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Laser acupuncture versus acupoint focused ultrasound in patients with knee osteoarthritis

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Abstract

Background: Knee osteoarthritis (KOA) is a common degenerative joint disorder that affects 250 million people globally. The most common treatment for KOA is non-steroidal anti-inflammatory drug administration. However, the analgesic effect is limited and often accompanied by multiple side effects. Hence, many KOA patients opt for complementary and alternative medicine. Acupuncture is one of the most popular complementary treatments with great analgesic effect and minimal side effect. Laser acupuncture is a photonic stimulation of acupoints and areas, initiating therapeutic effects similar to that of needle acupuncture and related therapies together with photobiomodulation. Acupoints focused ultrasound is the application of an ultrasound stimulus to the acupuncture meridian system

Objective: To investigate the difference between the effects of laser acupuncture versus acupoint focused ultrasound on knee osteoarthritis.

Subject and Methods: 51 Subjects of both genders with age range from (45-65) years old with grade 2 and 3 knee osteoarthritis was participate in this study and was conducted at outpatient physical clinics in Cairo University.

Three groups with 17 patients for each group, (group A) received laser acupuncture in addition traditional exercises for 3 sessions per week for four weeks, (group B) received acupoint focused ultrasound in addition to traditional exercise for 3 sessions per week for four weeks and (group C) received only traditional exercise for 3 sessions per week for four weeks. All patients were evaluated before and after the treatment using visual analogue scale, digital goniometer, Western Ontario and McMaster Universities osteoarthritis index (WOMAC).

Results: There was a significant decrease in VAS of group A compared with that of group B ($p = 0.001$) and group C ($p = 0.001$), There was a significant decrease in pain, stiffness and function scores of group A compared with that of group B ($p < 0.01$) and group C ($p < 0.001$), There was a significant increase in flexion ROM of group A compared with that of group B and group C ($p < 0.001$) and There was a significant increase in extension ROM of group A compared with that of group B ($p = 0.02$) and group C ($p = 0.02$).

Conclusion: application of laser acupuncture in conjunction with exercise for patients with KOA was more effective in pain relief and improvement of knee joint ROM and functional ability than acupuncture focused ultrasound conjunction with exercise and exercises alone.

Keywords: Knee osteoarthritis**,** laser acupuncture, acupoint focused ultrasound

Introduction

Osteoarthritis (OA) is a multifactorial disease related to genetic, hormonal, aging, mechanical and metabolic factors, which promote changes in focal areas causing loss of articular cartilage within synovial joints, associated with bone hypertrophy (osteophytes and subchondral bone sclerosis) and capsule thickening. [1] Every one hundred fifty individuals out of one million suffer from OA worldwide; therefore, it is ranked as the sixth major cause of moderate and severe disability. The prevalence and incidence of knee OA is ten times greater in patients between 30–65 years than in younger patients, indicating it is a disease mainly associated with the aging process. Approximately 80% of patients with knee OA suffer from some form of movement restriction, and 20% are unable to perform basic daily activities; indeed, 11% of sufferers require personal care. [2] Amongst the cardinal symptoms of OA, pain is the biggest concern, and motor disability and impaired proprioception are important secondary factors. [3]

Currently available modalities of management for knee OA include nonpharmacological, pharmacological, and surgical treatments during the past decade; much emphasis has been put on nonpharmacological management. It is widely recommended that the nonpharmacological intervention should be the first line of treatment for people with knee OA. [4] Acupuncture has been shown to be effective in pain relief and dysfunction associated with musculoskeletal conditions, including knee osteoarthritis. [5]

Laser acupuncture is one of recent technological developments (e.g., electro acupuncture) in the practice of acupuncture. Rather than mechanical stimulation produced by traditional needle therapy, acupoints irradiated by the laser acupuncture elicit physiologic effects at the cellular level with sufficient energy. Because it is a gentle, less-invasive and simple-to-perform non pharmacologic technique, laser acupuncture has become increasingly attractive for patients with needle phobias, as well as for elderly people and children. [6] in laser acupuncture traditional acupuncture points are stimulated

with low-energy lasers. There are practical and methodical advantages to this procedure compared to needle acupuncture: application is free of pain, there is no risk of infection, application is simple and not time-consuming, the stimulation technique and the parameters can be standardised and a physiologically inert placebo control can be carried out. [7]

Acupoints focused ultrasound is the application of an ultrasound stimulus to the acupuncture meridian system has been found safe and effective in many common clinical entities. [8] Ultrasound (US) treatment has been used as a non-invasive modality for the management of OA for more than 60 years because of its reputed ability to relieve pain, reduce edema, increase the range of motion, and accelerate tissue repair via thermal and non-thermal mechanisms (mechanical effects). [9] US can be administered in either a continuous or a pulsed mode. Pulsed US produces non-thermal effects and is beneficial for cartilage health, whereas continuous US aims to generate thermal effects that could enhance fibrous tissue extensibility, increase tissue metabolism, promote capillary permeability, and elevate the pain threshold. [9] Insertion of needles in acupuncture damages the skin, but ultrasound stimulation does not. Thus, ultrasound stimulation has a smaller risk of infection and users do not feel any pain during stimulation. Focused ultrasound stimulation uses almost the same intensity as ultrasound physical therapy (1–3 W/cm2). Temperature increase at the focal point can be suppressed by changing the supply voltage and waveform. [10]

Subjects, materials and methods

- The study was conducted at outpatient physical clinics in Cairo University through February to May 2023 to compare the effects of laser acupuncture versus acupoint focused ultrasound on knee osteoarthritis.
- Three groups with 17 patients for each group the first group received laser acupuncture in addition traditional exercises for 3 sessions per week for four weeks., the second received acupoint focused ultrasound in addition to traditional exercise for 3 sessions per week for four weeks and the third group received only traditional exercise for 3 sessions per week for four weeks.
- All patients were evaluated before and after the treatment using visual analogue scale, digital goniometer, Western Ontario and McMaster Universities osteoarthritis index (WOMAC).

The patients were selected according to the following criteria

1. Female or male patients with knee osteoarthritis according to the American College of Rheumatology criteria. [11]
2. An average pain intensity of ≥3 on a 10-cm visual analogue scale (VAS). [12]
3. Patients with unilateral knee osteoarthritis, for those patients with bilateral knee osteoarthritis the most painful knee were assessed. [12]
4. Patients will be referred by orthopedic physician.
5. Patients with body mass index <30Kg/cm^2

The patients were excluded if they have one of the following criteria [12]

1. Previous knee surgery.
2. serious valgus or varus deformity.
3. disease where laser and ultrasound treatment are contraindicated (cancer, uncontrolled diabetes mellitus, hypertension, etc).
4. current use of medications that might interfere with low level laser therapy treatment (e.g. corticosteroid injections).

Instrumentations and procedures for evaluation

Visual analogue scale (VAS)

Visual analogue scale (VAS): It will be used to assess pain. It consists of a 10 cm line. Patients will be asked to indicate the point along the line from 0-10 cm marked in 1 cm increments where 0 cm represents no pain and 10 cm the most severe pain imaginable. Visual analogue scale is a valid and reliable scale. [13]

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

The Western Ontario and McMaster Universities (WOMAC) index is an English-language questionnaire developed and validated by Bellamy *et al* in 1988. [14] This self-administered composite questionnaire includes five questions about pain, two about stiffness, and 17 about degree of difficulty in accomplishing daily life activities. The scores for the subscales on pain, stiffness, and disability are calculated separately, this score can vary, with pain ranging from 0 to 20 points; stiffness, 0 to 8 points; and physical function, 0 to 68 points. Higher scores represent worse pain, stiffness, and functional limitations. [14]

Arabic version of reduced Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess pain, stiffness, and physical function. Reliability and validity of the Arabic version of WOMAC have been established. Individual score of pain, stiffness, and physical functioning will be calculated separately and gross score also will be calculated according to interpretation guidelines. The ArWOMAC index is a reliable and valid instrument for evaluating the severity of knee OA, with metric properties in agreement with the original version. [15]

Digital goniometer

Absoulute + Axis™ Digital Goniometer; Fabrication Enterprises, Inc. White Plains, New York, USA. [16] fabrication enterprises Inc white plain Goniometer reads 0-185 degrees on LCD screen. Has ability to freeze angle measurement. Powered by one 9V battery. Goniometer exterior is powder-coated aluminum with inch/cm markings on the arm.

Procedures

- For measuring of knee flexion patients were asked to lie in supine position with lower extremities in anatomical position with a towel roll under ipsilateral ankle.
- Digital goniometer was aligned so the axis was placed on lateral epicondyle of the femur, with the stationary arm at the midline of the femur and moveable arm at the midline of the lateral malleolus, then instruction was given to patients to flex their knees through the available ROM by sliding foot along table toward pelvis.
- The number that appeared on the digital screen was recorded.
- For measuring of knee extension patients were asked to lie in supine position with lower extremities in

anatomical position with a towel roll under ipsilateral ankle.
- Digital Goniometer was aligned as in flexion.
- Instruction was given to patients to extend their knees through the available ROM by straighten knee as far as possible.
- The number that appeared on the digital screen was recorded.
- All patients were instructed about assessment and treatment procedures to gain their cooperation during the procedure.
- The patients signed a consent form in approval for administration of laser and ultrasound therapy.

Instrumentation and procedures for treatment

1. Laser apparatus

Multiwave locked system (MLS) laser therapy was used, the laser device Manufacture in Italy by ASA was for providing synchronized and overlapping continuous and pulsed emissions of Ga-Al-Ar laser emitted in a single hand piece. Mphi has a continuous emission of a wavelength of 808 nm with peak power of 1000 mW, mean power of 500 mW, spot diameter of 2 cm, and spot area of 3.14 cm2. Pulsed emission has a wavelength of 905 nm, peak MlS has a continuous emission of a wavelength of 808 nm with peak power of 1000 mW, mean power of 500 mW, spot diameter of 2 cm, and spot area of 3.14 cm. Pulsed emission has a wavelength of 905 nm, peak power of 25 W, and mean power of 54 mW.

Procedure of treatment
- Patients were asked to lie in a supine position, with the affected knee slightly flexed and supported by a rolled towel.
- The therapist and patients wore protective goggles to shield their eyes from active laser radiation.
- The device was set at:
- Frequency 420 Hz, energy density 18 J/cm^2. [17], duty cycle 50%, treatment duration 10 minute.
- The laser probe had been placed sequentially and perpendicularly in full contact with the skin at acupuncture points.
- The application was 100 seconds for each acupoint and the laser probe was glide to next point in the same side, then to other side.

The acupuncture points were selected according to the Traditional Chinese Medicine meridian theory to treat knee pain. [18] Which was Yanglingquan (GB34) IT is located at the depression anterior and inferior to the head of the fibula, Xuehai (Sp 10): is located 2 cm above the medial end of the upper border of patella, Liangqiu (St 34): It is 2 cm above and lateral to upper border of Patella, Dubai (St 35) It is in depression on the lateral side of ligamentum patellae, Neixiyan (EX-LE4) It is in depression on the medial side of ligamentum patellae, Yinlingquan (SP9)In the depression posterior and inferior to the medial condyle of the tibia, in the angle formed by the medial condyle and posterior border of the tibia.

Patient received 3sessions per week for 4 weeks

2. Ultrasound apparatus

Gymna Pulson 200 device was used, Manufacture in Belgium

Specifications

Frequency: Multifrequency head (1 and 3 MHz), 4 cm²

Mode: Continuous and pulsed mode (10–20–30–40–50-100%)

Mains voltages: 100-240-VAC, 50/60 Hz +/- 10%

Procedures for treatment
- Patients were asked to lie a supine position, with the affected knee slightly flexed and supported by a rolled towel.
- A couplant aquasonic gel was applied to the skin and ultrasound head to provide an air- free contact.
- The device was set at
- Frequency 1 Mhz, duty cycle 20% (1: 5) pulsed mode, intensity 1w/cm2, treatment duration 9 minute. [19-20]
- The treatment head was applied perpendicularly to the skin surface and was kept moving during treatment in continuous circular movements.
- the application was 1.5 minutes for each acupoint (GB34, SP9, SP10, ST34, ST35, and EX-LE4). [18] and the head was glide to next point in the same side, then to other side.
- Patient received 3sessions per week for 4 weeks

Traditional treatment

1. Stretch exercises [21]

1. Rectus femoris, iliotibial band, hamstring and self-stretch for calf muscle (3sets, each stretch 15-30 sec hold, between each set 5sec rests).

2. Strengthen exercises [21]

1. static quadriceps contraction (10 rep,3sets)
2. hip abductors strengthening 45 degree (10 rep,3sets),
3. hip extensor strengthening 15 degree (10 rep,3sets),
4. straight leg raising 45-70 degree (10 rep,3sets)
5. short arc knee extension (10 rep,3sets)

All exercises started active free then progress to, patients were hold in each exercise for (6-10) second.

The progression was done when patient was eased to do exercises, weight had been added according to DeLorme Principle for strengthening.

Data analysis

Subject characteristics were compared between groups using the MANOVA test. Fisher- Exact test was conducted for comparison of sex distribution between groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to test the homogeneity between groups. Mixed MANOVA was performed to compare within and between groups effects on VAS, WOMAC and knee ROM. 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) shows the subject characteristics of group A, B and C. There was no significant difference between groups in age, weight, height, BMI and sex distribution ($p > 0.05$).

Table 1: Basic characteristics of participants.

	Group A	Group B	Group C	p-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)	52.65 ± 6.35	53.76 ± 3.80	54.76 ± 5.97	0.53
Weight (kg)	74.94 ± 7.04	75.82 ± 7.62	73.94 ± 6.23	0.73
Height (cm)	162.94 ± 4.72	164.41 ± 5.78	162.18 ± 4.28	0.42
BMI (kg/m²)	28.18 ± 1.59	28.03 ± 2.29	28.12 ± 2.29	0.98
Sex, n (%)				
Females	12 (71%)	11 (65%)	14 (82%)	0.50
Males	5 (29%)	6 (35%)	3 (18%)	

SD, standard deviation; p-value, level of significance

Effect of treatment on VAS, WOMAC and knee ROM
Comparison within group

There was a significant decrease in pain, stiffness and function WOMAC scores in the three groups post treatment compared with that pre-treatment ($p < 0.001$). (Table 2).

There was a significant decrease in VAS and a significant increase in flexion and extension ROM in the three groups post treatment compared with that pre-treatment ($p < 0.001$) (Table 3).

Comparison between group

There was a significant decrease in pain, stiffness and function scores of group A compared with that of group B ($p < 0.01$) and group C ($p < 0.001$). There was a significant decrease in pain, stiffness and function scores of group B compared with that of group C post treatment ($p < 0.05$). (Table 2).

There was a significant decrease in VAS of group A compared with that of group B ($p < 0.001$) and group C ($p < 0.001$). There was a significant decrease in VAS of group B compared with that of group C ($p < 0.01$). (Table 3).

There was a significant increase in flexion ROM of group A compared with that of group B and group C ($p < 0.001$) and a significant increase of group B compared with that of group C ($p < 0.01$). There was a significant increase in extension ROM of group A compared with that of group B and group C ($p < 0.5$) while there was no significant difference between group B and group C ($p > 0.05$). (Table 3).

Table 2: Mean WOMAC pre and post treatment of group A, B and C:

WOMAC	Group A	Group B	Group C	p-value		
	mean ± SD	mean ± SD	mean ± SD	A vs B	A vs C	B vs C
Pain score						
Pre-treatment	11.12 ± 2.34	12.58 ± 2.85	11.53 ± 2.41	0.22	0.88	0.45
Post treatment	4.53 ± 1.42	6.35 ± 1.73	8.18 ± 2.07	0.01	0.001	0.01
MD (% of change)	6.59 (59.26%)	6.23 (49.52%)	3.35 (29.05%)			
	p = 0.001	p = 0.001	p = 0.001			
Stiffness score						
Pre-treatment	5.05 ± 1.03	4.94 ± 1.24	5.17 ± 0.95	0.94	0.94	0.8
Post treatment	1.88 ± 0.85	2.88 ± 0.99	3.64 ± 0.71	0.004	0.001	0.03
MD (% of change)	3.17 (62.77%)	2.06 (41.70%)	1.53 (29.59%)			
	p = 0.001	p = 0.001	p = 0.001			
Function score						
Pre-treatment	39.64 ± 7.63	40.76 ± 6.51	38.94 ± 5.08	0.87	0.94	0.69
Post treatment	17.88 ± 3.27	22.29 ± 3.16	28.58 ± 4.51	0.003	0.001	0.001
MD (% of change)	21.76 (54.89%)	18.47 (45.31%)	10.36 (26.61%)			
	p = 0.001	p = 0.001	p = 0.001			

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

Table 3: Mean VAS, knee flexion and extension ROM pre and post treatment of group A, B and C:

	Group A	Group B	Group C	p-value		
	mean ± SD	mean ± SD	mean ± SD	A vs B	A vs C	B vs C
VAS						
Pre-treatment	6.78 ± 1.39	6.58 ± 1.49	6.44 ± 1.49	0.91	0.77	0.95
Post treatment	2.12 ± 0.63	3.64 ± 0.94	4.50 ± 0.92	0.001	0.001	0.01
MD (% of change)	4.66 (68.73%)	2.94 (44.68%)	1.94 (30.12%)			
	p = 0.001	p = 0.001	p = 0.001			
Flexion ROM (degrees)		**Flexion ROM (degrees)**				
Pre-treatment	119.07 ± 7.19	121.12 ± 5.03	120.76 ± 5.02	0.56	0.67	0.98
Post treatment	134.29 ± 2.56	128.44 ± 3.77	124.76 ± 4.35	0.001	0.001	0.01
MD (% of change)	-15.22 (12.78%)	-7.32 (6.04%)	-4 (3.31%)			
	p = 0.001	p = 0.001	p = 0.001			
Extension ROM (degrees)						
Pre-treatment	177.38 ± 1.69	177.06 ± 1.52	177.4 ± 1.43	0.81	1	0.79
Post treatment	179.67 ± 0.77	178.75 ± 0.98	178.73 ± 1.17	0.02	0.02	0.99
MD (% of change)	-2.29 (1.29%)	-1.69 (0.95%)	-1.33 (0.75%)			
	p = 0.001	p = 0.001	p = 0.001			

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

Discussion: The study was conducted to compare between the effect of laser acupuncture and acupoint focused ultrasound in patients with knee osteoarthritis

Safari *et al*., 2020 reported that OA is the most common chronic joint disorder, is characterized by local inflammation and joint structural change, and is associated

with painful symptoms and loss of function leading to considerable impairment of quality of life. Globally, hip and knee OA are leading contributors to disability in terms of years lived with disability. [22]

The results of this study revealed that

- There was a significant decrease in VAS of group A compared with that of group B and group C. There was a significant decrease in VAS of group B compared with that of group C.
- There was a significant decrease in pain, stiffness and function scores of group A compared with that of group B and group C. There was a significant decrease in pain, stiffness and function scores of group B compared with that of group C post treatment.
- There was a significant increase in flexion ROM of group A compared with that of group B and group C and a significant increase of group B compared with that of group C. There was a significant increase in extension ROM of group A compared with that of group B and group C.

Pain is the most frequent symptom in knee OA and causes a reduction in functional capacity, which leads to restriction in daily activities and decrease in quality of life. [23]

The analgesic effect of laser therapy explained by Hagiwara *et al*., 2008, stated that reduction of pain after laser treatment is a result of its anti-inflammatory effects, increase in microcirculation, and stimulation of immunological processes, nerve regeneration and increased secretion of endogenous opioids such as β-endorphins, by which the pain is centrally inhibited. [24] And Hsieh *et al*., 2015, stated that the analgesic effect is due to inhibition of painful sensation at different levels. Histamine and bradykinin release from inflammatory tissue is reduced, and the pain threshold is increased. [25] Also, laser light reduces the secretion of substance P from peripheral nociceptors, thus reducing the pain relay and preventing the development of hyperalgesia. Also, Ferraresi *et al*., 2011, concluded that laser therapy has been shown to enhance muscle performance in strength training and maximum tests of effort in isokinetic dynamometry in humans. [26] Laser therapy is a safe treatment intervention that has been widely used in the treatment of patients with knee osteoarthritis. [27]

Laser penetration into tissue is dependent on the wavelength of the laser light, Wavelengths in the range 600–700 nm are used to treat superficial tissue, and longer wavelengths in the range 780–950 nm, which penetrate further, are used to treat deeper-seated tissues. [28] The laser device that used in this study provide combination of two wavelengths a continuous emission of a wavelength of 808 nm and Pulsed emission of a wavelength of 905 nm. The continuous component is less effective at relieving pain, rather it acts upon inflammation and edema, which the pulsed component does not. It is thought that the action of this mode is achieved by encouraging adenosine triphosphate production, stimulating blood and lymphatic circulation, and the subsequent faster reabsorption of fluid. [29]

These were in line with Helianthi *et al*.,2016, who performed RCT to compare the effectiveness of active laser acupuncture with placebo on reducing pain intensity and improving functional outcome in geriatric patients with knee osteoarthritis (OA). Interventions were carried out using a gallium aluminum arsenide laser device at the ST35 Dubi, ST36 Zusanli, SP9 Yinlingquan, GB34 Yanglingquan and EX - LE - 4 Neixiyan acupuncture points on the affected knee for ten sessions of treatment. Results was that VAS scores were significantly improved in the active laser acupuncture group compared to the placebo group. [30]

The study come in agreement with Al Rashoud *et al*.,2014, who evaluated the efficacy of low-level laser therapy applied at acupuncture points in knee osteoarthritis. They concluded that short-term application of LLLT to specific acupuncture points in association with exercise and advice is effective in reducing pain and improving quality of life in patients with knee osteoarthritis. [31]

These results were supported by Chiung-Hui *et al*.,2021, who made RCT to study the effect of laser acupuncture improves early outcomes of osteoarthritis patients' physical functional ability after total knee replacement, this randomized controlled trial demonstrated that ALLLT improves outcomes of knee joint function in terms of joint flexion and stiffness early in patients with osteoarthritis receiving TKR in the first three postoperative days. ALLLT, as a noninvasive, painless, and highly safe procedure, is a suggested regimen for clinical care of patients with osteoarthritis receiving TKR to improve knee physical function. [32]

These results were in consistent with the findings of Hung *et al*., 2021, who evaluate the treatment effectiveness of laser acupuncture (LA) in patients with musculoskeletal pain.in total, 20 articles comprising 568 patients receiving LA and 534 patients receiving sham treatment were included in the current study. They concluded that LA significantly reduced pain, disability, and functional impairment in patients with musculoskeletal disorders. [33] In contrast to Hinman *et al*., 2014 who performed RCT to determine the efficacy of laser and needle acupuncture for chronic knee pain. And concluded that in patients older than 50 years with moderate or severe chronic knee pain, neither laser nor needle acupuncture conferred benefit over sham for pain or function. Their findings do not support acupuncture for these patients. [34]

These results disagreed with Yurtkuran *et al*., 2007, the purpose of this study was to investigate the effects and minimum effective dose of laser acupuncture in knee osteoarthritis (KOA), and to determine if it is superior to placebo treatment (sham) in the evaluation of clinical-functional outcome and quality of life. Methods: In this randomized, placebo-controlled study, patients with grade 2 and 3 primary KOA were selected. Group I (n = 27) received 904-nm low-level laser irradiation with 10 mW/cm^2 power density, 4 mW output power, 0.4 cm^2 spot size, 0.48 J dose per session, and 120-sec treatment time on the medial side of the knee to the acupuncture point Sp9. and concluded that laser acupuncture was found to be effective only in reducing periarticular swelling when compared with placebo laser. [35]

Analgesia induced by therapeutic US may be due to both thermal and nonthermal mechanisms. The reduction of soft tissue pain by US could result from increased capillary permeability and tissue metabolism, enhancement of fibrous tissue extensibility and elevation of pain threshold by thermal mechanism. However, nonthermal mechanisms may act in pain relief by stimulating tissue regeneration, changing cell membrane permeability and increasing intracellular calcium in the nervous system. [36] The improvement in stiffness and ROM of knee and walking

time may depend on the healing and thermal effects of US on periarticular structures of knee joint. Deep heating with US can produce a temporary increase in the extensibility of highly collagenous structures such as tendons, ligaments and joint capsule. Besides its thermal effects, nonthermal effects of US can modulate cell diffusion, fibroblast production, collagen synthesis, alter extracellular matrix arrangement, break down adhesion and accelerate healing. [37] Therapeutic US is one of the suggested physical agents used to treat KOA. It is high-frequency mechanical energy consisting of alternative compression and rarefaction that may be continuous or pulsed. Pulsed US (PUS) is agreed to be the preferred mode, which is effective in pain alleviation and function improvement in KOA. [38]

These results were supported by Dantas *et al*., 2021, who performed systematic review and meta-analysis with grade quality assessment therapeutic ultrasound for knee osteoarthritis. Four studies (N = 234 participants) were eligible for inclusion in their primary analyses assessing therapeutic US versus sham. They concluded that use of therapeutic US provides pain relief and functional improvement when used as an adjuvant therapy in individuals with KOA. [39]

Similarly, Zhang *et al*., 2016, did systematic review and meta-analysis to explore the effects of therapeutic ultrasound with sham or no intervention on pain, physical function and safety outcomes in patients with knee osteoarthritis. Ten randomized controlled trials (645 patients) met the inclusion criteria. The authors suggested that therapeutic ultrasound is beneficial for reducing knee pain and improving physical functions in patients with knee osteoarthritis and could be a safe treatment. [40]

These come in agreement with Jia *et al*., 2016, who performed RCT to investigate the effects of focused low-intensity pulsed ultrasound (FLIPUS) therapy on the functional and health status of patients with knee osteoarthritis (KOA). A total of 106 subjects with bilateral KOA were randomized sequentially into two groups. Participants were assigned into group I (FLIPUS + diclofenac sodium sustained-release tablets) or group II (sham FLIPUS + diclofenac sodium sustained-release tablets) at a 1:1 ratio in a random and double-blinded manner. In group I the four US probes were close to the surface skin of the ST 35 acupoint, EX-LE 4 acupoint and interior and lateral knee joint spaces. And revealed that FLIPUS is a safe and effective treatment modality that causes pain relief and improves function and HRQoL in patients with knee OA. [41]

These results were supported by Yeğin *et al*., 2017, who studied the effect of therapeutic ultrasound on pain and physical function in patients with knee osteoarthritis. The study involved 62 patients. The patients were randomly divided into two groups. The patients in group 1 (n 5 30) were administered 1 W/cm2, 1 MHz continuous US, and the patients in group 2 (n 5 32) were administered sham US. And concluded that therapeutic US was shown to be an effective and reliable method for reducing pain and improving function in knee OA in the short term, but its beneficial effects did not persist in the long term. [42]

Similarly, Tascioglu *et al*., 2010, studied short-term effectiveness of ultrasound therapy in knee osteoarthritis. Patients were randomly assigned to three groups: group 1 received continuous ultrasound, group 2 received pulsed ultrasound, and group 3 received a 'sham' (placebo) ultrasound for 5 min each session. In conclusion, pulsed ultrasound therapy is a safe and effective treatment modality in patients with knee OA. [43]

Similarly, Cakir *et al*., 2014, performed RCT to study efficacy of therapeutic ultrasound for the management of knee osteoarthritis. The aim of this study was to compare whether the effectiveness of continuous ultrasound (US) was superior against pulsed US and against sham US in knee osteoarthritis. A randomized controlled study was carried out on 60 patients diagnosed with knee osteoarthritis according to American College of Rheumatology. The patients were randomized into the following three treatments: (1) continuous US (at a frequency of 1 MHz with intensity of 1 W/cm), (2) pulse US (same frequency and intensity on 1:4 pulse ratio), and (3) sham US. And concluded that all assessment parameters significantly improved in all groups without a significant difference. This result suggested that therapeutic US provided no additional benefit in improving pain and functions in addition to exercise training. [44]

Also, Ulus *et al*., 2012, conducted RCT to evaluate the short-term effectiveness of ultrasound (US) therapy on pain, physical function, ambulation activity, disability and psychological status in patients with knee OA. Forty-two inpatients with bilateral knee OA were randomized by an independent researcher not involved in the data assessment, to receive either therapeutic continuous US (group 1) or sham US (group 2). A 1-MHz US head was used, set to an intensity of 1 W/cm for 10 min. and concluded that US therapy is safe but use of US in addition to conventional physical therapy programs seems to have no further significant effect in people with knee OA. [45]

Muscle weakness, and in particular quadriceps weakness, has been implicated in knee OA, which increases knee pain; and there is strong evidence suggesting that exercises can reduce pain and improve function in patients with OA. [46] Therefore, exercises commonly used in clinical practice and supported by the findings of previous studies. [47, 48] were performed to enhance muscle strength mainly the gluteus maximus, gluteus medius and quadriceps. [49]

The study supported by Raposo *et al*., 2021, who performed systematic review to study Effects of exercise on knee osteoarthritis. total of 4499 studies were retrieved and 19 articles met the inclusion criteria. And concluded that exercise programmes appear to be safe and effective in knee osteoarthritis patients, mainly regarding pain and strength improvement. Pilates, aerobic and strengthening exercise programmes performed for 8–12 weeks, 3–5 sessions per week; each session lasting 1 h appear to be effective. Both aquatic and land- based programmes show comparable and positive effects. [50]

This is in line with Rocha *et al*., 2019, who performed a systematic review with meta-analysis, to study the effects of a rehabilitation, physical training program for the treatment of pain and muscle strength in knee osteoarthritis (OA). They analyzed studies published between 2008 and 2018 referenced at the Medline (National Library of Medicine) database, selecting 7 randomized controlled clinical trials about exercise programs to improve pain and muscle strength in patients with knee OA with Physiotherapy Evidence Database (PeDro) score higher than 8. and concluded that that there was an improvement of pain in all articles that performed muscle strengthening, but there is still an obstacle to the protocols used. [51]

Similarly, to Li *et al*.,2016 who analyze the effectiveness of resistance exercise in the treatment of knee osteoarthritis on pain, stiffness, and physical function. data from 17 randomized clinical trials including 1705 patients were integrated, and concluded that Resistance exercise is beneficial in terms of reducing pain, alleviating stiffness, and improving physical function in patients with knee osteoarthritis. [52]

In contrast to Bartholdi *et al*.,2017, who performed systematic review to analyze if exercise interventions for patients with knee osteoarthritis (OA) following the American College of Sports Medicine (ACSM) definition of muscle strength training differs from other types of exercise, and to analyze associations. A systematic search in 5 electronic databases was performed to identify randomized controlled trials comparing exercise interventions with no intervention in knee OA, and reporting changes in muscle strength and in pain or disability assessed as standardized mean differences (SMD) with 95% confidence intervals (95% CI). between changes in muscle strength, pain, and disability. And concluded that Exercise interventions following the ACSM criteria for strength training provide superior outcomes in knee extensor strength but not in pain or disability. [53]

Conclusion

The results of this study demonstrate that application of laser acupuncture in conjunction with exercise for patients with KOA was more effective in pain relief and improvement of knee joint ROM and functional ability than acupuncture focused ultrasound conjunction with exercise and exercises alone.

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