

Effects of High Power Laser Therapy on Patients with Chronic Discogenic Sciatica: A Randomized Clinical Trial.

Abstract

Back ground: Sciatica is a common clinical condition that can be extremely painful, disabling and life changing.

Objectives: The purpose of this study was to determine the influence of high power laser therapy on pain, degree of straight leg raise, six meter walk test and electrophysiological studies in patients with chronic discogenic sciatica.

Methods: Thirty-six male patients suffering from chronic unilateral sciatica due to lumbar disc herniation at L5-S1 was included in this study. The patients were assigned randomly into two equal groups, control group (G1) and study group (G2). The patients in control group (G1) received designed physical therapy program which consisted of electrotherapy and exercises whereas, the patients in the study group (G2) received the same physical therapy program as G1 in addition to, high power laser therapy. Clinical and electrophysiological studies (Hoffmann reflex) were used for assessment. The clinical assessment of discogenic sciatica consisted of assessing pain intensity through numerical pain rating scale (NPRS) and measuring degree of hip flexion during straight leg raise (SLR) and six meter walk test. Assessment was done before and after four weeks of treatment (end of treatment) for both groups.

Results: Results proved that post treatment; there was significant decrease in pain intensity and latency of Hoffmann reflex (H-reflex) in both groups. There was significant improvement of degree of hip flexion during straight leg raise (SLR), six meter walk test and amplitude of H-reflex in both group. There was a significant decrease in VAS and H reflex latency of study group compared with that of control group post treatment ($p < 0.01$). Also, there was a significant increase in 6MWD, SLR and H reflex amplitude of study group compared with that of control group post treatment ($p < 0.01$).

Conclusion: It can be concluded that suggested high power laser therapy is an effective method in treatment of patients with chronic discogenic sciatica.

Key words: Discogenic sciatica; Lumbar disc herniation; High power laser therapy; Hoffmann reflex; Numerical pain rating scale; Straight leg raise and Six meter walk test.

Introduction

Comment [dd1]: Include settings of study
Add duration of study
Add protocols of intervention

Comment [dd2]: Add statistics with pre to post measurements

Sciatica is well-defined as radicular leg pain localized to the dermatome of a pathologically affected **nerveroot**. Discogenic sciatica is induced by lumbar **discherniation** (LDH) and may be accompanied by **neurologicaldeficits**, such as leg pain, leg paresthesia, disability, and low back pain^{1,2}. The estimated prevalence of **sciaticaranges** from 1.2 to 43% in various regions¹. Discogenicsciatica, which accounts for nearly 90% of sciatica, is a **main reason mainreason** of morbidity; furthermore, it has a **significanteffecton** the economy due to the **highcosts** of health care and loss of work^{3,4}.

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The term LASER is an acronym for Light Amplification by Stimulated Emission of Radiation. It is a device that produces coherent, collimated and monochromatic light through a process of optical amplification based on the stimulated emission of electromagnetic radiation. Laser therapy uses light within the red and infrared parts of the electromagnetic spectrum. Treatment with class 3B lasers (with a power not exceeding 500 mW) is called low intensity power therapy (LPLT), whereas the use of therapeutic lasers with a much higher power (class 4 lasers) is called high power laser therapy (HPLT)⁵.

The high-intensity laser therapy (HILT), which involves **laserradiation** with high-intensity, is a kind of novel, powerful and painless mode and has significant effects on relieving pain. The HILT possesses its own photomechanical, photothermal, and the photo-chemical properties, and it has many therapeutic effects, containing anti-edema, analgesic and the biological stimulation⁶⁻¹¹. Another benefit of HILT, in particular the neodymium-doped yttrium aluminum garnet laser, is its higher power and penetration depth to the deep tissues¹². The application of HILT obviously decreases the degrees of pain in the chronic and acute diseases, for instance, carpal tunnel syndrome, chronic osteoarthritis, and rheumatoid arthritis, shoulder pain, the injuries of knee, fibromyalgia, as well as the pain after operation^{7,13-16}.

Comment [dd9]: Spelling mistake

There is no consensus in literature on the pulse power, application time, frequency and the dose of energy of laser therapy for the patients. At present, there are a few investigations on the effects of HPLT treatment on the lateral epicondylitis, frozen shoulder, and cervical radiculopathy, knee arthritis as well as post-mastectomy. However, in the chronic lumbar disc herniation, the literature on the treatment of HPLT is limited. Therefore, we conducted this research for the assessment of safety and efficiency of HPLT in patients with chronic discogenic sciatica.

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Materials and methods

Design:

Single blinded **randomized clinical trial**. This study was conducted at the outpatient clinic of faculty of physical therapy, Cairo University and the outpatient clinic of faculty of physical therapy Badr University and outpatient clinic of faculty of physical therapy, Cairo University. The protocol of this research was accepted by the ethical committee of the physical therapy faculty

Comment [dd11]: Clinical trial must be registered please attach clinical trial registry number

Randomization:

After inclusion in the study, every participant signed an informed consent. Patients were randomly assigned into two groups using random generator (www.randomization.com). The randomized list was done by a research assistant not involved in the study, and the allocation to one of the two groups was revealed to the patients at the time of confirmation of enrolment. The participants were assigned randomly into two equal groups: Control group (G1) and study group (G2). The participants in control group (G1) were treated by designed physical therapy program which consisted of electrotherapy (TENS and ultrasound) and therapeutic exercises (spinal extension exercises). The participants in study group (G2) were treated by the same physical therapy program and high power laser therapy (HPLT). Three sessions per week for one month.

Comment [dd12]: Informed consent and institutional review board certificate must be attached

Patients

Thirty-six male patients suffering from unilateral sciatica results from lumbar (L5-S1) disc herniation with pain for more than three months. The age of patients ranged from 22 to 44 years. Each patient was subjected to physical, neurological examination (motor assessment, sensory assessment) and electrophysiological assessment (H-reflex). Magnetic resonance imaging (MRI) was done to detect the level of lesion. Patients with the history of severe osteoporosis or lumbar injections in past 4 weeks, and the patients with acute trauma, inflammatory pain, lumbar instability, lumbar surgery and neurological disorders, patients with severe diseases and severe or uncontrolled cardiovascular, Other cases of sciatica as ligamentum flavum hyperatrophy, osteophyte formation or stenosis, as well as the patients with acute onset of pain (pain less than three months) and Patients with bilateral radiating pain were excluded.

Outcome measures and assessment procedures

- **A visual analog scale (VAS)** was used to measure pain intensity before and after therapy. Using a 10-cm VAS, patients have been asked to rate their wrist pain in the previous few days. Patients select the severity of their pain via putting a sign on a line, with 0 (no agony) and 10 (the worst pain imaginable) indicating the endpoints of the VAS line. VAS is a valid and accurate measure for assessing chronic pain (interclass correlation coefficient (ICC) = 0.87).

- **Range of motion assessment of straight leg raise (SLR)** using uni-level inclinometer (ISOMED). From supine lying position on a flat plinth towards the side of the examiner, with the neck in neutral position. The examiner places one hand under the Achilles tendon and the other hand held the inclinometer. The inclinometer must be held in a vertical position during the SLR test by the examiner's hand between the index and the middle fingers and center of inclinometer was positioned on the lower third of tibia. The leg was lifted perpendicular to the point at which the patient expressed the perception of pain and the therapist prevented any knee flexion.

- **Performance and Scoring of the 6 meter walk test (6WT):** Participating subjects were instructed on how to download and install the free 6WT app, using standardized information sheets in plain language and augmented by figures/illustrations. Those sheets also contained instructions on the optimal testing environment, being a sufficiently long, straight, and relatively level path without high-rises (or other objects blocking the GPS signal) and without obstacles

(such as red traffic lights), in agreement with prior research. A person and contact number were provided to help resolve questions, should any occur.

- **Hoffmann reflex (H-reflex)** was recorded from soleus muscle (TOENNES Neuro Screen plus 1.70C), via stimulation of the tibial nerve using one ms pulse at 0.2 pps of H-max. For each subject, the peak -to-peak amplitude of the maximum obtained H-reflex and the latencies of four separated traces were averaged for both lower extremities. The soleus H-reflex is mainly by the S1 spinal segment. It was elicited by stimulation of the tibial nerve at the popliteal fossa. The patient was positioned in prone lying with the head in mid position. The skin over the calf area and the popliteal fossa behind the knee was cleaned by alcohol. The recording electrodes were attached by tape. Conductive gel was used for electrodes. Active (black) recording electrode was placed two cm distal to the bifurcation of the gastrocnemius in the midline and in line with Achilles tendon. Reference (red) recording electrode was placed three cm distal to the active electrode. Ground electrode was placed on gastrocnemius between recording electrodes and stimulating electrodes. The recording electrode and the ground electrode were connected to the preamplifier and the differential amplifier unit of the electromyography (EMG) unit. The stimulating electrode was placed longitudinally in the middle of the popliteal fossa with the active electrode (cathode) proximally placed and the anode distally placed. The patient was asked to fix patient's head, legs, or arms during the test. The intensity of electrical stimulation was started by the lower amplitude and increased gradually until planter flexion of the foot appeared in response to electrical stimulation. Increase the stimulus intensity until the maximum amplitude of the H-reflex (H maximum) was reached. Four repetitive H-maximums were recorded in the lower extremity (affected). The average was calculated. Procedure was repeated for the other lower extremity (sound) to compare amplitudes and latencies and to record side to side difference of H-reflex latencies. Electrical stimulation parameters were: stimulus duration: 0.5-1 ms, stimulus rate: 1 pulse every 5 seconds (0.2 pps) and stimulus intensity: subthreshold to the action potentials.

Treatment procedures

High power laser therapy

A Zimmer Opton pro, integrated High-power class IV laser device (serial N: 15200013306 & REF: 4682, made in Germany, manufactured by Zimmer MedizinSysteme), was used for treatment. Zimmer Opton Pro emits energy in the infrared spectrum to provide topical heating for the purpose of elevating the tissue temperature. The simultaneous application of laser light of two wavelengths (810 and 980nm) opens up a wide range of therapy options for the user.

The subject was putted in prone, exposing the treatment area and pillows kept under the head and legs for the relaxation; the lumbar area was scrubbed with an alcohol soaked gauze pad. Both the therapist and the participant wore protective goggles for safety during the treatment time.

The characteristics of laser beam included: wave length 904 nm; frequency 3000 Hz; power output 25 mW; spot size 1 cm². Application mode stationary in contact with skin, anatomical site local 4 points, 2 cm laterally from spinous process of involved and next distal spinal segment. The doses were chosen according to recommended anti-inflammatory doses for Gallium-Arsenide (GaAs) lasers by the World Association of Laser Therapy (WALT) 30 and energies that were used in clinical trials for lumbar spine pain.

Designed physical therapy treatment:

It consisted of electrotherapy (transcutaneous electrical stimulation and ultrasound) and back extension exercises. Transcutaneous electrical nerve stimulation (TENS) was applied for 20 minutes, three times per week for one month. The patient lied prone and electrodes were placed one electrode on each side of low back area. Parameters of TENS were train of high frequency (100-120 Hz), pulse width or pulse duration ranged from 200- 300 msec and amplitude or intensity according to the patient's tolerance. Ultrasound was used for five minutes with continuous mode on low back area. Frequency was 1 MHz and power was 1.5 watt / cm². Acoustic gel was used as occupying medium. The program of therapeutic exercises consisted of upper and lower back exercises. Each exercise was repeated from ten to fifteen times, five repetitions in three sets with rest one to two minutes between the sets. The repetition of each exercise varied according to the physical ability of each patient.

Sample size calculation

Sample size calculation was performed using G*POWER statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany) based on data of H reflex amplitude from pilot study performed on 5 subjects in each group. The required sample size for this study was 18 subjects per group. Calculations were made using $\alpha=0.05$, $\beta=0.2$ and effect size = 0.98 and allocation ratio $N2/N1 = 1$.

Statistical analysis

Unpaired t-test was conducted for comparison of subject characteristics between groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to ensure the homogeneity between groups. Mixed design MANOVA was performed to compare within and between groups effects on VAS, 6MWD, SLR and H reflex. Post-hoc tests using the Bonferroni correction were carried out for subsequent multiple comparison. The level of significance for all statistical tests was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

- Results

- Subject characteristics:

Table (1) showed the subject characteristics of the study and control groups. There was no significant difference between groups in age, weight, height and BMI ($p > 0.05$).

Table 1. Comparison of subject characteristics between study and control groups:

	Mean \pm SD		MD	t- value	p-value
	Study group	Control group			
Age (years)	33.88 \pm 7.23	35.27 \pm 6.72	-1.39	-0.59	0.55
Weight (kg)	82.77 \pm 6.03	83.27 \pm 5.34	-0.5	-0.26	0.79
Height (cm)	177.11 \pm 3.69	176.5 \pm 3.79	0.61	0.49	0.62
BMI (kg/m ²)	26.31 \pm 0.92	26.74 \pm 1.82	-0.43	-0.88	0.38

SD, Standard deviation; MD, Mean difference; p-value, level of significance

Effect of treatment on VAS, 6MWD, SLR and H reflex:

There was a significant interaction of treatment and time ($F_{(5,30)} = 26.08$, $p = 0.001$, $\eta^2 = 0.81$).

There was a significant main effect of time ($F_{(5,30)} = 834.76$, $p = 0.001$, $\eta^2 = 0.99$). There was no significant main effect of treatment ($F_{(5,30)} = 1.64$, $p = 0.17$, $\eta^2 = 0.21$).

- Within group comparison

There was a significant decrease in VAS and a significant increase in 6MWD and SLR of the study and control groups post treatment compared with that pre treatment ($p < 0.001$). The percent of change of VAS, 6MWD and SLR of study group was 57.38, 80.85 and 48.1% respectively and that of control group was 47.05, 53.93 and 32.34% respectively. (table 2).

There was a significant increase in H reflex amplitude and a significant decrease in H reflex latency of the study and control groups post treatment compared with that pre treatment ($p < 0.001$). The percent of change of H reflex amplitude and latency of study group was 190.4 and 13.39% respectively and that of control group was 97.26 and 9.44% respectively. (table 3).

- Between groups comparison:

There was no significant difference between groups pre-treatment ($p > 0.05$). There was a significant decrease in VAS and H reflex latency of study group compared with that of control group post treatment ($p < 0.01$). Also, there was a significant increase in 6MWD, SLR and H

reflex amplitude of study group compared with that of control group post treatment ($p < 0.01$). (table 2,3).

Table 2. Mean VAS, 6MWD and SLR pre and post treatment of study and control groups:

	Study group	Control group	MD (95% CI)	p- value
	Mean \pm SD	Mean \pm SD		
VAS				
Pre treatment	6.5 \pm 0.85	6.61 \pm 0.91	-0.11 (-0.71: 0.49)	0.71
Post treatment	2.77 \pm 0.64	3.5 \pm 0.85	-0.73 (-1.23: -0.21)	0.007
MD (95% CI)	3.73 (3.47: 3.97)	3.11 (2.85: 3.36)		
% of change	57.38	47.05		
	<i>p = 0.001</i>	<i>p = 0.001</i>		
6MWD (meters)				
Pre treatment	239.05 \pm 30.72	247.61 \pm 39.62	-8.56 (-32.57: 15.46)	0.47
Post treatment	432.33 \pm 54.02	381.16 \pm 46.93	51.17 (16.88: 85.44)	0.005
MD (95% CI)	-193.28 (-215.32: -171.23)	-133.55 (-155.59: -111.51)		
% of change	80.85	53.93		
	<i>p = 0.001</i>	<i>p = 0.001</i>		
SLR				
Pre treatment	45.61 \pm 7.78	45.67 \pm 9.06	-0.06 (-5.77: 5.66)	0.98
Post treatment	67.55 \pm 7.02	60.44 \pm 8.11	7.11 (1.96: 12.25)	0.008
MD (95% CI)	-21.94 (-23.65: -20.23)	-14.77 (-16.49: -13.07)		
% of change	48.1	32.34		
	<i>p = 0.001</i>	<i>p = 0.001</i>		

SD, Standard deviation; MD, Mean difference; CI, Confidence interval; p-value, Level of significance

Table 3. Mean H reflex amplitude and latency pre and post treatment of study and control groups:

	Study group	Control group	MD (95% CI)	p- value
	Mean \pm SD	Mean \pm SD		
H reflex amplitude (mV)				
Pre treatment	1.98 \pm 0.79	2.19 \pm 1.18	-0.21 (-0.89: 0.47)	0.53
Post treatment	5.75 \pm 0.85	4.32 \pm 1.45	1.43 (0.62: 2.24)	0.001
MD (95% CI)	-3.77 (-4.05: -3.48)	-2.13 (-2.41: -1.84)		
% of change	190.4	97.26		
	<i>p = 0.001</i>	<i>p = 0.001</i>		
H reflex latency (ms)				
Pre treatment	33.67 \pm 1.44	34.1 \pm 1.69	-0.43 (-1.49: 0.63)	0.42
Post treatment	29.16 \pm 1.82	30.88 \pm 1.41	-1.72 (-2.82: -0.61)	0.003
MD (95% CI)	4.51 (4: 5.01)	3.22 (2.71: 3.72)		
% of change	13.39	9.44		
	<i>p = 0.001</i>	<i>p = 0.001</i>		

SD, Standard deviation; MD, Mean difference; CI, Confidence interval; p-value, Level of significance

Discussion

This come in consistency with the work of **Monici et al.**¹⁷ who concluded that high intensity laser therapy has been used for a wide range of painful conditions, the efficacy of the pulsed Nd:YAG laser has been proven in the treatment of many musculoskeletal diseases and it is believed to have anti-inflammatory, anti-edema, analgesic, and reparative effects.

The improvement in this study may be attributed to the analgesic effect of HPLT is based on different mechanisms of action, including its ability to slow the transmission of the pain stimulus and to increase the production of morphine-mimetic substances in the body¹⁸. In addition, it may have a direct effect on nerve structures, which could increase the speed of recovery from conduction block or inhibit A δ - and C-fiber transmission¹⁹. The treatment also increases blood flow, vascular permeability, and cell metabolism²⁰.

The HILT pain control is because of several mechanisms, as the discharge of endogenous opioids, for example, the β endorphins in the central nervous system is expanded by HILT therapy and these could diminish the pain sensations centrally, while the substance P which

sensitizes pain transmitting neurons in the peripheral nervous system, that leads to hyperalgesia, however, the laser therapy lead to diminish the substance P discharge through the peripheral receptors^{2,22}.

More recently, the pulsed neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, a form of high-intensity laser therapy (HILT), was introduced to the field of physical therapy. This laser is considered to be a non-painful and noninvasive therapeutic modality. It is able to stimulate areas that are difficult to reach with the low-power laser, such as the large and/or deep joints²³. The use of the pulsed Nd:YAG laser has been increasing, with patients reporting significant pain reduction²⁴. Studies have documented the anti-inflammatory, anti-oedematous, and analgesic effects of the Nd:YAG laser, justifying its use in patients with pain issues²⁵.

Our result showed improvement in the exercise, laser group and this come in agreement with **Alayat et al.**²⁶ who showed that exercise therapy is clinically able to decrease pain, increase ROM, and improve function. It is proving to be economical, practical, and safe to emphasize the importance of an active exercise program in rehabilitation aimed at functional recovery. The combined use of HILT combined with exercise is more effective and has a more prolonged effect than sham laser with exercise or laser alone in increasing lumbar ROM and in decreasing pain and functional disability, with effects lasting up to 3 months.

A study by **Kolu et al.**²⁷ revealed that using HILT in chronic lumbar radiculopathy patients, was effective treatment method as it decreased the VAS and Oswestry Disability Index scores four weeks after the treatment sessions, likewise the findings of the study by **Song et al**²² showed that the HILT treatment for back and neck pain significantly diminished pain and disability scores.

Comment [dd13]: Whole the discussion part is needed to rewrite because author did not compare the results of study with national and international resources.

Conclusion

The results of this study show that the high power laser therapy is effective in reducing lumbar and legpain without side effects in patients with chronic discogenic sciatica.

Limitations:

Small number of patients because of economic reasons and the lack of evaluation of long term results.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is

absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References

1. Konstantinou K, Dunn KM. Sciatica: review of epidemiological studies and prevalence estimates. *Spine*. 2008; 33(22): 2464–2472.
2. Ergun T, Lakadamyali H. CT and MRI in the evaluation of extraspinal sciatica. *Brit J Radio*. 2010; 83(993):791–803.
3. Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *Spine J*. 2008; 8(1): 8–20.
4. Asche CV, Kirkness CS, McAdam-Marx C, Fritz JM. The societal costs of low back pain: data published between 2001 and 2007. *J Pain and Palli CarePharma*. 2007; 21(4): 25–33.
5. Santamato A, Solfrizzi V, Panza F, Tondi G, Frisardi V, Leggin, BG, et al. Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment of people with subacromial impingement syndrome: a randomized clinical trial. *Phys Ther*. 2009; 89(7): 643-652.
6. Boyraz I, Yildiz A, Koc B. Comparison of high-intensity laser therapy and ultrasound treatment in the patients with lumbar discopathy. *Biomed Res Int*. 2015;2015:304328. doi: 10.1155/2015/304328.
7. Fiore P, Panza F, Cassatella G³
8. Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment of low back pain: a randomized controlled trial. *Eur J Phys Rehabil Med*. 2011;47:367–73.
9. Venosa M, Romanini E, Padua R, et al. Comparison of high-intensity laser therapy and combination of ultrasound treatment and transcutaneous nerve stimulation in patients with cervical spondylosis: a randomized controlled trial. *Lasers Med Sci*. 2019;34:947–53.
10. Kolu E, Buyukavci R, Akturk S, et al. Comparison of high-intensity laser therapy and combination of transcutaneous nerve stimulation and ultrasound treatment in patients with chronic lumbar radiculopathy: a randomized single-blind study. *Pak J Med Sci*. 2018;34:530–4.

11. Alayat MSM, Aly THA, Elsayed AEM, et al. Efficacy of pulsed Nd:YAG laser in the treatment of patients with knee osteoarthritis: a randomized controlled trial. *Lasers Med Sci* 2017;32:503–11.
12. Santamato A, Solfrizzi V, Panza F, et al. Short-term effects of high intensity laser therapy versus ultrasound therapy in the treatment of people with subacromial impingement syndrome: a randomized clinical trial. *Phys Ther* 2009;89:643–52.
13. Zielińska P, Nicpoń J, Kielbowicz Z, et al. Effects of high intensity laser therapy in the treatment of tendon and ligament injuries in performance horses. *Animals (Basel)* 2020;10:E1327.
14. Qaseem A, Wilt TJ, McLean RM, et al. Clinical Guidelines Committee of the American College of Physicians. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2017;166:514–30.
15. Glazov G, Yelland M, Emery J. Low-level laser therapy for chronic nonspecific low back pain: a meta-analysis of randomised controlled trials. *Acupunct Med* 2016;34:328–41.
16. Huang Z, Ma J, Chen J, et al. The effectiveness of low-level laser therapy for nonspecific chronic low back pain: a systematic review and meta-analysis. *Arthritis Res Ther* 2015;17:360.
17. Nambi G, Kamal W, Es S, et al. Spinal manipulation plus laser therapy versus laser therapy alone in the treatment of chronic non-specific low back pain: a randomized controlled study. *Eur J Phys Rehabil Med* 2018;54:880–9.
18. Monici M, Cialdai F, Fusi F, Romano G, Pratesi R. Effects of pulsed Nd:YAG laser at molecular and cellular level. A study on the basis of Hiltterapia. *Energy for Health; Int J Information Scientific Culture*. 2009; 3:26–33
19. Zati A, Valent A. Physical therapy: new technologies in rehabilitation medicine Ed Minerva Medica. 2006:162–185.
20. Chow R, Armati P, Laakso EL, Bjordal JM, Baxter GD. Inhibitory effects of laser irradiation on peripheral mammalian nerves and relevance to analgesic effects: a systematic review. *Photomed Laser Surg*. 2011; 29(6):365–381.
21. Kujawa J, Zavadnik L, Zavadnik I, Buko V, Lapshyna A, Bryszewska M. Effect of low-intensity (3.75–25 J/cm²) near-infrared (810 nm) laser radiation on red blood cell ATPase activities and membrane structure. *J Clin Laser Med Surg*. 2004; 22(2):111–117.
22. Clijisen R, Brunner A, Barbero M, Clarys P, Taeymans J. Effects of low-level laser therapy on pain in patients with musculoskeletal disorders—a systematic review and meta-analysis. *Eur J Phys Rehabil Med*. 2017; 53:603–613.
23. Song HJ, Seo H-J, Lee Y, Kim SK. Effectiveness of high-intensity laser therapy in the treatment of musculoskeletal disorders: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2018;97:e13126.
24. Santamato A, Solfrizzi V, Panza F, Tondi G, Frisardi V, Leggin BG, Ranieri M, Fiore P. Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment

- of people with subacromial impingement syndrome: a randomized clinical trial. *Phys Ther.* 2009; 89(7):643–52
25. Viliani T, Ricci E, Mangone G, Graziani C, Pasquetti P. Effects of Hilterapia vs. Viscosupplementation in knee osteoarthritis patients: a randomized controlled clinical trial. *Energy for Health. Int j inform scien cul.* 2009; (3): 14–17.
26. Saggini R, Bellomo RG, Cancelli F. Hilterapia and chronic ankle pain syndromes. Abstract from *Energy for Health. Int j inform scien cul.* 2009; 3 (3):22–25: 38.
27. Alayat MS, Atya AM, Ali MM, Shosha TM. Long-term effect of high-intensity laser therapy in the treatment of patients with chronic low back pain: a randomized blinded placebo-controlled trial. *Lasers Med Sci.* 2014;29(3):1065-73. doi: 10.1007/s10103-013-1472-5.
28. Kolu E, Buyukavci R, Akturk S, Eren F, Ersoy Y. Comparison of high-intensity laser therapy and combination of transcutaneous nerve stimulation and ultrasound treatment in patients with chronic lumbar radiculopathy: A randomized single-blind study. *Pak J Med Sci.*2018; 34:530-534

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