA (cm^2), in group (A) before application of laser (pre) was 20.24 ± 3.93 , after 10 days (post I) was 9.16 ± 4.09 and after 21 days (post II) was 2.32 ± 2.35 . There was significant decrease in the WSA after 10 days and 3 weeks compared to initial measurement (before treatment), $p<0.05$ as shown in table (II).

Results for group (B): The mean value and standard deviation of WSA (cm^2), in group (B) at the beginning of the study (pre) was 21.44 ± 5.26 , after 10 days (post I) was 14.35 ± 3.62 and after 21 days (post II) was 6.33 ± 3.53 . There was decrease in the WSA after 10 days and 3 weeks compared to initial measurement (pre), $p<0.05$ as shown in table (II).

Results for group (C): The mean value and standard deviation of WSA (cm^2), in group (C) at the beginning of the study (pre) was 21.45 ± 4.6 , after 10 days (post I) was 18.26 ± 5.03 and after 10 days (post II) was 13.57 ± 3.7 . There was decrease in the WSA after 10 days and 3 weeks compared to initial measurement (pre), $p<0.05$ as shown in table (III).

Patient demographic data	Group (A) (n=15)	Group (B) (n=15)	Group (C) (n=15)	P- value
Age (years)	27.93±5.92	30.26±5.17	27.2±6.03	0.32*
Sex (male/ female)	7/8	8/7	6/9	0.561*
TBSA (%)	29.6±3.71	29.33±2.28	30.26 ±2.46	0.66*
Cause of burn (flam/scald)	10/5	9/6	8/7	0.75*
WSA (cm ²)	20.24±3.93	21.44±5.26	21.45±4.6	0.72*

X= Mean, SD= Standard deviation, P-value = Probability level, WSA= Wound surface area

*Non- Significant. (P >0.05)

Table II: statistical analysis of the demographic & clinical characteristics of patients among 3 groups at the beginning of the study. Results of wound surface area (cm²) for 3 groups pre, post (I) and post (II).

Group	Statistical value	Wound Surface Area (cm ²)			P-value
		Pre	Post (I)	Post (II)	
Group (A)	Mean±SD	20.24±3.93	9.16±4.09	2.32±2.35	0.001*
Group (B)	Mean±SD	21.44±5.26	14.35±3.62	6.33±3.53	0.001*
Group (C)	Mean±SD	21.45±4.6	18.26±5.03	13.57±3.7	0.001*

X= Mean, SD= Standard deviation, P-value = Probability level, WSA= Wound surface area

*Non- Significant. (P >0.05)

Table III: statistical analysis of WSA (cm²) for group (A), group (B) and group (C) at (pre), (post-I) and (post-II).

Comparing the mean values of WSA between groups (A), (B) and (C)

Comparing the mean values of WSA between group (A), group (B) and group (C) before treatment (pre), after 10 days (post I) and after 3 weeks (post II) we found that before treatment (pre), there were no significant differences between the three groups, $p > 0.05$. After 10 days (post I), and after 21 days (post II) there was a highly significant reduction in WSA in group (A) and group (B) compared to group (C) ($p < 0.05$).

HeNe is more effective in decreasing WSA and improving the photographic pictures, although the value results not significant.

In relation to photographic pictures: HeNe Group Results

Figures 1, 2 and 3 taken by using digital camera show differences in wound status and surface area in the three groups.

DISCUSSION

Wound healing is a biologically complex sequence of overlapping events and is a natural restorative response to tissue injury [13].

Delayed wound healing is continuing challenge in rehabilitation medicine despite some recent advances in understanding of its basic principles and problems in wound healing that continue to cause significant morbidity and mortality. A great number of studies have been conducted on acceleration of wound healing, attainment of normal breaking strength and prevention of keloid and scar formation by using many physical methods such as therapeutic ultrasound, laser therapy and electrical stimulation [14].

This study was designed to study and compare between the effect of two types of low intensity laser (HeNe and GaAs). The result of this study showed that, there was significant decrease in WSA in groups

(A, B), after 10 days and 3 weeks of laser treatment, compared to control group (C).

HeNe is more effective in decreasing WSA and improving the photographic pictures. These results are consistent with previous reports that have demonstrated elevation of several metabolic indices of ATP synthesis fibroblast proliferation [15, 16] and collagen synthesis, as well as increases in the biomechanical indices of tissue healing.

There is evidence in the literature that low energy laser irradiation has a therapeutic effect on wound healing. The results of our study support the observation that low energy laser irradiation positively affects wound healing. It was reported that analysis of the fibroblastic proliferation indicated that when Laser used at appropriate doses, wavelength, potency density and time of exhibition positively it influences fibroblastic proliferation and production of collagen [17].



Figure (1): The pictures representative of patients treated with HeNe laser



Fig (2): The photographic pictures for patient treated with GaAs laser: pre, (post I) and (post II).



Fig (3): The photographic pictures for patient from the control group: pre, (post I) and (post II)

Several indices of tissue repair are positively affected by laser treatment. In vivo studies and clinical reports indicated that laser therapy promotes wound healing by accelerating collagen synthesis, inflammation course, healing time and strength acquisition [18, 19].

DNA microarray technique was used to investigate the gene expression profiles of human fibroblasts irradiated by low-

intensity red light. The gene expression profiles revealed that 111 genes were regulated by the red light irradiation. Most of these genes directly or indirectly play roles in the enhancement of cell proliferation and the suppression of apoptosis 38 mitogen activated protein kinase signaling pathway and the platelet-derived growth factor signaling pathway, were found to be involved in cell growth induced by irradiation of low-

intensity red light. Several genes related to antioxidation and mitochondria energy metabolism were also found to express differentially upon irradiation [20].

LLLT has no effect until its photon absorbed, the photons have different effects on amino acids, nucleic acid bases and other groups called chromophores. The former is the basis for DNA and proteins. The latter involves porphyrins,

which are bio-organic molecules, such as hemoglobin and melanin. Porphyrins reinforce the immune function of the body through increasing serum gamma-globulin, rosette formation rate of B and T-lymphocytes and increasing phage percentage and phagocytic index of T-lymphocytes and neutrophilic leucocytes in blood. Such effect could be utilized in accelerating the healing process of wound [21].

Laser stimulation leads to increased production of ATP from ADP molecules. The basis of the study of Madrado et al., [22], which evaluated the effects of laser therapy in experimental cutaneous wound healing and concluded that a dose of 4 J/cm² was more effective to that of 8 J/cm². In addition, Hawkins and Abrahams [23, 24] reported that a dose of 5 J/cm² generated by a HeNe laser stimulates mitochondrial activity, leading to reestablishment of cellular functions, and induces proliferation and migration of fibroblasts, thus hastening wound closure. In contrast, a dose of 10 J/cm² was associated with a significant amount of cellular and molecular damage. Pereira et al [25] studied the effect of a 120 mW GaAs diode laser on fibroblasts, and concluded that a dose of 3 J/cm² stimulated fibroblast proliferation without impairing procollagen synthesis.

In two non-controlled studies conducted by Schindl et al.,1999 [26] and Kawalec et al., 2001 [27] laser therapy was administered to small sample sizes of 20 and 19 patients. Following HeNe laser therapy, given 3 times per week for a median of 12 weeks, all ulcers healed. Instead, following 8 weeks of GaAs laser treatment given once every 2 weeks, 39 ulcers healed, average wound size decreased 9.4% and bacterial count decreased 45.9%.

The study of Tawfic et. al (2001): was designed to accelerate burn wound using different laser system, such as HeNe laser with varying energy density 1, 2, 4 j/cm² as well as GaAlAs laser with varying energy density 1, 2, 4 j/cm². The result reported that laser therapy may be of value in accelerating the burn healing and HeNe Laser is more effective in healing of rat's burn than GaAlAs Laser, and the optimal dosage was 2-4 J/cm².

In agreement with outcomes of previous studies our results completely support the hypothesis that healing process of partial thickness burn is favored by low intensity (HeNe or GaAs) laser. However HeNe laser seemed more effective than GaAs, although the value results not significant. Both types of laser were safe and effective for the treatment of partial thickness thermal burn, and induces a significant decrease in WSA as demonstrated by evaluation of the wounds at 10 days and after 3 weeks.

CONCLUSIONS

It is important to develop new strategies and standardize protocols for treating burn injury which result in decrease of cost and faster time of wound healing. Both Helium Neon and Gallium Arsenide laser are useful tool in accelerating wound healing; they reduces wound surface area. HeNe is more effective in decreasing WSA and improvement in the photographic pictures.

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The title page (page 1) should include:

- A concise and informative title (capital bold font; not exceeding 120 characters)
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Each paper must be preceded by an abstract (page 2) that summarizes in no more than 250 words a brief introduction, the aim of the study, materials and methods; main results and conclusions. It shouldn't contain any reference.

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After the abstract, in the same page, a list of 4-6 keywords should be supplied for indexing purposes.

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The introduction should describe the state of the art, give a short review of pertinent literature, state the purpose of the investigation. It should be as concise as possible, without subheadings.

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The “materials and methods” section should follow the introduction and should provide enough information to enable the experiments to be reproduced.

Patients (clinical studies): typology of patients (age, sex...), criteria for enrolment in the study, etc.

Experimental model: cellular, animal, etc.

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"In the case that laser sources are considered, authors are requested to specify all the necessary technical data pertinent to the experiment(s): laser type and wavelength, emission mode (continuous, pulsed), laser power (peak and average power in case of pulsed emission), laser beam dimensions, beam intensity (Watt/cm² spot area), total energy dose on the irradiated area in a single treatment (J/cm²), duty cycle. In case of laser treatment of cultured cell models, as well as in vivo and ex vivo treatments, authors are requested to specify the dimensions of the treated region, treatment duration and timing modalities (e.g. one session, multiple sessions)."

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The discussion should be an interpretation of the results and their significance, also with reference to works by other authors. The relevance of the results in the research and clinical applications should be explained.

CONCLUSIONS

They should be concise and effective, with reference to possible involvements in the future.

ACKNOWLEDGEMENTS

Concise acknowledgements may be addressed to persons, public and private organizations, companies.

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Reference should be made only to articles that are published or in press. The list of references should only include papers that are cited in the text. They must be progressively numbered (in square brackets) in the order in which they appear in the text and listed at the end of the paper in numerical order. Each reference should cite article title and the authors. Abbreviations of journal titles should follow those used in Index Medicus.

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Reference to a journal publication:

1. Boyle WJ, Simonet WS, Lacey DL. Osteoclast differentiation and activation. *Nature*, 2003, 423: 337-342.

Reference to a book:

2. Michaeli W. *Extrusion Dies*. Hanser Publishers, Munich, Vienna, New York, 1984.

Reference to a chapter in an edited book:

3. Gmünder FK, Cogoli A. Effect of space flight on lymphocyte function and immunity. In: Fregly MJ, Blatteis CM, eds. *Handbook of Physiology*. Oxford:University Press, 1996, vol. 2, pp 799-813.

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