Clinical science

APPLICATION OF HIGH-INTENSITY LASER IN PAIN TREATMENT OF PATIENTS WITH KNEE OSTEOARTHRITIS

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Citation: Koevska V, Dimitrova E, Mitrevska B, Savevska C, Gjerkaroska-Savevska M, Goccevska M, Kalcovska B. Application of high-intensity laser in pain treatment of patients with knee osteoarthritis. Arch Phy Health 2021; 13(2):1-13.
donline:10.3869/aph.2021.6008

Key words: high-intensity laser, low-intensity laser, knee osteoarthritis, VAS scale

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Received: 19-Jun-2021; Revised: 26-Jul-2021; Accepted: 7-Aug-2021; Published: 30-Aug-2021

Abstract

Osteoarthritis is a rheumatic disease characterized by degeneration and decay of cartilage in the joints. As the disease worsens, the joint space narrows causing numbness and pain, which often impairs movement. In addition to pharmacological therapy, low-intensity laser (LILT), high-intensity laser (HILT) and exercise are used to treat osteoarthritis (OA) of the knee. HILT is a new modality in our country and the experience from its application is small, especially in the treatment of OA of the knee. Aims of the paper was to compare the effect of HILT with LILT in the treatment of OA of the knee. Material and methods: This was a randomized comparative unilateral blind study involving 72 patients divided into two groups. The first group was treated with HILT, the second group treated with LILT. Outcome measure was the visual analogue scale (VAS) for pain, which was made on the first and tenth day of treatment. Statistical significance was defined as p < 0.05. Results: We found a significant difference between the two groups in terms of VAS score after 10 therapies in favor to a significantly lower score, that is, less pain in the HILT group (p = 0.0055). The comparison of the VAS score between the two times in the two groups separately showed that in both, the HILT and the LILT groups, the VAS score after 10 days of therapy was significantly lower compared to that at 0 time, for consequently p = 0.0001. Conclusion: Treatment with HILT and LILT significantly reduces pain and stiffness in patients with OA. Patients treated with HILT had better results, i.e., had a significant reduction in pain than patients treated with LILT. HILT was more effective than LILT.

Извадок

Остеоартрит е ревматолошко забољување које се карактеризира со депеноизација и распад на роговицата во зглобовите. Сопственото помеѓу болеста и пробитото пространство на зглобот често го нарушува движењето. Освен фармаколошката терапија, во лекувањето на остеоартритот (ОА) на коленото се применува нискоинтензивен ласер (НИЛТ), високоинтензивен ласер (ВИЛТ) и вежби. ВИЛТ е нов модел во нашата земја и искуството од неговата примена е мал, особено во лекувањето на ОА на коленото. Цел на трудот е да се спореди ефектот на ВИЛТ во однос на НИЛТ во лекувањето на ОА на коленото. Извабот во однос на НИЛТ има значајно намалување на болката, а ВИЛТ ги добива значајно по-добри резултати. Коишто постои статистичка значајност помеѓу двата групи со VAS скорот по 10 терапии за HILT против ЛИЛТ (p=0.0055). Споредбата на VAS скорот помеѓу двата време во двата групи со еднаков период од 10 денови покажа дека уште по веднашна терапија биле значајни разлики помеѓу ВИЛТ и ЛИЛТ. Точеното анализирање на времето за консеквативно p=0.0001 залева дека ВИЛТ биле значајно по-добри од ЛИЛТ.
Introduction

Osteoarthritis (OA) is a very common cause of chronic musculoskeletal pain and disability in the adult population. In fact, all people over 60 years have some degenerative changes in their joints; 70-85% of them have signs and symptoms such as pain and short-term morning stiffness. One of the most common forms of osteoarthritis found in clinical practice is osteoarthritis of the knee (OAK). Radiographic evidence of OAK is present in about 30% of men and women over the age of 65\(^1\).

Pain and functional limitations lead to a reduction in quality of life and reduced participation in social and societal activities\(^2\). Osteoarthritis of the knee is characterized by degeneration and disintegration of the cartilage of the joint which over time leads to narrowing of the joint space. The ligaments and surrounding tendons may be affected, and bone growths may develop, or these-called osteophytes. Pain, morning stiffness, and limited knee mobility are characteristic symptoms of OAK. Over time, typical deformities, such as varus or valgus may develop. Pain occurs due to changes in the synovial membrane, bone microfractures in the subchondral bone, mechanical irritation from osteophytes, and involvement of extraarticular structures of the knee such as bursitis, tendinitis, entesopathy, and enthesitis and eye spasm. Last but not least, pain is influenced by psychological and social factors\(^3\).

Analgesics, nonsteroidal anti-rheumatic drugs, glucosamine sulfate, and chondroitin sulfate are recommended to reduce pain and improve functional ability. So far, several physical modalities such as tension, low-intensity laser and therapeutic ultrasound have been shown to be effective in treating OAK pain\(^4,5,6\).

Several recent studies have shown results where low-intensity laser therapy (LILT) reduces pain in patients with OAK\(^7,8,9,10\). High-intensity laser is a relatively new non-invasive physical modality in the treatment of OAK. In 2020, several reviews of research on the effectiveness of high-intensity laser therapy (HILT) in the treatment of pain were published. In the conclusion, the authors commented that in the future more research is needed with a larger sample of patients\(^11,12\). The results of several randomized trials of patients showed a significant reduction in pain and improvement in physical function in OAK\(^13,14\). LILT has a biostimulatory effect. It occurs primarily locally in tissues that have absorbed the laser beam. Its main action is to accelerate the regeneration of damaged and diseased tissues, reduces swelling and pain and has an anti-inflammatory effect. The advantage of these lasers is their minimal thermal effect\(^15\).

In Ray M.’s review, several studies from 1980-2017 were analyzed examining the impact of laser therapy on both HILT and LILT in animal models. The laser has been shown to have a bistimulatory effect on cartilage and surrounding muscle and ligament tissue in joints as well as a positive effect on pathoanatomical changes in OA. It has also improved symptoms in this disease along with functioning, particularly emphasizing the HILT effects\(^16\).

High-intensity lasers also have a thermal and mechanical effect and
induce an electromagnetic field, as well as photoelectric, electrochemical, and other changes in exposed tissues. The advantage of HILT is that by increasing power the depth of penetration is increased, and thus the effects in deep structures, despite the presence of regression of the quantity and quality (coherence, polarization) of light electromagnetic energy\(^{17,18}\). HILT in the tissue causes a photochemical effect, such as increased oxygenation in the mitochondria and formation of ATP, which leads to an increased absorption of edema by increasing metabolism and microcirculation\(^{19}\).

A systematic search of PubMed, SAGE, HINARI databases showed that a small number of studies have compared the impact of HILT and LILT on pain and physical functioning in patients with OAK. So far, in our country no comparative study of the impact of HILT and LILT in patients with osteoarthritis of the knee has been conducted. This is a motive to conduct research in our country, which results would contribute to a better and higher quality treatment of patients with knee OA and enable better quality of life. The results of the research would help to establish protocols for treatment of OA with physical therapy.

The aim of this study was to compare the effect of HILT and LILT in reducing pain in OAK.

**Material and methods**

This was one-sided blind randomized comparative study, conducted at the University Clinic for Physical Therapy and Rehabilitation in Skopje. The study included 72 patients who had previously been diagnosed with osteoarthritis of the knee based on the clinical picture and X-ray.

Inclusion criteria: patients with pain due to osteoarthritis of the knee no longer than 3 months.

Exclusion criteria: application of corticosteroids and hyaluronic acid in the last 3 months, malignant diseases, fractures, tendon injury, meniscus, ligament, diseases of the hip and ankle, operated knee, rheumatoid arthritis, diseases with contraindications to laser therapy, personal reasons.

Patients were assigned into two groups.

1. The first group consisted of patients receiving a high-intensity laser therapy

2. The second group consisted of patients receiving a low-intensity laser therapy.

Patients in both groups received 10 sessions of laser therapy. They were monitored for one month, during which period two controls were performed. The first control was after 10 sessions of treatment, and the second control was at the end of the 30 days follow-up.

A visual analog scale (VAS) was used to assess pain. It is a one-dimensional measure of pain intensity (0-100 mm), used in different adult populations, including those with rheumatic diseases (20). A higher result indicates a greater intensity of pain. We noted the intensity of pain as 0 if there was no pain (0-4 mm), 1 for mild pain (5-44 mm), 2 for moderate pain (45-74 mm) and 3 severe pain (75-100 mm).\(^{21}\). The pain assessment was made at the beginning and 10 days after the treatment of the patient. Assessment of physical function, stiffness, and
knee pain was determined by the WOMAC index (or Western Ontario and McMaster Universities Osteoarthritis Index). The index contains 24 questions, 5 related to pain, 2 to stiffness and 17 to physical function. It can be used to monitor the course of the disease or to determine the effectiveness of various interventions (pharmacological, surgical, physiotherapy, etc.)^{22}.

**High-Intensity Laser Treatment Protocol**

For high-intensity laser therapy, a VIKARE electro-medical device of Italian production was used with a power of 4-8 W. The application uses a standardized protocol presented in the device, every day, for a total of 10 days. The patient receives 8.00 J / cm² per one session, for a period of 10 minutes. The patient lies in a supine position with a knee flexion of 30°. The application of laser radiation is by scanning transversally and longitudinally on the anterior, medial and lateral side of the knee joint with special emphasis on the femoral and tibial epicondyle^{23}. 

**Low-Intensity Laser Treatment Protocol**

For low-frequency laser treatment, Eco Medico Laser device of Electronic Design, Ser.Nº1116 made in Serbia was used. A standardized protocol for application presented in the device was used. The application dose is 5J / cm², with a power of 200Hz. The patient lies in a supine position, with a knee flexion of 30°. Knee skin is cleansed with alcohol. The application is performed with a probe at acupuncture-trigger painful points on the medial, anterior and lateral side of the knee, a total of 14 points. Each point takes a third of 25 seconds, the total duration of one application is 6 minutes. The patient is treated daily, with a weekend break, receiving 10 sessions in a 2-week-period. The patient and the doctor wear goggles during the application of LILT and HILT. The data obtained during the study were statistically analyzed using the SPSS software package, version 22.0 for Windows (SPSS, Chicago, IL, USA). A significance level of p <0.05 was used to determine the statistical significance.

**Results**

The distribution of patients by gender in the HILT and LILT groups showed representation of 23 (63.89%) vs 31 (86.11%) women, and 13 (36.11%) vs 5 (13.89%) men, respectively. We observed a significantly higher proportion of male patients in the group treated with HILT (p = 0.0294) (Table 1). 

The mean age of patients in the HILT and LILT groups was 61.36 ± 8.14 vs 60.36 ± 7.45 without a significant difference between the two groups (p = 0.7105). The proportion of patients in the age groups of 50-59 and 60-69 years was equal in both the HILT and the LILT groups, that is, 13 (36.11%) vs 14 (38.89%), consequently. In both groups, the proportion of patients aged 40-49 was lowest, followed by 70-79. The analysis of BMI indicated an average value of 30.68 ± 4.49 kg / m² in the HILT and 30.29 ± 4.49 kg / m² in the LILT group without a significant association between the BMI level and the group to which the patients belonged (p = 0.6162).
Table 1. General characteristics by groups

| Parameters                  | HILT N=36 | LILT N=36 | p         |
|-----------------------------|-----------|-----------|-----------|
| Gender- N (%)               |           |           | Pearson Chi-square test=4.7407; df=1; p=0.0294* |
| Female                      | 23 (63.89%) | 31 (86.11%) |           |
| Male                        | 13 (36.11%) | 5 (13.89%) |           |
| Age (years)                 |           |           | Mann-Whitney U Test: Z=0.3716; p=0.7105 |
| ± SD                        | 61.36±8.14 | 60.36±7.45 |           |
| Min/Max                     | 45/76     | 45/72     |           |
| Median (IQR)                | 62 (55-68) | 61 (55-66.5) |           |
| Agegroups - N (%)           |           |           | Fisher-Freeman-Halton exact test: p=0.8094 |
| 40-49                       | 2 (5.56%) | 3 (8.33%) |           |
| 50-59                       | 13 (36.11%) | 14 (38.89%) |           |
| 60-69                       | 13 (36.11%) | 14 (38.89%) |           |
| 70-79                       | 8 (22.22%) | 5 (13.89%) |           |
| BMI (kg/m²)                 |           |           | Mann-Whitney U Test: Z=0.5012; p=0.6162 |
| ± SD                        | 30.68±4.49 | 30.29±4.49 |           |
| Min/Max                     | 22.25/40.40 | 22.55/40.40 |           |
| Median (IQR)                | 30.24 (27.51-33.47) | 29.38 (27.35-32.43) |           |

*significant for p<0.05

Anamnestic data

The anamnestic data on knee pain by groups is given in Table 2. Most of the patients from both groups (HILT/LILT) had no experience of previous knee pain - 26 (72.11%) vs 29 (80.56%) respectively, without a significant association of the existence of this type of experience with the group to which patients belonged (p = 0.4051). The time from the last episode of pain was without a significant difference between the groups and it was 7.64 ± 8.96 months for the HILT and 8.11 ± 8.66 months for the LILT group. In 50% of patients from both groups, the time to the last episode of pain was longer than 5.5 months, and the longest time in both groups was 36 months. Previous treatment of knee pain was reported by 20 (55.56%) patients in the HILT and 17 (47.22%) of those in the LILT group. We found no significant association between the positive history of previous treatment and the group to which patients were assigned (p = 0.4793).

Most of the patients in the HILT group, 12 or 60%, was previously treated with antirheumatic drugs followed by physical + antirheumatic drugs, 5 (25%), and physical therapy, 3 (15%) patients. In the LILT group, most of the knee pain was treated with physical + antirheumatic drugs, 7 (41.18%), followed by an equal proportion of 5 (29.41%) who were treated with physical therapy, i.e., only with antirheumatic drugs. The
analysis did not establish a significant association between the group to which patients belonged and the type of previous treatment of knee pain \( (p = 0.1742) \).

**Table 2.** Analysis of anamnestic data on knee pain by groups.

| Parameters                        | HILT N=36          | LILT N=36          | p               |
|-----------------------------------|--------------------|--------------------|-----------------|
| Pain for the first time - N (%)   |                    |                    | Pearson Chi-square test = 0.6930; df = 1; \( p = 0.4051 \) |
| No                                | 26 (72.11%)        | 29 (80.56%)        |                 |
| Yes                               | 10 (27.78%)        | 7 (19.44%)         |                 |
| Last episode (month)              |                    |                    | Mann-Whitney U Test: Z = -0.2083; \( p = 0.8349 \) |
| ± SD                              | 7.64±8.96          | 8.11±8.66          |                 |
| Min/Max                           | 0/36               | 0/36               |                 |
| Median (IQR)                      | 5.5 (0-12)         | 5.5 (3-12)         |                 |
| Previous treatment- N (%)         |                    |                    | Pearson Chi-square test = 0.5004; df = 1; \( p = 0.4793 \) |
| No                                | 16 (44.44%)        | 19 (52.78%)        |                 |
| Yes                               | 20 (55.56%)        | 17 (47.22%)        |                 |
| BMI (kg/m²)                       |                    |                    | Fisher-Freeman-Halton exact test: \( p = 0.1742 \) |
| Physical therapy                 | 3 (15%)            | 5 (29.41%)         |                 |
| Physical therapy+ NSAIL           | 5 (25%)            | 7 (41.18%)         |                 |
| NSAIL                             | 12 (60%)           | 5 (29.41%)         |                 |

*significant for \( p < 0.05 \)

**Table 3.** Comparison at VAS scale for knee pain between groups and intergroups at two times.

| VAS     | N    | ± SD     | Min/Max | Median (IQR) | p               |
|---------|------|----------|---------|--------------|-----------------|
| 0-time  |      |          |         |              |                 |
| HILT    | 36   | 7.14±1.62| 3/10    | 7 (6-8) | Mann-Whitney U test: Z = -0.7433; \( p = 0.4573 \) |
| LILT    | 36   | 6.81±1.62| 3/10    | 7 (6-8) |                 |
| 10-therapies |      |          |         |              |                 |
| HILT    | 36   | 2.22±1.74| 0/5     | 2 (1-4) | Mann-Whitney U test: Z = -2.9169; \( p = 0.0035 \)* |
| LILT    | 36   | 3.56±1.78| 0/7     | 4 (2-5) |                 |

*Wilcoxon signed-rank test 0/10: VILT: Z = 5.2316; \( p = 0.00001 \) NILT: Z = 5.0119; \( p = 0.00001 \)*

*significant < 0.05
Knee pain in patients of both groups was assessed according to VAS at two times, at 0 time and after 10 therapies (Table 3). At 0 time the average VAS score in the HILT and LILT group was 7.14 ± 1.62 vs 6.81 ± 1.62, with a min / max value in both groups of 3/10 or 50% of patients in whom the pain had a VAS score higher than 7. We found no significant difference between the two groups regarding VAS score level (p = 0.4573). After 10 therapies, the average VAS score in the HILT and LILT groups was 2.22 ± 1.74 vs 3.56 ± 1.78 with a min / max score of consequently 0/5 vs 0/7 and 50% of patients with VAS score lower than consequently 2 vs 4. There was a significant difference between the two groups in terms of the VAS score level after 10 therapies in favor of a significantly lower score or less pain in the HILT group (p = 0.0035) (Figure 1).

Additionally, we compared the VAS score between the two times in the two groups separately. We found that in both groups, HILT and LILT, the VAS score after 10 days of therapy was significantly lower compared to that at 0 time for consequently p = 0.00001 vs p = 0.00001 (Figure 1).

**Figure 1.** Comparison of VAS for group and intergroup knee pain at two times

**Discussion**

Our study included two equal groups of 36 (100%) subjects; the first was treated with high-intensity laser therapy (HILT), and the second with low-intensity laser therapy (LILT). The general characteristics by groups are given in Table 1. We observed a significantly higher proportion of male patients in the group treated with HILT (p = 0.0294). The mean age in the HILT and LILT groups was without a significant difference between the two groups (p = 0.7105). Also, there was no significance between the BMI level and the group to which patients belonged (p = 0.6162). In 50% of patients from both groups, the time to the last episode of pain was longer than 5.5 months, and
the longest time was 36 months. We found no significant association between the positive history of previous treatment and the group to which patients belonged (p = 0.4793). The analysis showed no significant association between the group to which patients belonged and the type of previous treatment of knee pain (p = 0.1742).

VAS scale
At 0 time we did not find a significant difference between the two groups in terms of the VAS score (p = 0.4573). We found a significant difference between the two groups in terms of the VAS score after 10 therapies in favor to a significantly lower score, i.e., less pain in the HILT group (p = 0.0035).

Additionally, we compared the VAS score between the two times in the two groups separately. We found that in both groups, HILT and LILT, the VAS score after 10 days of therapy was significantly lower compared to that at 0 time for consequently p = 0.00001 vs p = 0.00001.

Our study demonstrated statistically significantly better results in the group of patients treated with HILT than in the group treated with LILT. In the available literature, LILT is considered an effective modality in the treatment of knee OA. In previous studies, it was used alone or in combination with acupuncture or exercise. In several studies, the authors did not find an allergic effect of LILT in patients with OA of the knee. In contrast, other authors demonstrated efficacy in the treatment of pain with LILT. In addition, LILT was shown to be superior to ultrasound therapy in treatment of patients with OAK.

In our study, we examined the effectiveness of LILT in treating pain by using VAS at least 1 week after treatment. The results obtained in our study about the LILT impact are similar to several previous studies that applied the same outcome measure. LILT reduces pain directly by reducing the conduction velocity of sensitive nerves and raising the pain threshold, or indirectly by increasing tissue oxygenation and subsequently reducing swelling. Meanwhile, it has been reported in the literature that LILT reduces the intensity of the inflammatory process and improves microcirculation. Recently, HILT has been used in the treatment of pain in neurological and musculoskeletal disorders. For e.g., the study of Paul et al comprising former athletes with osteoarthritis showed HILT to be effective in reducing chronic pain. In addition, HILT has been shown to be effective in reducing low back pain, chronic ankle pain, neck pain, and carpal tunnel syndrome. HILT also showed a positive short-term effect in frozen shoulder, a long-term positive effect in reducing lateral epicondylitis inflammation, and in Bell’s palsy.

Several recent surveys from 2015 and 2017 that reviewed the results of several studies about the LILT treatment of OA reported that LILT had limited effects on the treatment. In contrast, a number of randomized trials on the efficacy of HITL in the treatment of chronic pain has increased in recent years. One of them is our study where HILT has proven to be a simple, non-invasive, and effective choice for physiotherapy or physical modalities. HILT is simple to apply (“point-and-shoot”) and has almost no side effects. The only known side
effect is a temporary change in skin color (redness) and a burning sensation if the head of the laser probe is located near the surface of the skin. The study conducted by Villiani et al. demonstrated that analgesic effect and better functionality in OA of the knee can be achieved, after application of only 5 procedures, continuously every day\(^4\).

There are several studies in the literature that have examined only the analgesic efficacy of VAS with HILT in OA of the knee\(^46,11,13\). One of them is the study of Kim et al.\(^46\), which included 28 patients, who showed a significant reduction in pain (\(P <0.05\)) after half a month of knee treatment. Similarly, in the study of Stiglitz-Rogoznica et al.\(^11\) where 96 patients were randomized, pain was also evaluated at the VAS scale before and after 10 days of treatment. The results showed a statistically significant reduction in pain (\(p <0.001\)). In the randomized pilot study of Ilijeva and Angelova comprising 72 patients, the results showed that there was a significant reduction in pain after seven days of treatment in the group of patients treated with HILT (\(p <0.001\))\(^47\).

There are several studies in the literature that compared the effectiveness of HILT with conservative physical therapy (ultrasound, interference currents, and exercise). One of them is the study of Goal-Joo\(^48\), where patients were assigned into two groups and received 12 treatments. The results of VAS and K-VOMAK showed that HILT was more effective in pain treatment of patients with OAK than conventional therapy.

A recent one-sided blind comparative study by Nazari et al. published in 2020 compared the efficacy of HILT with conventional physical therapy in OA of the knee. In this study, the results of HILT were superior to conventional physical therapy in relieving pain and improving function. The study was conducted in 93 respondents, who were randomly assigned into three groups; the first one treated with HILT and exercise, the second with conventional physical therapy and the third group with exercise only. The HILT group was treated for 12 sessions. The results of VAS, timed up and go test, 6-min walk test, Western Ontario and McMaster Universities Osteoarthritis (WOMAC) questionnaire showed a significant improvement in the first group treated with HILT and exercise\(^49\).

This study conducted in our institution supports the fact that the effect of the laser depends on the characteristics of the laser itself such as wavelength and coherence. The effectiveness of HILT is based on the specific and high-peak power of the laser pulse with a certain frequency and width of the pulse. Thanks to this high-energy peak, a large amount of energy is supplied in a short time (vertical effect), unlike the traditional delivery of the same amount of energy for a longer time and the risk of heating and tissue damage (horizontal effect). The advantage of HILT compared to LILT is that by increasing power the depth of penetration increases, and thus the effect in deep structures. The reduction of pain occurs through the so-called “Gate control system”. This system is the result of the stimulating effect of radiation on the regeneration of nerve fibers. The anti-inflammatory effect is realized by modulating the components of the inflammatory reaction, exudation, change and pro-
liferation, blocking cyclooxygenases and lipoxygenases and synthesis of prostaglandins and prostacyclin.

**Conclusion**

The results of our study showed that treatment with HILT and LILT significantly reduces pain in patients with OA. Patients treated with HILT showed better results, i.e., had a significant reduction in pain compared to patients treated with LILT. The use of HILT has been shown to be clinically relevant in providing a rapid and potent pain-reducing effect.

In the future, these findings might be compared to changes in muscle contraction and strength. The effect of laser therapy, especially HILT, on the cartilage of the knee, can also be the subject of further research if we start from the assumption that it can improve cartilage regeneration. New comparative studies are needed in the future where the sample and follow-up time should be longer to see the long-term effect of HILT. All this would contribute to the development of an appropriate protocol for the treatment of OA of the knee.

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