



Efficacy of high-intensity laser therapy in comparison with conventional physiotherapy and exercise therapy on pain and function of patients with knee osteoarthritis: a randomized controlled trial with 12-week follow up

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Abstract

Knee osteoarthritis (KOA) is one of the most common musculoskeletal disorders causing pain and functional impairment. The purpose of the study is to compare the effects of high-intensity laser therapy (HILT), conventional physical therapy (CPT), and exercise therapy (ET) on pain and function in patients with KOA. The study was designed as an assessor-blind randomized controlled trial. Ninety-three patients (aged between 50 and 75 years) with proved KOA were included and randomly allocated into three groups, and received 12 sessions of HILT, CPT, or ET. The outcomes were pain intensity measured by visual analog scale (VAS), knee flexion range of motion (FROM), timed up and go test (TUG), 6-min walk test (6MWT), and functionality of knee measured by the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) questionnaire. Statistical analyses were done to compare the amounts at the baseline, immediately after treatment and after 12 weeks. HILT was significantly more effective than the other groups in decreasing the VAS, increasing FROM and improving the scores of WOMAC (total and function subscale) both after treatment and after 12 weeks. The effect of HILT and CPT on the TUG, 6MWT, and WOMAC pain subscale was not significantly different after treatment, and both were better than ET. HILT was significantly better than the others after follow-up, particularly more effective on the stiffness subscale of WOMAC. HILT combined with exercise therapy, as a useful therapeutic approach, could have positive influences on KOA patients.

Keywords Exercise therapy · High-intensity laser therapy · Knee osteoarthritis · Pain · Physical therapy · RCT · WOMAC

Introduction

Knee osteoarthritis (KOA) is one of the most debilitating conditions associated with pain and functional impairment which

negatively affect quality of life [1]. It is characterized by deterioration of the articular cartilage and subchondral bone sclerosis [2] due to biomechanical and metabolic factors [3, 4]. The prevalence of KOA is increasing; Davatchi et al. have shown a high prevalence of KOA (41.9%) in Iran urban population over 40 years of age [5] which often leads to loss of dependence [6]. Current therapeutic strategies focus on improving function and relieving symptoms especially pain as the main symptom and the major cause of disability. Conservative management for KOA is aimed at the symptomatic relief including medication, intra-articular injection, physical modalities, exercise therapy, etc. [7–9].

Exercise therapy alone or with other modalities play an important role in improving symptoms and physical function in KOA [10, 11]. There are several pieces of evidence showing the positive effect of regular exercise therapy on increasing muscle strength and endurance, reducing joint stiffness, enhancing proprioceptive efficiency, improving balance, and

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the quality of life of the patients [12–15]. Also, available evidence has shown that physical modalities plus exercise can improve clinical outcomes in KOA patients [16, 17].

High-intensity laser therapy (HILT) that involves higher-intensity laser radiation is a new, painless, and powerful modality that showed significant results in pain reduction [18]. HILT with its own photo-chemical, photothermal, and photo-mechanical actions has many therapeutic benefits including analgesic, anti-edema, and biostimulating effects [19, 20]. Another advantage of HILT, especially neodymium-doped yttrium aluminum garnet (Nd: YAG) laser, is its greater power and depth of penetration in deep tissues [21, 22]. HILT has satisfactory effects in treating pain [19, 20] but its analgesic effect in osteoarthritis is less studied [20].

A few studies have been conducted to compare the effectiveness of HILT with other therapeutic methods. The aim of the present study was to evaluate the effectiveness of different therapeutic methods: HILT, conventional physical therapy (CPT), and exercise therapy (ET) alone on pain and function in patients with KOA.

Materials and methods

The study was designed as an assessor-blind randomized controlled trial (IRCT ID: IRCT 201701025486N5) with ethical approval from the Research Ethics Committee of Iran University of Medical Sciences (95-04-30-28639) based on the latest version of the Declaration of Helsinki and carried out during 2016–2017 in the Sports Medicine Department, Hazrat Rasool Hospital, Iran University of Medical Sciences.

Participants One hundred and two patients, of both sexes aged between 50 to 75 years, with proven KOA based on the American College of Rheumatology criteria were initially recruited through notices in the university hospitals in Tehran and provided with a brochure explaining the purpose of the study.

The inclusion criteria were as follows: (1) X-ray stages II and III osteoarthritis according to the criteria proposed by Kellgren and Lawrence; (2) age between 50 and 75 years; (3) BMI equal to or less than 30; (4) Knee pain lasted at least 6 months with intensity at least 3 on VAS scale in activities such as going up- and downstairs, sitting and squatting; (5) no history of acute traumatic injuries; (6) no history of previous surgery or injury in the knee and lower extremities; (7) lack of neuromuscular disease; (8) normal mental state; (9) absence of bone implants; (10) no history of new fractures; (11) lack of cancerous tumors; (12) no history of chronic disease and any condition that affect the study; (13) not participating in sports programs and physical therapy in the recent 3 months; and (14) no history of knee intra-articular injection in the past 6 months. The Exclusion criteria were (1) unwillingness to

participate in the study; (2) uncompleted evaluation/treatment programs; (3) any damage to the knee joint during the study; and (4) using any treatment other than prescribed therapeutic protocols.

Randomized allocation Initially, 102 patients were enrolled to study; nine subjects did not fulfill the inclusion criteria. Main participants were 93 patients who were randomly divided into three groups: (1) HILT in combination with exercise, (2) CPT in combination with exercise, and (3) ET alone. Three patients (one from each group) were excluded due to different reasons at the next stage (Fig. 1).

The patients who met the inclusion criteria randomly assigned to one of the three groups in a ratio of 1:1:1 using a computer-generated random allocation sequence through the stratified block randomization method.

The patients, the assessor, and the researchers who were responsible for the evaluation, treatment, and analyzing of the data were blinded to the randomization results.

Sample size To determine the sample size, a power analysis was performed to detect the effect size of two scores in pain improvement scale (VAS), as a primary outcome measure with a standard deviation of two points. A sample size of 26 in each group was found with a power of 80% and $\alpha = 0.05$ (2 tailed). To allow for a 20% dropout rate, the sample size increased to 31 patients per group.

The patients who were included in the study signed university-approved written informed consent forms prior to participation and completed demographic data sheets. All participants were allowed to be excluded at any time, if they did not want to continue the study.

Outcome measures Outcome measures were consisted of knee pain intensity by VAS, the range of active knee flexion (FROM), timed up and go test (TUG), 6-min walk test (6MWT), and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Ebrahimzadeh et al. assessed validity and reliability of WOMAC and demonstrated its suitability for Persian speaking patients with KOA [23]. The outcome measures were done at three intervals: at the baseline or pre-intervention, post-intervention (at 4 weeks), and at the end of follow up (at 12 weeks).

Intervention protocols The participants began a 12-session program (three times per week) in each group after pre-intervention assessment.

High-intensity laser therapy protocol The HILT group received HILT with pulsed mode of E20780 - laser YAG HT (Fysiomed, Belgium). The laser therapy consisted of Nd: YAG laser with wavelength of 1064 nm. HILT was performed in a slow manual scanning in longitudinal and perpendicular

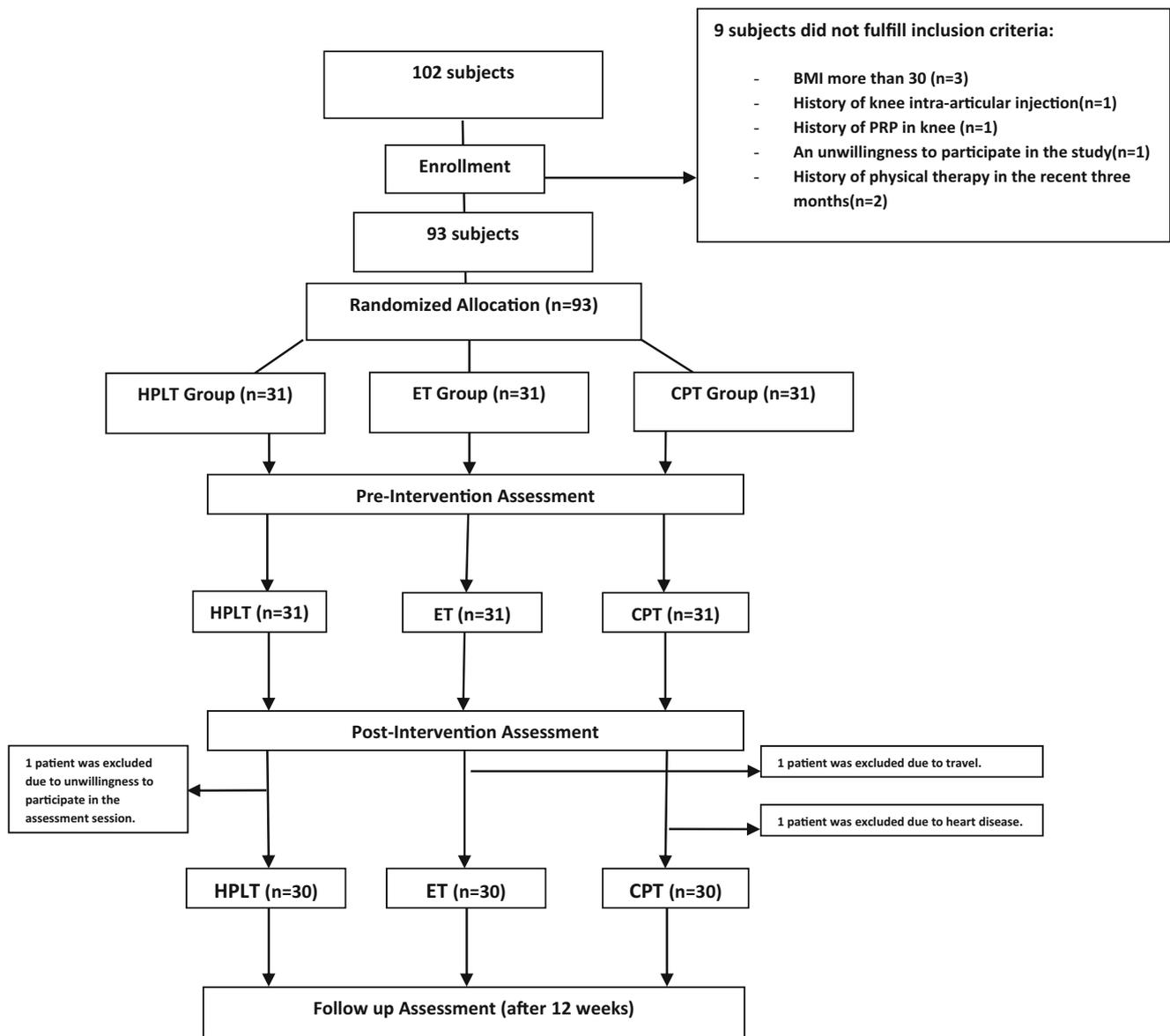


Fig. 1 Flow diagram of recruitment and allocation of the participants

direction on the medial and lateral sides of the knee with a 6-cm probe. The probe was placed vertically in contact with the joint line while the patient was in a supine position and the knee flexed at 30° for 8 min, at a frequency of 30 Hz with a peak power of 5 W (which is below the level of HILT power in other studies), a duty cycle of 70%, energy density of 60 J/cm², and total energy of 2400 J during one session.

Conventional physical therapy protocol The participants in the CPT group were treated by Combined BTL-4825 S Topline, UK, including transcutaneous electric nerve stimulation (TENS) and ultrasound (US) for 12 sessions, on alternate days.

The TENS was delivered by two self-adhesive electrodes which were placed on the medial and lateral parts of the knee

joint line. The TENS was applied to the patients using a frequency of 100 Hz, pulse width of 50–100 μs, and quadratic biphasic symmetrical pulse shape for 20 min. The intensity (mA) was set at the individual threshold of a tingling sensation.

The US protocol consisted of continuous ultrasonic waves of 1 MHz frequency and 1 W/cm² intensity applied with a 5-cm diameter applicator. The patients were placed in a supine position, and the US was applied to the medial and lateral parts (5 min on each side) of the knee in circular movements with the probe at right angles to ensure maximum absorption of the energy.

Exercise therapy protocol An exercise protocol was designed to be easily carried out at home with no need to attend any

special facility. Participants were educated on how to do the exercises correctly during the first session.

All groups received the same, standardized exercise protocol for KOA which consisted of nine exercises including muscle strengthening and flexibility training [11, 24] as follows:

1. Warm-up exercises: Walking at the usual speed on a flat surface for 10 min with hamstring and calf gentle stretches.

2. Major exercises for KOA: Straight leg raise (SLR), quadriceps setting, pillow squeeze, heel raise, one leg balance, step ups, and quadriceps strengthening exercises.

The exercises were done in three sets of ten repetitions with a 3-min rest between them. The ET group received above mentioned protocol alone as a home-based exercise program without any physical modalities.

All patients were provided an exercise booklet including the illustrations, the numbers, and the sets of the exercises and were strongly advised to do the exercises two times daily for 12 weeks. A family member was asked to confirm that the patient has done the exercises at home. In order to unify the participants' medications, all patients were asked to stop taking their medications 1 week before the beginning of the study and acetaminophen was prescribed for a dose of 2 g per day to use if they had pain.

Statistical analysis The SPSS (version 23; SPSS Inc., Chicago, IL, USA) was used to conduct the analysis. Dropout data was not included for analysis. The Kolmogorov-Smirnov test was used to assess data normality, and it revealed that only FROM had a normal distribution. The ANOVA was used for comparing means value of demographic data at the baseline. The intragroup results were analyzed by the Friedman test to compare baseline, at fourth and 12th week; repeated measure ANOVA was only applied for analyzing the values of FROM. The parametric (one-way ANOVA) and nonparametric (Kruskal-Wallis) methods were used to detect the significant changes in the data among the groups and in three stages of assessments. The LSD and Dunnett tests were also used to identify the between-group differences. The significance level was set at $p < 0.05$.

To assess the intra-tester reliability of objective tests, ten healthy subjects had repeated measurements 7 days apart in a pilot study. Test-retest reliability of TUG and 6MWT was assessed using interclass correlation coefficients (ICC) with a 95 level of confidence. The ICCs between the first and second measurements were 0.90 and 0.95, respectively, for TUG and 6MWT.

Results

A total of 93 patients participated in this study, but 90 patients (49 females and 41 males) completed the study and assessments.

There were no significant differences among the groups before the study in terms of the demographic variables listed in Table 1 using ANOVA, indicating the groups were well matched. Also, there were no significant differences clinical data (VAS, FROM, 6MWT, TUG, and WOMAC total and subscales) among the three groups at the baseline (Table 2).

Intragroup comparisons There were significant differences in VAS, FROM, 6MWT, TUG, and WOMAC (total and subscales) at each group in the three phases of assessments. After 12 weeks of follow-up, the abovementioned variables showed somewhat deterioration, but they were significantly better than the pre-intervention stage (Table 2).

The highest improvements were revealed in VAS, TUG, 6MWT, and WOMAC (total and subscales) in the HILT group. There was also a significant difference in FROM among the groups, but the best result was observed similarly in the HILT group (Table 2).

Comparison between the groups Between-group differences were analyzed using ANOVA and Kruskal-Wallis test on post-intervention data. Also, the LSD and Dunnett tests were used to compare the post-intervention data between the groups. The results of the comparison among the groups were expressed in the following:

Pain A significant difference in pain reduction was detected between the groups by Kruskal-Wallis test. Comparing the values of VAS at fourth and 12th week among the groups revealed a more significant decrease in pain in the HILT using Dunnett test (Fig. 2).

Flexion range of motion Improvement of FROM has been revealed in the HILT group by ANOVA and LSD tests at the fourth week and 12th week (Fig. 3).

There were also significant differences in TUG, 6MWT, and WOMAC (total and subscales) variables between groups using Kruskal-Wallis test at the fourth week and 12th week (Table 2).

Timed up and go test No significant difference was seen in the TUG between the HILT and the CPT at the fourth week, however, it was significantly better in HILT and CPT comparing to the ET. Furthermore, TUG showed a significant improvement in the HILT group, with a non-significant difference shown in both the ET and CPT groups at 12th week (Fig. 4).

Six-minute walk test 6MWT did not differ between the HILT and the CPT at the fourth week, but there was a significant difference between the groups in favor of HILT and CPT. After 12-week follow-up, no significant differences in the 6MWT were shown between CPT and ET, but there was a significant difference between the abovementioned groups

Table 1 Baseline demographic and clinical characteristics of the participants

	HILT group (<i>n</i> = 30) mean (SD)	CPT group (<i>n</i> = 30) mean (SD)	ET group (<i>n</i> = 30) mean (SD)	<i>p</i> value (<i>p</i> ≤ 0.05)
Age (years)	61.5 (3.9)	62.4 (3.14)	62.24 (3.87)	0.325 ^a
BMI (kg/m ²)	27.7 (1.4)	27.2 (1.6)	27.5 ± 1.8	0.132 ^a
History of KOA (years)	3 (1.3)	2.3 (0.7)	2.6 (1.9)	0.224 ^a
Gender (%)				
Female	17 (57%)	16 (54%)	16 (54%)	0.601 ^a
Male	13 (43%)	14 (46%)	14 (46%)	
K-L radiological stage (%)				
Grade II	19 (64%)	17 (57%)	18 (60%)	0.512 ^a
Grade III	11 (36%)	13 (43%)	12 (40%)	0.509 ^a
Involved knee (%)				
Right	18 (60%)	19 (64%)	16 (54%)	0.774 ^a
Left	12 (40%)	11 (36%)	14 (46%)	

^a Non-significant difference (one-way ANOVA test)

and the HILT. The values of 6MWT were greatly improved in HILT at 12th week (Fig. 5).

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The results of WOMAC pain subscale in the HILT group were similar to those in the CPT group. It was improved at the end of treatment and after the follow-up with a non-significant difference between the groups at fourth and 12th week (Fig. 6).

No significant difference was found between the HILT and CPT in WOMAC stiffness subscale post-intervention, and Dunnett test showed the superiority of the HILT group from the others. There was no significant difference between CPT and ET at 12th week, but the HILT significantly improved the stiffness of the patient with KOA (Fig. 6).

There were significant differences between the groups in WOMAC function subscale post-intervention and after follow-up. The statistical analysis confirmed the superiority of the HILT in improving the WOMAC function scores of the patients after the end of treatment and after 12 weeks follow-up.

The same results as function subscale were obtained for WOMAC total scores.

Discussion

The present research was conducted to study the effect of HILT on pain and function of the patients with KOA in comparison with CPT and ET. Our findings indicated the superiority of HILT on reducing pain, increasing FROM, improving function, and WOMAC scores as compared to the conventional treatment.

Furthermore, we observed significant differences between groups in VAS, WOMAC (total and subscales), TUG, 6MWT, and FROM after 12-week follow-up which all proved the effectiveness of the HILT. There are several reports about the positive effects of pulsed Nd: YAG laser therapy on some musculoskeletal disorders, such as shoulder pain [2], chronic ankle pain [6], low back pain [1], lateral epicondylitis [5], and chronic neck pain [19], but very few studies have investigated the efficacy of HILT on KOA.

Pain The outstanding finding in the study was the immediate and long-lasting (3 months) effect of HILT on decreasing knee pain that demonstrated HILT supremacy over the other interventions. Moreover, no adverse effect was reported by the patients during or after HILT. The result is consistent with the previous researches by Viliani et al. [25], Kheshie et al. [19], Sabbahi [26], Štiglic-Rogoznica et al. [20], Kim et al. [27], Angelova et al. [28], and Wyszynska et al. [29] in terms of pain relief of KOA.

Based on our results, it might be suggested that HILT is an effective modality in controlling patient's pain for short-term due to its specific characteristics including analgesic effects on nerve endings [20], photochemical and photothermic effects that increase blood flow [29], vascular permeability, and cell metabolism [25].

HILT could control inflammation by reducing prostaglandin, C-reactive protein, interleukin 1, and neopterin levels [18, 29].

The photomechanical effect of HILT is the main reason for its immediate analgesic effect [30]. Also, based on an in vitro observation, HILT may play an effective role in the reorganization of connective tissues and healing process [31] which is somewhat similar to low level laser therapy (LLLT). Also, there was some evidence which stated that the pain-relieving

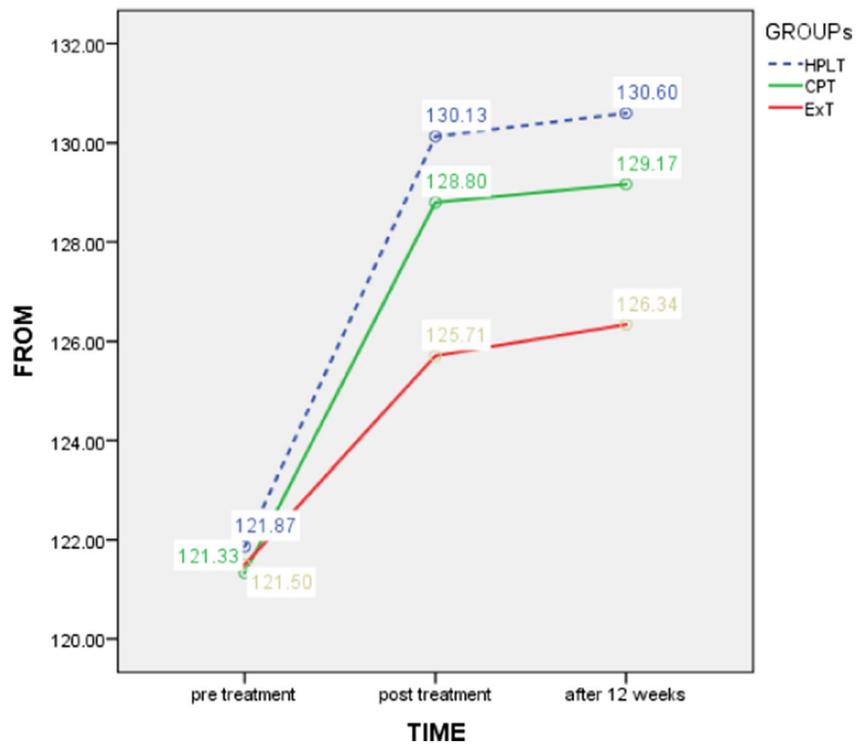
Table 2 Changes in VAS, FROM, 6MWT, TUG, and WOMAC (total and subscales) between the groups

	HILT group (<i>n</i> = 30) mean (SD)	CPT group (<i>n</i> = 30) mean (SD)	ET group (<i>n</i> = 30) mean (SD)	<i>p</i> value (<i>p</i> ≤ 0.05)
VAS (0–10)				
Pre-intervention	6.68(0.4)	6.73(0.5)	6.58 (0.7)	0.387 ^c
Post-intervention	3.79(0.54)	4.28(0.56)	5.22(0.6)	< 0.001 ^a
After 12 weeks	4.14(0.68)	5.21(0.59)	5.64(0.5)	< 0.001 ^a
<i>P</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	
FROM (degree)				
Pre-intervention	121.87 (4.09)	121.33 (4.27)	121.51 (4.22)	0.898 ^c
Post-intervention	130.13 (3.02)	128.80 (2.99)	125.71 (2.81)	< 0.001 ^b
After 12 weeks	130.60 (2.59)	129.16 (2.24)	126.34 (2.07)	< 0.001 ^b
<i>P</i> value	< 0.001 ^d	< 0.001 ^d	< 0.001 ^d	
TUG (second)				
Pre-intervention	9.63 (0.70)	9.72 (0.75)	9.57 (0.68)	0.609 ^c
Post-intervention	8.30 (0.66)	8.53 (0.66)	8.91 (0.73)	< 0.001 ^a
After 12 weeks	8.60 (0.81)	9.01 (0.71)	9.22 (0.65)	0.001 ^a
<i>P</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	
6MWT (m)				
Pre-intervention	389.77 (22.1)	391.70 (21.54)	390.56 (21.52)	0.714 ^c
Post-intervention	431.26 (22.78)	422.13 (21.70)	399.29 (21.08)	< 0.001 ^a
After 12 weeks	415.93 (21.29)	406.03 (20.05)	402.37 (20.36)	0.007 ^a
<i>P</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	
WOMAC pain subscale				
Pre-intervention	9.20 (0.88)	8.73 (0.98)	8.94 (0.74)	0.076 ^c
Post-intervention	4.13 (0.62)	4.43 (0.85)	7.24 (0.81)	< 0.001 ^a
After 12 weeks	5.36 (0.66)	5.66 (0.92)	7.78 (0.90)	< 0.001 ^a
<i>P</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	
WOMAC stiffness subscale				
Pre-intervention	3.93 (0.73)	3.83 (0.79)	3.81 (0.68)	0.733 ^c
Post-intervention	1.73 (0.69)	2.13 (0.73)	2.61 (0.75)	< 0.001 ^a
After 12 weeks	2.56 (0.62)	3.13 (0.77)	3.32 (0.78)	< 0.001 ^a
<i>P</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	
WOMAC function subscale				
pre-intervention	33.63 (2.93)	32.86 (2.16)	33.25 (2.37)	0.345 ^c
post-intervention	13.66 (1.42)	15.50 (1.27)	24.72 (1.82)	< 0.001 ^a
after 12 weeks	16.43 (1.22)	18.56 (1.19)	25.83 (1.25)	< 0.001 ^a
<i>p</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	
WOMAC total score				
Pre-intervention	46.76 (4.32)	45.43 (3.60)	45.87 (4.04)	0.225 ^c
Post-intervention	19.53 (2.12)	22.06 (2.16)	34.57 (2.27)	< 0.001 ^a
After 12 weeks	24.36 (1.84)	27.36 (2.20)	36.93 (1.68)	< 0.001 ^a
<i>P</i> value	< 0.001 ^e	< 0.001 ^e	< 0.001 ^e	

^a Significant difference post-intervention among groups (Kruskal-Wallis test)^b Significant difference post-intervention among groups (ANOVA)^c Non-significant difference in the baseline (Kruskal-Wallis test) (*p* > 0.05)^d Significant difference based on repeated measure ANOVA^e Significant difference based on the Friedman test

FROM, flexion range of motion

Fig. 2 Mean VAS score changes among treatment groups over time ($p < 0.001$)



effects of laser therapy might be due to increased levels of the neurotransmitters implicated in pain modulation such as

serotonin (25), releasing α and β endorphins which binds to the nociceptors (26), decreasing the afferent conduction

Fig. 3 Mean flexion range of motion (FROM) changes among treatment groups over time ($p < 0.001$)

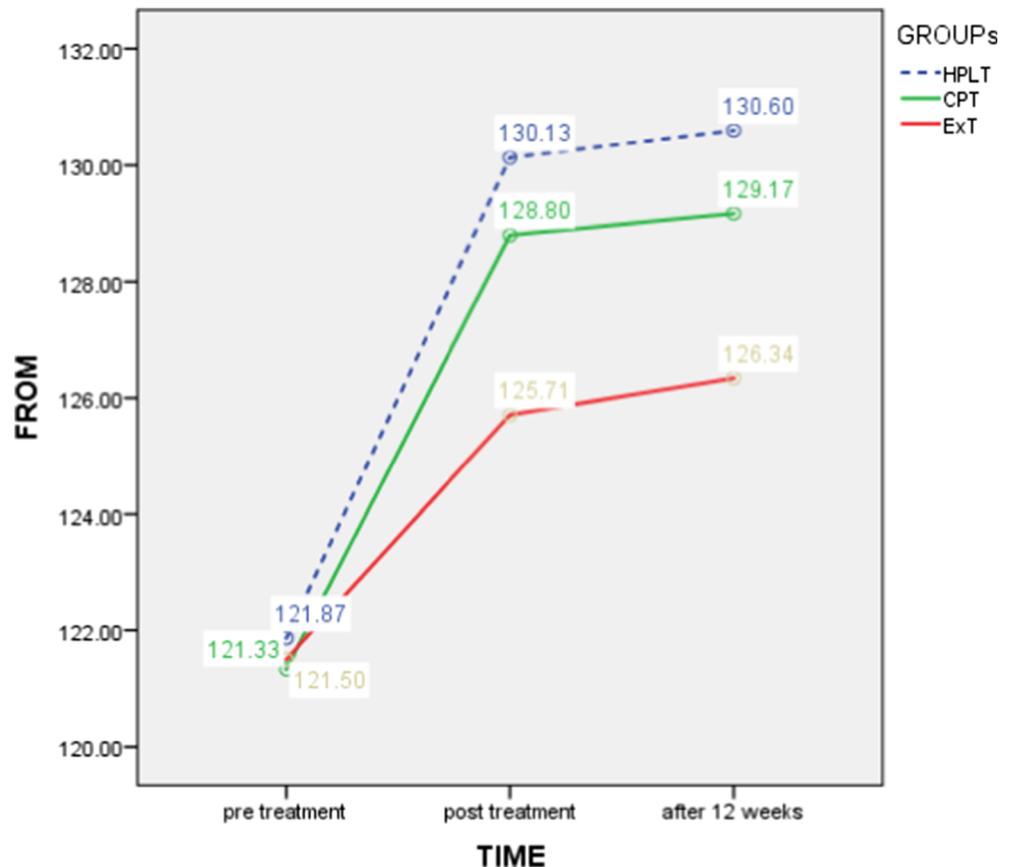
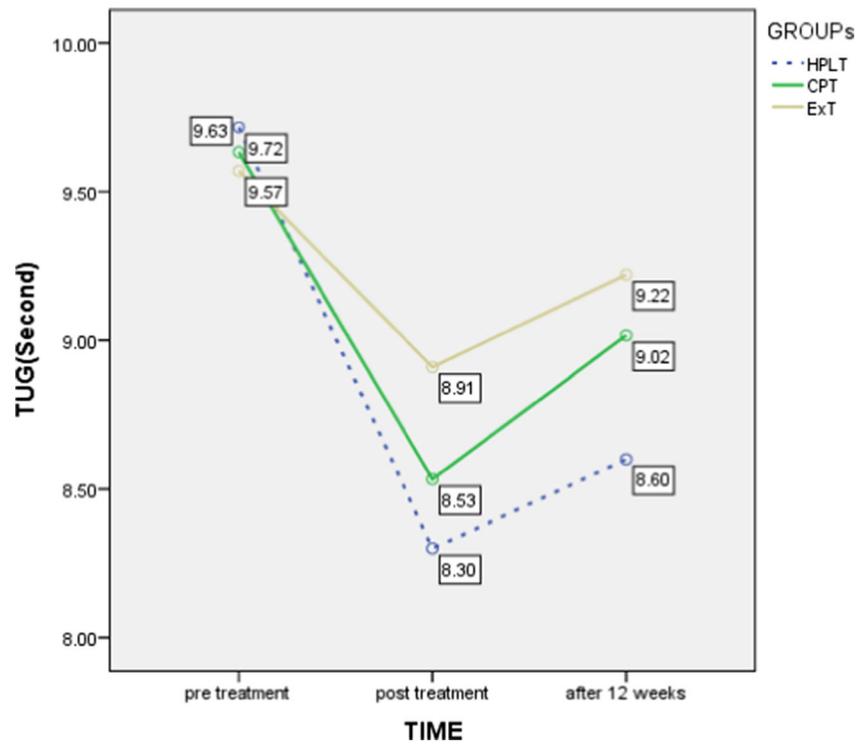


Fig. 4 Mean TUG score changes among treatment groups over time ($p < 0.001$)



velocity, decreasing effusion, inhibition of nociceptive activity by laser irradiation at peripheral nerves [32], raising the nociceptors' threshold [33], altering the release of histamine and bradykinin from injured tissues [34], and of substance P

from the peripheral nociceptors [35, 36], an anti-edema effect [37], increasing microcirculation and local temperature on treatment area [37, 38], enhancing oxygenation of treatment area [33], and increasing local metabolism [39].

Fig. 5 Mean 6MWT changes among treatment groups over time ($p = 0.005$)

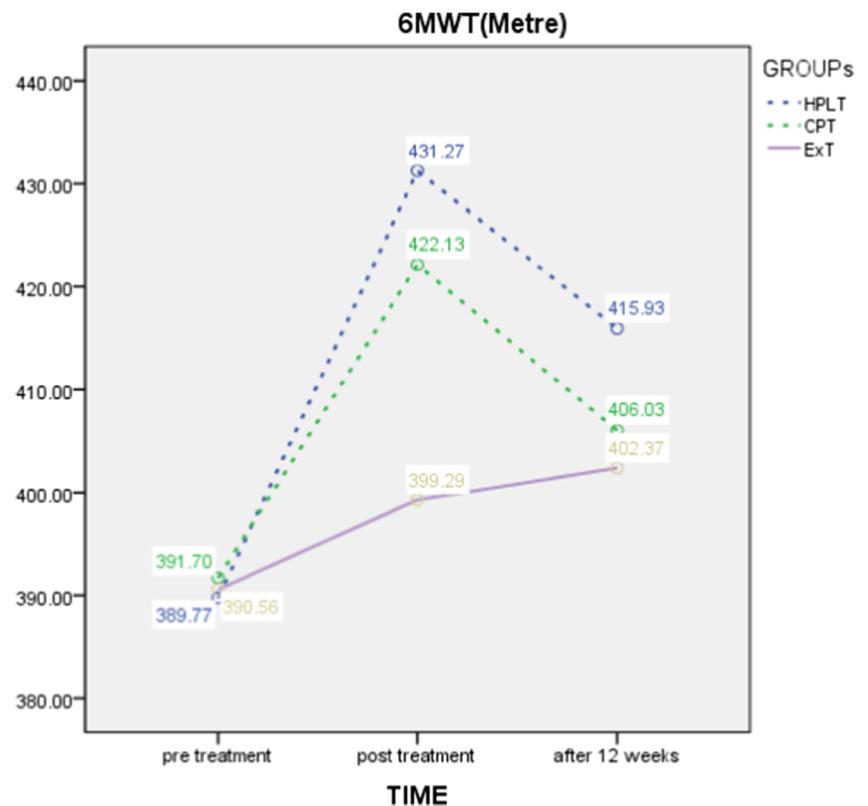
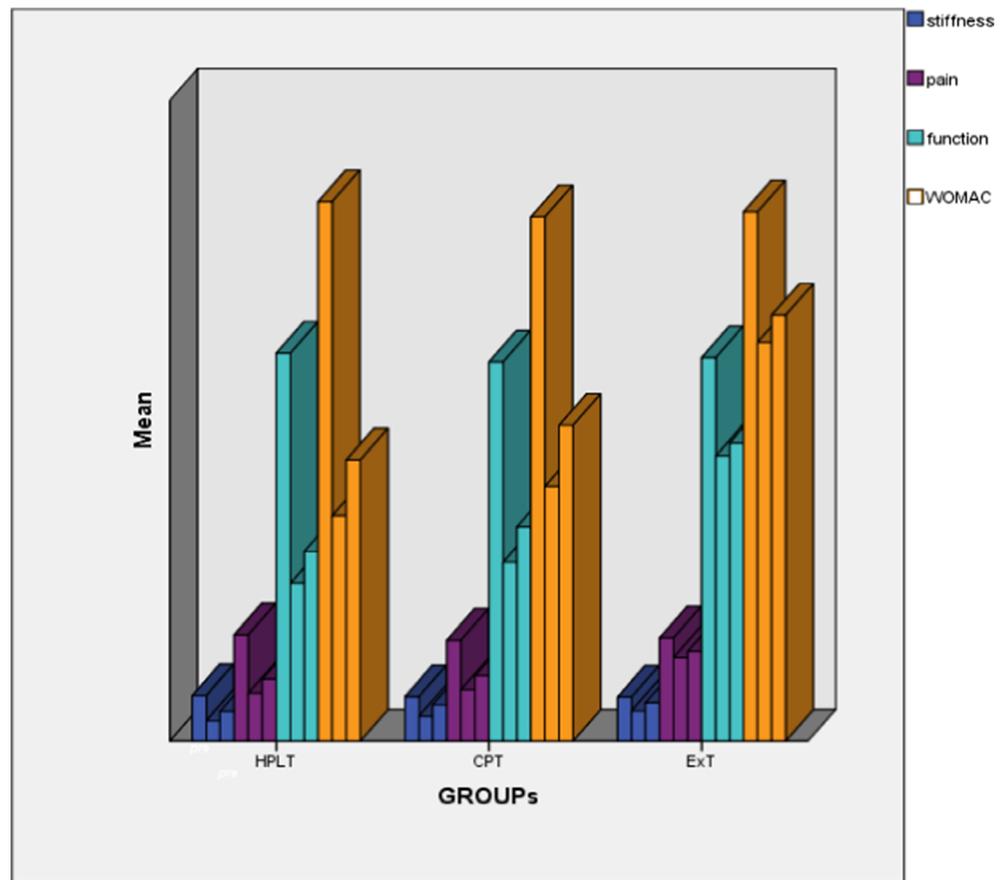


Fig. 6 Mean WOMAC and subscales changes among treatment groups over time ($p < 0.001$)



Gate control mechanism and nerve fiber regeneration are among the most important mechanisms justified relieving pain effect of HILT [28, 40].

Analgesic mechanisms of LLLT are also true for HILT with different intensity and penetration depth of HILT which is greater than LLLT [19, 20]. After conducting a comparative study between HILT and LLLT in patients with KOA, Kheshie et al. stated that HILT was more effective than LLLT [19].

Our results indicated the greater effectiveness of HILT on pain alleviation than US and TENS used in the CPT group. Similar to our findings, Santamanto et al. found greater effects of HILT than ultrasound in the treatment of shoulder subacromial impingement [30]. It has also been shown in Hsieh et al. study that LLLT was superior to ultrasound in the treatment of patients with KOA which is in line with our findings, though LLLT was applied in their study [35].

Sabbahi has declared that the analgesic and anti-inflammatory effects of HILT are far greater and more durable compared to ultrasound effects [26] which are confirmed by the present findings.

The present study supported the better result of HILT on pain control than conventional physiotherapy modalities. It seems the modalities such as TENS and US have limited and short-lasting effects on pain [25] as the result of the present study. Our findings indicated that the pain

improvement in the HILT and CPT groups was much greater than exercise therapy alone. In other words, the pain reduction in the HILT group was faster and more dramatic than the other groups. Therapeutic exercise is an effective, safe, and economical treatment for the KOA. ET was also able to decrease pain but not as much as and as quickly as the other modalities as shown in the study. However, a combination of exercise with HILT or other modalities, as has been shown in the present study, can play a more beneficial and rapid role in pain control similar to the Kheshie et al. findings [19]. Just like the post-intervention findings, the same results were obtained at follow-up which means the continuation of pain-relieving effect even after 12 weeks, especially in the HILT group, was similar to the findings of Angelova et al. [28].

Biological effect of HILT is determined by the radiation wavelength, its mode (continuous or pulse), pulse duration, energy, and power. Laser radiations with the wavelength in range of 600–1064 nm have the deepest penetration, and the penetration depth of the pulsed Nd: YAG laser used in the study is up to 100 mm [18, 40] which provides energy to the cell for its own metabolism without histological and disruptive changes. Nd: YAG laser affects the cells' microenvironment through mechanical stress which lead to cellular bio-stimulation, venous and lymphatic microcirculations,

increasing the cells mitotic index, activating extracellular ion transport, and stimulating healing process [40, 41]. According to available evidences, it is assumed that the photomechanical and thermodynamic of pulsed Nd: YAG laser are responsible for HILT analgesic, anti-edematous, anti-inflammatory, and reparative effects [18–21, 25, 28, 29, 32, 37, 40–42].

Our findings have confirmed that the analgesic effects of HILT have still remained after 3 months, and the patients were satisfied with their treatment, which is one of the strengths of this research that proved the short-term effect of HILT in pain relief.

Flexion range of motion Pain and inactivity in patients with KOA cause the peri-articular tissue fibrosis and adaptive shortening of muscles which lead to limitation of knee ROM [43]. Unfortunately, the effect of HILT on knee ROM has not been evaluated; only Alayat and his colleagues have shown that HILT with exercise could improve the range of lumbar region [44]. Sabbahi et al. found an improvement in performing squat in the KOA patients; however, they did not evaluate the knee ROM [26].

Our finding has shown a significant difference in the FROM between the groups post-intervention and after follow-up. The HILT group had a remarkable improvement in the FROM over the other groups that might be due to increasing local temperature on treatment area [38] or as a consequence of pain reduction. Rayegani et al. found no significant difference in knee ROM after laser therapy in a systematic review due to insufficient evidence. But, the results are similar to those reported by Youssef et al. in increasing knee range after using LLLT in the KOA patients [45]. The results of the study confirmed the effect of the HILT over ultrasound thermal effect in increasing FROM. It seems that adding HILT as a deep heating modality to other therapies could be more useful in increasing ROM and flexibility of soft tissue structures in the KOA patients.

Functional tests According to our findings, the functional tests showed significant differences between the different phases of evaluation in each group. Functional disability of the KOA patients is often due to pain, muscle weakness, and limited ROM in affected joints [46]. HILT and CPT with exercise had a great effect on TUG and 6MWT outcomes and improving physical performance of the patients' post-intervention by decreasing the pain and increasing ROM as well as muscle strength.

HILT with exercise therapy has had a better therapeutic effect on physical function after 12-week follow-up; it was due to the continued relief of pain, increasing ROM, and strength in the patients.

In agreement with the current study, Sabbahi showed an increase in a 6MWT-walking distance in the HILT group [26].

Kheshie et al. [19] and Viliani et al. [25] also showed significant differences in the function of the patients of the HILT group.

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WOMAC is the most common self-declaration questionnaire for the KOA patients to evaluate pain, stiffness, and function. There was no significant improvement in WOMAC pain subscale in the HILT and CPT groups, but the results of the two groups showed a significant difference with the ET group. According to patients' statements in this subscale, the results of the HILT and CPT have been similar at fourth and 12th weeks, and both had more sedative effects than ET alone.

As previously stated, HILT was determined as the better modality for pain reduction over the other interventions by VAS, while HILT and CPT were estimated to have similar analgesic effects in the WOMAC pain subscale; perhaps the reason for this can be attributed to different methods of pain evaluation.

WOMAC total score, as well as stiffness and function subscales, have been shown to have significant improvement, manifested by a decrease WOMAC scores in the HILT at fourth and 12th weeks which could be due to the effect of HILT on affected tissues. In agreement with our findings, Alayat et al. revealed a significant difference in WOMAC (total and other subscales) in all groups after the end of intervention; but contrary to our results, non-significant differences were observed after 3 months of follow-up [19]. Similar to our results, a decrease in WOMAC scores was indicated in the systemic review of Wyszynska et al. [29].

Kheshie et al. showed that a significant difference in WOMAC scores in HILT and LLLT [19] is in confirmation of our results. All the three groups in Viliani et al. study showed a highly statistically significant improvement in WOMAC scores after HILT which was maintained at follow-up after 4 months similar to our findings [25]. Kim et al., in a similar research, studied the effect of HILT in comparison with conservative physical therapy in KOA and showed that the HILT had a significant improvement in both the VAS and the Korean WOMAC than the other group [27].

Most likely, the reason for improving WOMAC scores in the HILT group should be attributed to a significant reduction in pain and its persistence. Because of the chronic pain experience, the patients with KOA show a slight tendency to any physical activities despite the benefits of exercise, and the patients have often reduced their mobility in order to avoid pain. This causes a great decline in their ability to use their joints, which results in a weakening of muscle strength, increasing joint stiffness, reducing ROM, and decreasing physical performance.

Limitations

Our study, however, has some limitations such as a small number of patients and lack of full control over the daily activities or the prescribed exercise protocol of the participants. Furthermore, sonographic assessment was not used for following the probable repairing process. In addition, absence of a long-term follow-up (more than 3 months) is another limitation of this study. Therefore, a variety of future studies should be conducted to compensate for the limitations and also some studies should be designed with a different protocol of HILT for KOA.

Conclusion

The finding supports the feasibility of application of HILT for the patients with KOA as a safe and well-tolerated modality. The HILT combined with ET was more effective than CPT combined with ET and exercises alone in improving pain and function of the patients with KOA and in the other cases; its therapeutic effects have been similar to CPT.

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Compliance with ethical standards

Ethical approval The Research Ethics Committee of Iran University of Medical Sciences approved the study (95-04-30-28639) and the study has been performed based on the latest version of the Declaration of Helsinki.

Conflict of interest statement The authors declare that they have no conflict of interest.

Informed consent The patients signed a written Persian consent form and announced their agreement to study and for publication of the results with respect to the confidentiality of personal data.

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