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RESEARCH ARTICLE

Effect of pulsed electromagnetic field versus pulsed high intensity laser in the treatment of men with osteopenia or osteoporosis: a randomized controlled trial [version 1; peer review: awaiting peer review]

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Abstract

Background: Osteoporosis has been related to a negative impact on several aspects of patient health, including physical, mental, and emotional well-being. The objective of this study was to examine the effects of pulsed electromagnetic fields (PEMF) and pulsed Nd-YAG laser therapy (HILT) on men with osteopenia or osteoporosis.

Methods: Ninety-five men with osteopenia or osteoporosis (mean age, 52 years; mean height, 176 cm; mean weight, 83 kg; mean body-mass index (BMI), 26.86 kg/m²) took part in the study, and they were randomly assigned to one of three groups: Group 1 received PEMF and exercise program (PEMF +EX), Group 2 received HILT and exercise program (HILT+EX), and Group 3 received exercise program only (EX). PEMF was applied three times per week for 12 weeks using a full-body mat, while HILT was applied to the lower back and hip regions with a total dose of energy of 3000 J delivered in two treatment stages. Flexibility, aerobic exercise, strength, weight-bearing, and balance exercises are included in exercise program, which is followed by whole-body vibration training. Bone mineral density (BMD) of the total hip and lumbar spine, bone markers, health-related quality of life (HRQoL), and fall risk are all outcome measures.

Results: There were no significant differences in the parameters between the groups at the baseline ($P > 0.05$). Patients in all groups, however, showed significant improvements in all measured parameters following treatment ($P < 0.05$), with Group 1 and Group 2 showing much greater improvements than Group 3.

Conclusion: After 12-weeks of treatment, PEMF combined with

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exercise is more effective than HILT combined with exercise or exercise alone in increasing BMD and promoting bone formation, suppressing bone-resorption markers, and improving quality of life and fall risk, with the effects lasting up to six months.

This study was registered in the ClinicalTrial.gov PRS ([NCT05029440](#), 26/08/2021).

Keywords

Pulsed electromagnetic field, pulsed high intensity laser, Exercise program, bone mineral density, osteopenia, osteoporosis.

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Introduction

Osteoporosis (OP) is a systemic bone disease characterized by a gradual loss of bone mass and tissue degradation, resulting in impaired bone strength, significant deterioration of bone microarchitecture, and decreased bone mass, caused by bone resorption outpacing bone formation, resulting in increased bone fragility and a high fracture risk.^{1,2} Osteopenia is a condition marked by low bone mineral density (BMD) that can lead to OP. Because patients have no early symptoms, most OP cases are detected after a fracture.³

Osteoporosis and the fractures that accompany it are a major public health concern around the world. OP is estimated to affect over 200 million people worldwide, resulting in over 8.9 million fractures each year.⁴ OP affects 34% of women and 30.7 % of men aged 50 to 79 years in Saudi Arabia.⁵

Osteoporosis has been related to a negative impact on several aspects of patient health, including physical, mental, and emotional well-being, with hip and vertebral fractures having the greatest impact on patients' quality of life.⁶ An increase in fragility fractures is a major complication of OP, which leads to severe morbidity, mortality, disability, and a deterioration in patients' quality of life.^{7,8}

Despite current advancements in healthcare systems, the prevalence of OP among older adults in Saudi Arabia continues to increase, and proven effective medication to treat low BMD and decrease the risk of fractures is becoming more widely available.⁹ Unfortunately, because OP is asymptomatic, its care is currently inadequate, and the illness is frequently undiagnosed and untreated until it has progressed to the point where fractures occur.¹⁰

There is currently no universally approved strategy for therapeutic decision-making in men. To minimize fracture risk, a daily calcium intake of 1000-1200 mg (from dietary sources or supplements) and adequate vitamin D intake to achieve 25 (OH) D concentrations of >30 ng/ml are recommended.¹¹ Men should participate in regular weight-bearing and muscle-strengthening physical exercise, as well as quit smoking and reduce their alcohol consumption.¹²

Exercise is a well-known method of preventing bone loss as we age, but high-intensity loading is required to trigger a beneficial adaptive response.¹³ Progressive resistance training combined with weight-bearing impact activity is most likely the most advanced form.¹⁴ Closed kinetic chain exercises can help postmenopausal women with OP increase their BMD and decrease their fall risk. As a result, these activities should be used in conjunction with other OP therapy strategies.¹⁵

Pulsed high-intensity laser therapy (HILT) penetrates the tissue deeply, triggering chemical and mechanical changes as well as thermal mechanisms.¹⁶ Physical properties of HILT beams, such as mechanical and thermal effects, may be responsible for the profibrinolytic effects. Inflammation and painful sensations are promptly reduced by HILT.¹⁷ It employs a waveform with regular amplitude peaks and shot duration that induce photochemical and photothermic effects in deeper tissues, resulting in increased blood flow, vascular permeability, cell metabolism, and tissue photomechanical level, all while requiring relatively short application times.³

Pulsed electromagnetic field (PEMF) has a lot of potential to become a stand-alone or adjuvant treatment approach for musculoskeletal disorders such as osteopenia and OP because of its noninvasiveness, safety, and efficacy.¹⁸ Several studies have investigated at the underlying cellular and subcellular mechanisms of PEMF stimulation on a variety of musculoskeletal disorders, providing a molecular basis for expanding its therapeutic application.^{19–22}

The paucity of studies focusing on such a high-impact population in Saudi Arabia is making it difficult to establish effective intervention programs that address specific concerns for this group.^{23,24} The goal of this research was to compare the effects of PEMF and HILT in the treatment of men with osteopenia or osteoporosis.

Methods

Ethical declaration and trial registration

This was a randomized regulated study with three measurement intervals. Umm Al-Qura University's Biomedical Research Ethical Committee accepted and deemed this project properly achievable (Approval number: HAPO-02-K-012-2021-540). The study was also listed with the Clinical Trial Registry (Clinical [Trials.gov](https://www.trials.gov) ID: NCT05029440).

Power assessment

The proper sample size was calculated using G-power for Windows, with estimated power = 0.95 and = 0.05. The effect size was 0.30 utilizing evaluation of variance (ANOVA) with in-between interface in three groups and three assessment times. A minimum of 92 patients was identified in all therapy groups.

Participants

Ninety-five men over the age of 45 were enrolled in the study (mean age, 52.02 ± 1.83 years; average height, 176 ± 1.89 cm; mean weight, 83.21 ± 2.34 kg; average BMI, 26.86 ± 1.34 kg/m²). All applicants were initially evaluated for the enrollment requirements. The screening method included a health and psychiatric record, involving height, weight, and BMI, in addition physical and lab analysis. Every participant was physically evaluated to determine their level of physical activity. During the examination, any gait difficulties, muscular distress, or joint discomfort were reported. If applicants had physical treatment or a shift in their pharmacological treatment in the prior three months, they would not be allowed to use any extra treatments, specific regimens, or aerobic training options for the duration of the study.

Participants were told to approach their standard exercises as regular all through the preliminary and to stay away from any methodical exercise preparing programs. Each of the patients were determined to have osteopenia or osteoporosis (T-scores of <-1.5) utilizing dual-energy X-ray absorptiometry (DEXA). All members were assessed by a similar assessor before treatment, following 12 weeks of treatment, and six months after the end of the treatment. Follow-up was done simultaneously following a half year assessment to control for diurnal varieties. Following the pre-treatment assessment, the review objectives were tended, and all members gave composed informed assent for their interest and the distribution of their review results. The study's stream outline shows the entirety of the proposal means (Figure 1).

Diabetes, intraocular focal points, coagulation record, cardiopulmonary disorders, extreme vascular and kidney sickness, thyroid illness, heart pacemaker, life-threatening blood pressure, advanced neurological manifestation, persistent impairing joint pain, utilization of any drugs that influence bone mineralization, serious liver sicknesses, presence of

Figure 1. Flow chart of the study based on CONSORT criteria.

osteoporotic crack, critical sickness, neuropsychiatric problems (e.g., dementia), alcohol misuse, extreme sadness, bipolar syndrome, or psychosis and BMI <19 kg/m² or >31 kg/m² were completely avoided from the scheme.

Randomization

The applicants were arbitrarily allocated to one of three groups after the initial evaluation of using an electronic GraphPad Prism (RRID:SCR 002798; R is an open access alternative). Group 1 received PEMF combined with an exercise program (PEMF+ EX), Group 2 received HILT combined with an exercise program (HILT+ EX), and Group 3 received an exercise program only (EX).

Outcome measures

Age (years), tall (cm), weight (kg), and BMI (kg/m²), BMD of the lumbar spine (L2-L4) and entire hip, HRQoL, and fall risk, were all measured in all participants. Bone tests such s-OC, s-NTX, s-CTX, BSAP, PTH, and Vit D were assessed Pre-treatment, 12-weeks post-treatment, and six-months as follow-up estimations were taken from all groups.

BMD evaluation

BMD was measured in all applicants at the lumbar spine (L2-L4) and overall hip pre-treatment, after 12 weeks of therapy, and at six-months as a follow-up utilizing a PRIMUS DEXA densitometer (OsteoSys, CO. LTD Korea). The manufacturer's Middle East (ethnicity) reference database was applied to determine T-scores for assessing osteopenia and OP. Before the assessments, the machines were calibrated on a daily basis applying spine phantoms provided by the company. Throughout the trial, the same operator performed all measures on all participants.

Bone markers

Blood samples were collected from all applicants by means of plan vacutainer tubes and handled to harvest serum, which was put away at -20°C until required for examination of osteocalcin (s-OC), N-terminal telopeptide of type I collagen (s-NTX), carboxy-terminal collagen crosslinks (s-CTX), bone-explicit antacid phosphatase (BSAP), parathyroid hormone (PTH), and 25-hydroxy nutrient D (Vit D). All examples were dissected in three-time.

Health related quality of life (HRQoL)

A self-controlled ECOS-16 survey was used to assess all patients' HRQoL. ECOS-16 has been shown to have high psychometric qualities and is a helpful tool for assessing HRQoL in older people with OP in both research and clinical practice. Physical function, pain, anxiety of sickness, and psychosocial work are all addressed in the ECOS-16 questionnaire. Each item's score runs from 1 (best HRQoL) to 5 (worst HRQoL).

Fall risk assessment

A Biodex balance device was used to assess the risk of falling (Biodex, New York, USA). A fall hazard test protocol is an accessible test that measures the stability of participants over 50 with varying balancing abilities and allows for the detection of potential falls. While the platform was moving, the applicants stood on the stand and concentrated to keep their base of gravity inside the middle of the bottom of support. The stage stability is rated from 1 to 12, with 1 being the most unstable. The platform becomes less stable as the resistance level drops. The test lasted 20 seconds; the stage was eight, and the attitude was bilateral with eyes open. The applicant did three test replications with a 30 second break between sets. The results were assessed to those of an age-corresponding healthy person.

Treatment Interventions

Full-body pulsed electromagnetic field

A 68"×23"×1.5" mat applicator and an 8"×10"×2.5" pillow applicator from Sedona Pro PEMF Systems, Portland Oregon USA Ltd, were used to apply PEMF to the full body. The complete-body full strength is 30 gauss (3,000 micro-Tesla), while the pillow is 101 gauss (10,000 micro-Tesla). This mat emits a PEMF with a frequency range of 0.01-15,000 Hz, using sinusoidal, rectangular, multi-resonance, impulse, or sawtooth waveforms (10,000 micro-Tesla). Each participant lay on the mat for 30 minutes three points a week for a total of 12 weeks.¹⁹

High-intensity laser therapy

HILT was delivered by a HIRO 3 (Asalaser, Arcugnano, Italy). A pulsed Nd-YAG laser with a highest power of 3 kW, an usual power of 10.5 W, a wavelength of 1064 nm, a fluency level of 510-1780 mJ/cm², a brief duration of 120-150 ls, a low frequency of 10-30 Hz, 0.1 percent duty cycle, a probe diameter of 0.5 cm, and a spot size of 0.2 cm² are all included in the HILT machine. For a time of 12 weeks, all applicants received three sessions per week. The scan was done longitudinally and transversely in the lower back region to encompass the lumbar vertebrae, paraspinal muscles, and upper part of the gluteus maximus. The anterolateral, lateral, and posterolateral parts of the proximal hip region were also

treated with the laser. A total dose of energy of 3000 J was delivered in two treatment stages. The primary period was completed with rapid manual imaging at 510, 610, and 710 mJ/cm² in three successive subphases and 500 J in each subphase for a total of 1500 J. The last stage was similar the primary stage excluding that the imaging was slow. The mean area for the higher thigh or lower back was 200 cm² with a normal fluency of 15 J/cm², and the treatment time for each region was about 18 minutes. HILT was calibrated for constant output throughout the study period by the manufacturer.³

Exercise training program

The exercise schedule lasted 12 weeks and comprised of three 60-minute meetings per week, all of which took place in the exercise lab under the supervision of the researchers. Each session started with a 40-minutes including (flexibility, aerobic, strengthening, weight-bearing, and stability exercises), followed by a WBV training exercise. Starting with a warm-up and progressively increasing the strength of the training session is recommended in the initial training program. Patients in all groups were trained to do the similar exercise schedule at home once per day. WBV training involved a low-rate (30–40 Hz) vibration incentive delivered in a controlled setting (2–4 mm peak to peak). The pulsation spotlight began with one set of 30 seconds at 2 mm amplitude and 30 Hz, then progressed to two sessions of 5 minutes each at a high amplitude of 35 Hz. At the end of the session, they engaged in a cool-down phase that included relaxation and stretch exercises. All of the patients were encouraged to walk for half an hour every day. They were given a booklet describing the exercises, as well as a report on exercise compliance. Patients would be dropped out of the study if they missed three consecutive exercise sessions. Refer to the previous study for a more detailed description of the exercise protocol.¹⁹

Statistical analysis

Based on the power study, G-Power 3.1 for Windows was applied to determine the expected sample size. SPSS for Windows, version 21 (statistical Package of Social Science, IBM, USA), was applied to analyze patient demographic information such as age, weight, height, and BMI. To compare intervals between management groups, an ANOVA with a post hoc Bonferroni test was implemented. The starting point, after-therapy, and six-month follow-up evaluations in each group were calculated applying a frequent measures ANOVA with a post hoc Bonferroni test. The degree of significance was approved at 0.05 for all groups.

Results

For this study,⁵⁹ a total of 110 men were selected as potential participants (Figure 1). The presence of 15 were ruled out (nine not meeting the inclusion criteria, and five refused to participate). A total of 95 men were randomly allocated to one of three groups in this study. Between the three groups, there were no significant differences in mean age, weight, height, BMI, or vitamin D levels (Table 1). After treatment, all participants were 100% adherent with their exercise programs.

BMD of the lumbar spine and total hip

Pretreatment scores for BMD of the lumbar spine and total hip between the three groups were not significantly different ($P>0.05$) at baseline (Table 2). There were significant differences ($P<0.05$) when comparing pre and post scores in the

Table 1. Baseline values among treatment groups.

	Group 1 (PEMF+EX)	Group 2 (HILT+EX)	Group 3 (EX)	F value	P value
Age (years)	52.28± 1.80	52.15±2.00	51.61±1.66	1.185	0.310**
Weight (kg)	82.57 ± 2.69	83.28 ± 2.28	83.79 ± 1.89	2.212	0.115**
Height (cm)	1.75 ± 2.06	1.76± 1.73	1.77 ± 1.35	0.001	0.999**
BMI (kg/cm ²)	26.96 ± 1.30	26.89± 1.32	26.75 ± 1.40	0.199	0.819**
Vitamin D level (ng/mL)	25.72±5.58	27.40±5.90	26.62±6.07	0.660	0.519**
Number of patients	32	32	31		
Number, osteopenic/ osteoporotic hip (%) −1.1<T< −2.4	20 (63%) /12 (37%)	22 (69%) /10 (31%)	21 (68%) /10 (32%)		
Number, osteopenic/ osteoporotic lumbar (%) −1.1<T< −2.4	21 (66%) /11 (34%)	21(66%) /11 (34%)	22 (71%) /9 (29%)		

BMI, body-mass index; EX, exercises; PEMF, pulsed electromagnetic field; HILT, Pulsed high intensity laser; P, probability value.

**Non-significant differences in the same measurement interval among treatment groups (one-way ANOVA; $P > 0.05$).

PEMF+Ex and HILT+EX groups after 12 weeks and six months of treatment, with significant improvement in the PEMF+EX group over the HILT+EX group, but no significant differences ($P>0.05$) in the EX-group (Table 2).

Health related quality of life (HRQoL)

At baseline, there were no significant differences in HRQoL scores between the three groups ($P>0.05$) (Table 2). There were significant differences ($P<0.05$) in the three groups' baseline, 12 week, and six-month scores, with significant improvement in the PEMF+Ex group compared to the HILT+EX and EX groups, as shown in Table 2.

Fall risk

As shown in Table 2, there were no significant differences ($P>0.05$) in pretreatment fall risk scores between the three groups at baseline, but there were significant differences ($P<0.05$) in the three groups after 12 weeks of treatment and after six months of follow up after treatment, with significant improvement in the PEMF+Ex group compared to the HILT+EX and EX groups.

Bone markers

The s-OC, s-NTX, BSAP, PTH were declined markedly in the PEMF+ EX group after treatment in comparison with baseline values ($P<0.001$). While the total calcium and 25(OH) VD were non-significant difference at baseline, and 12 weeks after treatment in the PEMF+ EX group ($P>0.05$). Regarding the HILT+EX group the s-OC, s-NTX, BSAP, PTH were significantly reduced after treatment in comparison with baseline values ($P<0.001$). Meanwhile the total calcium and 25(OH) VD were insignificantly change at baseline, and 12 weeks after treatment in the HILT+EX group ($P>0.05$). Simultaneously the amount of s-OC, s-NTX, BSAP, PTH showed significant reduction in EX group after treatment in compare with baseline values ($P<0.001$). On the other hand, total calcium and 25(OH) VD revealed non-significant difference at baseline, and 12 weeks after treatment in the EX-group ($P>0.05$) as displayed in Table 3.

In the post-treatment group, the s-OC, s-NTX, BSAP, PTH were significantly reduced in the PEMF+ EX when compared with the HILT+EX and EX groups. Also, those parameters were significantly reduced in the HILT+EX as compared with EX group. While the total serum calcium and 25(OH) VD were non-significant change between all treated groups as showed in Table 3.

The S-OC was significant decreased in the PEMF+ EX group as compared with HILT+EX and EX groups after follow-up at six months. The s-NTX was reduced markedly in the PEMF+ EX and HILT+EX when compared with EX. While the BSAP and PTH were significantly lowered in the PEMF+ EX groups compared with HILT+EX and EX groups after follow-up six months, while those parameters were lower in the HILT+EX than the EX-group. The total calcium and 25(OH) VD were non-significant change between all groups after six months follow-up as displayed in Table 3.

Discussion

The study's main findings show that following 12 weeks of treatment, PEMF combined with exercise has a greater effect than HILT+EX or EX alone in boosting BMD and enhancing bone formation, suppressing bone-resorption indicators, improving quality of life, and reducing fall risk, with these effects persisting up to six months after treatment.

The PEMF effects

The effects of PEMF on living organisms are well documented. Cells in organisms have membrane that electrically charged and closely controls the electrically charged ions concentration which act as potent signal mediators, such as Ca^{+2} or Na^{+} .²⁵ As a result, it's believed that the membrane level is site of the majority of PEMF effects in cells. PEMF has been proven to act on the concentrations and dependent pathways of Ca^{+2} ,^{26,27} while Varani *et al.* have recently demonstrated that PEMF regulates Adenosine receptors.²⁸ In fact, the recent evidence that the transducing PEMF effects in cells is the role for primary cilia by Yan *et al.*²⁹ and Xie *et al.*³⁰ could be one of a wide activity on membrane passaging, which includes receptor trafficking. PEMF has been demonstrated to change defenses against oxygen species reaction,³¹ bioactive factor synthesis, and pathways between cells such as the sAC–cAMP–PKA–CREB signaling pathway.²¹

PEMF stimulation enhances the anabolic actions in skeleton of the unloaded hindlimb of rats, as proved by biochemical, mechanical, micro-computed tomography, and morphometric results, according to Jing and colleagues.³² They further show that portmanteau signaling may be involved in PEMF's anabolic actions on bone. PEMF, with no side effects method, could become a useful treatment modality for osteopenia and/or osteoporosis, as well as a countermeasure for bone loss, according to their findings.³²

Recently in a review, the PEMFs signaling pathways in bone repair have been summarized, including Ca^{+2} , Wnt/-catenin, mitogen-activated protein kinase, fibroblast, vascular endothelial and transforming growth factor/bone morphogenetic proteins, insulin-like growth factor, and cAMP/protein. Also, the mammalian target of the pathway of rapamycin has

Table 2. Changes in bone mineral density, HRQoL and fall risk among treatment groups.

	Group 1 (PEMF+EX)				Group 2 (HLT+EX)				Group 3 (EX)				P value	
	Pre	12wk	6M		Pre	12wk	6M		Pre	12wk	6M		Pre	6M
Lumbar spine (BMD) Mean $\pm$ SD	0.93 $\pm$ 0.05	1.05 $\pm$ 0.09	1.07 $\pm$ 0.07		0.92 $\pm$ 0.06	1.01 $\pm$ 0.08	1.02 $\pm$ 0.08		0.92 $\pm$ 0.05	0.95 $\pm$ 0.07	0.96 $\pm$ 0.09			
P value	< 0.0001*				< 0.0001*				0.121**				0.505**	< 0.0001*
F value	32.46				16.44				2.17				0.688	10.626
Total hip (BMD) Mean $\pm$ SD	0.92 $\pm$ 0.05	1.02 $\pm$ 0.09	1.05 $\pm$ 0.09		0.92 $\pm$ 0.06	0.97 $\pm$ 0.08	0.99 $\pm$ 0.08		0.92 $\pm$ 0.05	0.94 $\pm$ 0.07	0.96 $\pm$ 0.08			
P value	< 0.0001*				0.001*				0.052**				0.935**	< 0.0001*
F value	21.10				7.86				3.05				0.067	9.524
HRQoL Mean $\pm$ SD	45.71 $\pm$ 2.15	29.50 $\pm$ 1.41	23.68 $\pm$ 1.74		44.81 $\pm$ 2.14	31.62 $\pm$ 1.56	27.50 $\pm$ 1.96		45.45 $\pm$ 2.47	34.22 $\pm$ 2.09	31.93 $\pm$ 2.32			
P value	< 0.0001*				< 0.0001*				< 0.0001*				0.2651**	< 0.0001*
F value	1426				723.1				315				1.347	131.8
Fall Risk Mean $\pm$ SD	3.57 $\pm$ 0.08	3.09 $\pm$ 0.09	3.03 $\pm$ 0.05		3.56 $\pm$ 0.07	3.40 $\pm$ 0.08	3.26 $\pm$ 0.08		3.54 $\pm$ 0.06	3.41 $\pm$ 0.09	3.40 $\pm$ 0.08			
P value	< 0.0001*				< 0.0001*				< 0.0001*				0.302**	< 0.0001*
F value	461.55				544.23				20.25				1.213	212.691

12W, 12weeks; 6M, 6 Months; BMD, bone mineral density; HRQoL, health related quality of life; SD, standard deviation.

*Significant difference in the same measurement interval among treatment groups (one-way ANOVA; $P < 0.05$).

**Significant difference among the repeated measurement intervals in each treatment group (repeated measures ANOVA; $P < 0.05$).

***Non-significant differences.

Table 3. Changes in bone markers among treatment groups.

	Group 1 (PEMF+EX)				Group 2 (HILT+EX)				Group 3 (EX)				P value	
	Pre	12wk	6M		Pre	12wk	6M		Pre	12wk	6M		pre	6M
s-OC (ng/ml)	25.05±6.82	14.42±2.64	15.90±3.44		25.30±7.09	16.75±3.33	18.65±6.86		23.65±7.1	18.35±2.55	19.62±4.41			
P value	<0.0001*				<0.0001*				0.0002*				0.598**	0.013*
F value	48.33				17.87				9.58				0.515	4.50
s-NTX (nmol/L)	26.55±7.66	14.71±4.70	15.76±3.56		26.40±7.61	18.42±7.20	17.67±5.18		27.10±7.2	21.52±7.52	22.35±6.40			
P value	<0.0001*				<0.0001*				0.005*				0.927**	<0.0001*
F value	44.13				16.45				5.64				0.076	13.53
BSAP (U/L)	85.71±16.4	35.47±11.3	42.10±8.85		89.32±11.2	50.50±11.19	53.75±12.60		88.2±11.8	63.50±8.31	76.52±12.57			
P value	<0.0001*				<0.0001*				<0.0001*				0.544**	<0.0001*
F value	150.6				108.8				38.76				0.612	73.24
PTH (pg/mL)	84.40±7.31	55.60±6.83	58.85±7.09		86.90±3.98	61.60±11.91	56.32±12.22		85.32±4.6	73.9±11.30	77.01±12.05			
P value	<0.0001*				<0.0001*				<0.0001*				0.190**	<0.0001*
F value	158.9				83.54				11.02				1.691	34.83
T. Calcium mg/dl	9.06±0.61	9.27±0.89	9.41±0.75		9.24±0.598	9.48±0.711	9.30±0.91		9.19±0.73	9.35±0.731	9.44±0.73			
P value	0.184**				0.416**				0.397**				0.521**	0.765**
F value	1.725				0.885				0.931				0.657	0.268
25(OH) VD (ng/mL)	25.72±5.58	27.97±6.99	28.38±6.71		27.40±5.90	28.07±7.13	28.32±6.48		26.62±6.1	29.02±6.77	26.40±6.93			
P value	0.213**				0.844**				0.229**				0.520**	0.417**
F value	1.575				0.170				1.499				0.659	0.883

12W, 12weeks; 6M, 6Months; s-OC; Serum osteocalcin 2-11; s-NTX; Serum amino-terminal cross-linking telopeptide of type I collagen; BSAP; Bone Serum Alkaline Phosphatase; PTH; Parathyroid hormone; 25(OH) VD; vitamin D.

*Significant difference in the same measurement interval among treatment groups (One-way ANOVA; $p < 0.05$). **Non-significant differences.

(Repeated measures ANOVA; $p < 0.05$).

been shown to be the PEMF signaling pathway involved in bone building. PEMF exposure affected the formation of growth factors, enhancing the formation of extra-cellular matrix proteins and enhancing tissue repair.¹⁵

Physical therapy has gained more attention in recent years, in addition to pharmacotherapy, for this type of disease.³³ PEMF has been shown to have potential effect in the treatment of OP^{21,34} as an effective physiotherapy for various disorders of bone. Management of postmenopausal osteoporosis with PEMF at particular dosage (8 Hz, 3.82 m T, 40 minutes per day, and six sessions per week) had the same treatment effect for 24 weeks, according to a randomized, active-controlled clinical trial.³⁴

Ebid *et al.* concluded in a recent randomized controlled study of osteoporotic men that PEMF with an exercise program has an obvious role in management of osteoporosis, in increasing BMD, and enhancing bone formation than exercise alone and PEMF alone, and suppresses the markers of bone-resorption following 12-weeks of treatment, and the effect continued up to six months.¹⁹

Because of its efficacy and non-side effects, PEMF has a lot of potential as alternative treatment method for musculoskeletal problems. Many studies have investigated into the PEMF stimulation on various musculoskeletal disorders including underlying cellular and subcellular mechanisms, as a molecular basis presenting its clinical application. The unknown issues as the deeper mechanisms and the optimal using parameter, remains unresolved. As a result, further research from well-designed, high-quality studies is necessary before they can be widely used in clinical situations to know the deeper mechanisms, the best treatment dosage, and establish the ideal protocol for decision-making about health-care. In conclusion, with suitable patient selection, well defined indications, and consistent treatment strategies, PEMF have the potential to play a significant role in the management of musculoskeletal disorders in the future.¹⁸

Effect of HILT

Comparing to baseline scores, the combined HILT and exercise effectively improve the lumbar and hip BMD. By stimulating cytochrome oxidase in the mitochondrial activity of osteoblast cells,³⁵ laser treatment can modify cellular metabolism by contributing in the production of an electrochemical potential and the production of oxygen molecules that are utilized to generate adenosine triphosphate.³⁶ Lasers stimulate proliferation by providing energy to tissues and growth factor secretion, as well as improve tissue function by enhancing DNA and RNA synthesis,³⁷ resulting in new bone formation and enhanced osteopenic fracture repair.³⁵

Previous HILT studies have shown this to be effective for treating musculoskeletal pain with no adverse effects or histological risks. The unique properties of HILT enable a laser with a wavelength of 1064 nm and pulsed high-power to penetrate deeper layers, resulting in laser energy diffusion in all directions, stimulating cytochrome oxidase and increasing mitochondrial oxidative reaction while enhancing photochemical and photobiological effects.^{38,39} Furthermore, with low-frequency high-power emissions, very brief durations, and paused time intervals, HILT are believed to have a photomechanical effect and repetitive mechanical stimulation may can reach the bone tissue.⁴⁰

The mechanoreceptive cells in bone tissue, known as osteocytes, adapt to mechanical stimuli by transmitting signals through the bone matrix to stimulate osteoblast bone formation. This mechanical stimulation may help to promote bone health by increasing or maintaining BMD.⁴¹ The study's results are in agreement with previous studies, that found HILT in combination with exercise was better than exercise alone in enhancing BMD of lumber region following treatment for 24 weeks and its effects continue up to a year.⁴²

In comparison to baseline scores, the combination of HILT and exercise successfully reduces the risk of fall and improves quality of life post-treatment. HILT may have the impact of reducing exercise-related pain as well as relieving accompanying issues such as muscular spasms and back pain.⁴³ The calming effect of HILT may be due to its ability to reduce pain impulses conduction and increase the rate of substance production in tissue, which is comparable to morphine's action.¹⁷ It may also improve circulation, the permeability of blood vessels, and cellular metabolism by blocking pain transmission through Ad- and C-fibers.⁴⁴

HILT may improve muscular efficiency during exercise and help muscle recovery from exercise-induced fatigue.⁴³ Regular physical activity enhanced strength, balance, and proprioception.⁴⁵ Exercise regimens may also help people reduce their risk of fall.⁴⁶ Programs of moderate intensity exercise designed specifically for preventing falls improved balance, the strength of the muscles, ambulation, and decrease fall risks, according to previous studies.⁴⁷

The findings of this study are consistent with previous studies that found that exercises improved BMD and decrease fall risk in women with OP.¹⁵ In addition, the current study found that the group of HILT had a better quality of life in

comparing with the exercises group, as demonstrated by higher scores in all five EHP-5 domains and a significant difference in the quality-of-life scores mean value, which is consistent with previous research.⁴⁸

Effect of exercises

In comparison to pre-treatment scores, exercise effectively increased both lumbar and total hip BMD in men with OP following treatment of 12 weeks and at six-months later, but there was no significant effect between 12 weeks and six-month follow-up scores in this study. The results of this study, which were in agree with the previous clinical trials, suggest that exercise had a small, statistically significant, but potentially obvious effect on postmenopausal women with OP.⁴⁹

A significant and relevant long-term effect on bone density at the lumbar region and neck of femur was demonstrated with an exercise program adapted to the subject's priorities.⁵⁰ Although there is no linear effect, an increase in daily living activity using simple, performed activities can help prevent decreases of post-menopausal BMD.⁵¹ Mechanical loading exercise regulates bone vascularization by regulating angiogenic mediators, which are important for skeletal health.⁵² Exercise enhanced BMD in the neck of femur and lumbar region by 1.8 % and 1.5 %, respectively, with a significant increase in muscle strength.⁵³ Resistance training combined with weight-bearing activities may help prevent osteoporosis by preventing or delaying the loss of BMD in men at middle-aged and older.⁵⁴

Exercises also enhance muscle strength, as well as static and dynamic balance. The findings of this study opposed previous clinical trials that suggested resistance exercises does not improve femur bone density more than walking for 30 minutes three times a week.⁵⁵ Differences in age ranges, as well as the kind, period and intensity of exercise, may explain the differences between results of this study and those of previous studies.

In comparison to baseline scores, the exercise effectively reduces the risk of fall and improves quality of life. Resistance training decrease pain and enhance wellbeing, mood status, and cognitive abilities, improve quality of life,⁵⁶ and lower falls risk,⁵⁷ all of which reduce the risk of fracture,⁵⁸ according to the results of this study.

Conclusions

PEMF in combination with program of exercise is better than HILT combined with exercise or exercise alone in improving BMD and promoting bone synthesis, suppressing bone-resorption markers, and improving quality of life and risk of fall following treatment of 12-weeks and the effect continue up to six months.

Recommendation

The benefits of such treatments should be studied for extended periods of time in various musculoskeletal disorders, as well as in women with osteoporosis. As a result, further research from well-designed, high-quality studies is needed to understand deeper mechanisms, standardize treatment parameters, and determine the appropriate techniques for health-care decision-making before they can be widely used in healthcare situations.

Limitations

In terms of limitations, the findings of this investigation should be regarded with caution because our trial's six-month follow-up time was insufficient to determine the efficacy of PEMF and HILT on BMD and bone turnover indicators. Bone metabolism takes a long time to adapt to exercise, according to previous research. All of the study participants were instructed to maintain a well-balanced diet and follow a home exercise program that included 30 minutes of daily walking and exercise compliance monitoring. Because none of the participants reported any drawbacks, major side effects, or new-onset local discomfort, we regarded the home-based exercise program to be a limiting factor in this study. Although the results of this study are encouraging, more trials with fewer inclusion and exclusion criteria would yield more generalizable results. Long-term research as well as comparisons to different therapies are warranted.

Data availability

Underlying data

Figshare: Age, height and weight raw data, <https://doi.org/10.6084/m9.figshare.16920130>.⁵⁹

Figshare: BMD total hip raw data, <https://doi.org/10.6084/m9.figshare.16920151>.

Figshare: BMD lumbar spine raw data, <https://doi.org/10.6084/m9.figshare.16920163>.

Figshare: Bone markers raw data, <https://doi.org/10.6084/m9.figshare.16920184>.

Figshare: HRQoL raw data, <https://doi.org/10.6084/m9.figshare.16920190>.

Figshare: Fall risk raw data, <https://doi.org/10.6084/m9.figshare.16920196>.

Extended data

Figshare: Tables, <https://doi.org/10.6084/m9.figshare.16920250>.

Reporting guidelines

Figshare: CONSORT Checklist, <https://doi.org/10.6084/m9.figshare.16920253>.

Figshare: Flow chart of the study, <https://doi.org/10.6084/m9.figshare.16920232>.

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

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