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Healing time response to low intensity pulsed ultrasound in hip fractured osteoporotic postmenopausal women

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Osteoporotic fractures are an important public health issue as it results in disability and diminishes quality of life. The aim of the current study was to investigate the healing time response to the application of low intensity pulsed ultrasound (LIPUS) in hip fractured osteoporotic post-menopausal women. As an additional non-invasive physical therapy modality that can accelerate fracture healing process. Forty osteoporotic postmenopausal women ,their age ranged between 64 to 76 years diagnosed with stable intertrochanteric hip fracture underwent internal fixation with dynamic hip screw (DHS) were recruited in this study. They were randomly assigned into two equal groups :(LIPUS) group and control group. (LIPUS) group received traditional post-operative physical therapy program, In addition to low intensity pulsed ultrasound over the fracture site three days per week for 16 successive weeks. While the control group received only traditional post-operative physical therapy program .All patients were evaluated by antero-posterior and lateral views X-rays immediately post-operative, at 4th weeks, 12th weeks, and 16th weeks for fracture healing assessments using the radiographic union scale for hip (RUSH score).showed significant difference in healing time between (LIPUS) group and the control group, which reflected a decrease in radiographic healing time in (LIPUS) group compared to control group ($p<0.05$). It was concluded that low intensity pulsed ultrasound can reduce healing time in hip fractured post-menopausal women and can be added to rehabilitation programs as a non-invasive treatment option proved to have a clinical benefit on osteoporotic fractures.

Keywords: Healing time; Osteoporosis; Hip Fracture; Low Intensity Pulsed Ultrasound.

INTRODUCTION

Osteoporosis is a silently progressing metabolic bone disease widely prevalent in post-menopausal women it leads to a skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue, leading to enhance bone fragility and increase the risk of fractures especially with low energy trauma (Hernlund et al., 2013).

Among all osteoporotic fractures, hip fracture has been given the most attention as they have high rates of morbidity and mortality; Patients are prone to delayed union and non-union which make fracture healing as a priority of patient outcomes (Blomfeldt et al., 2005).

Low intensity pulsed ultrasound (LIPUS) is a

form of mechanical energy transmitted transcutaneously through biological tissues by high-frequency acoustic pressure waves, and is considered as non-thermal and non-destructive waves (Pasco et al., 2005).

The US Food and Drug Administration (FDA) and the UK National Institute for Health and Care Excellence (NICE) have approved the usage of low intensity pulsed ultrasound (LIPUS) for fracture healing based on radiographic outcomes of patients with different fractures site and consider the usage of (LIPUS) as an additional non-invasive treatment to improve bone healing (www.nice.org.uk/guidance/ipg374/history).

Bone regeneration involves a complex process such as inflammation, cellular proliferation and differentiation, chemotaxis, synthesis of an extracellular matrix and finally remodelling (Harwood and Ferguson, 2015).

Bone cells are sensitive to strains caused by physical loading; Mechanoreceptors convert biophysical stimuli into biochemical responses that alter gene expression and cellular adaptation (Rutten, 2013).

There are Several potential mechanisms of LIPUS that may have a positive effect on bone fracture healing such as Mechanical signal transduction , activation of enzymes in response to heat energy, increased vascularity at the fracture site, modulation of intracellular calcium, enhanced cartilage calcification and maturation (siska et al .,2008).

MATERIALS AND METHODS

Forty postmenopausal osteoporotic women aged between 64 and 76 years, with a body mass index (BMI) between 24.2 to 28.2 Kg/m ^{2}and T-score of bone mineral density (BMD) (-2.5 SD or below the young adults mean) diagnosed with intertrochanteric hip fracture and underwent intra-operative management for internal fixation using dynamic hip screw (DHS) were included in the study. Patients were excluded if they had multiple fractures, head injury, Secondary osteoporosis, Metabolic bone diseases or tumors, Diabetes Mellitus, hypo–hyperthyroidism and hyperparathyroidism, chronic renal failure, chronic liver disease, under steroid treatment, Smokers, Recurrent hip fractures of the same side, under current medical treatment for osteoporosis during the study duration .Patients were randomly assigned into two equal groups; (LIPUS) group, n= 20 and control group, n=20.

Ethical committee approval:

The study was approved by research ethical committee, faculty of physical therapy, Cairo University (NO:P.T.REC/012/00820).

All patients gave their written consent to be enrolled in this study.

Procedures

The study was controlled clinical trial conducted at outpatient clinics in Dr / Souad Kafafi Memorial medical Centre, Misr University for Science and Technology (MUST).The aim of the study was to investigate healing time response to low intensity pulsed ultrasound (LIPUS) in hip fractured osteoporotic post-menopausal women, who underwent internal fixation with dynamic hip screw (DHS). Study started with full medical assessment for all participants to ensure they fulfil the inclusion criteria. The treatment protocol for both groups started during Patients hospitalization period (48 hours post-surgery) with traditional post-operative physical therapy program consists of range of motion, stretching, strengthening exercises and gradual weight bearing training established during the treatment protocol according to fracture stability and surgeon recommendations. Only For (LIPUS) group, low intensity pulsed ultrasound treatment added 7-10 days post-operative over the fracture site three days per week for 16 successive weeks.

Low Intensity pulsed Ultrasound bone healing system (OSTEOTRON IV) made in Japan ,was used in the study ,it provides Ultrasound frequency 1.5+/- 5% MHZ, Modulating signal burst width 200 +/- 10% microsecond ,Repetition ratio 1.0 +/- 10 % kilohertz (KHz) Effective radiating area 3.88 +/-1% square cm (cm2) ,Temporal average power 117 +/- 30% mille watts. During treatment sessions the device transducer covered totally by ultrasound coupling gel and placed over the fracture site by adjustable device strap.

The fracture site was specifically determined during the surgical procedures by using the c-arm guide to place a permanent mark over the skin indicating the exact fracture site.

All Patients underwent antero-posterior and lateral views X-rays at intervals of; immediately post-surgery at 4thweeks, 12th weeks, and 16th weeks for fracture healing assessments.

All patient X-rays radiographs during the period of the study were assessed independently by two orthopaedic surgeons to judge about radiographic fracture healing using The

radiographic union scale for hip (RUSH score) (Bhandari et al., 2013).
The total time needed for radiographic healing in both groups were calculated in weeks and compared with each other to examine the fracture healing time in response to (LIPUS) by the end of the study

Data collection:
Prior to final analysis, data were screened, for normality assumption test and homogeneity of variance. Normality test of data using Shapiro-Wilk test was used, that reflect the data was normally distributed after removal outliers that detected by box and whiskers plots. All these findings allowed the researchers to conducted parametric and non-parametric analysis.

Statistical analysis
The statistical analysis was conducted by using statistical SPSS Package program version 20 for Windows (SPSS, Inc., Chicago, IL).

The following statistical procedures were conducted
Unpaired (Independent) t-test to compare between the (LIPUS) and control group for age, BMI, number of years after menopause, days of Hospitalization and healing time in weeks.
Mann-Whitney test to compare between the (LIPUS) and control group for Rush score values.
All statistical analyses were significant at 0.05 level of probability ($P \leq 0.05$).

RESULTS

Demographic data of patients
The statistical analysis by independent t-test revealed that there were no significant differences ($P>0.05$) in mean values of general descriptive data (age, BMI, number of years after menopause, days of hospitalization) between the control group and (LIPUS) group as shown in (Table 1), (figure 1).

Healing time in weeks
Table (3) and Figure (3) represented the comparative mean values of healing time in weeks between LIPUS and control group. The mean ±SD values of healing time in weeks for (LIPUS) and control group were 11.45 ±0.51 and 15.75 ±0.44, respectively. The statistical analysis by independent t-test revealed that there were significant differences on healing time ($P=0.0001$; $P<0.05$) between LIPUS and control groups.

Table (1): Comparison of descriptive data mean values between (LIPUS) and Control group.

Items	Age (year)	BMI (kg/m^2)	No. of years after menopause	Days of hospitalization
LIPUS group	69.00 ±3.61	25.70 ±1.03	18.75 ±2.53	7.85 ±1.46
Control group	69.05 ±3.63	26.40 ±1.04	19.25 ±3.05	8.35 ±1.04
t-value	0.044	0.631	0.563	1.247
P-value	0.965	0.540	0.577	0.220
Significance	NS	NS	NS	NS

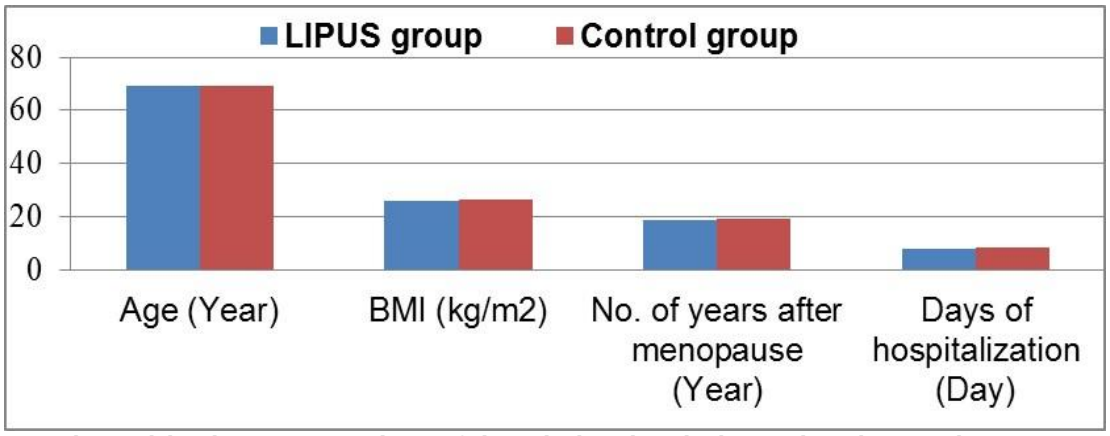

Figure (1): Show mean values of descriptive data in (LIPUS) and control group.

The statistical analysis by Mann-Whitney test revealed that there were no significant differences in Rush score between both groups at zero time (P=1.000; P<0.05), while there were significant differences at 4th weeks (P=0.004; P<0.05), 8th weeks (P=0.0001; P<0.05), 12th weeks (P=0.0001; P<0.05), and 16th weeks (P=0.0001; P<0.05) as shown in Table (2) and Figure (2).

Table (2): Comparison median values of Rush score between (LIPUS) and control group.

Items	Rush score				
	Zero	4thweek	8thweek	12th week	16thweek
LIPUS group	10 (10, 10)	18 (17, 18)	23 (22, 24)	30 (29, 30)	30 (30, 30)
Control group	10 (10, 10)	16 (15, 17)	21 (20, 22)	24 (22, 25)	26 (25, 26)
Z-value	0.000	2.846	4.121	5.501	5.571
P-value (P<0.05)	1.000	0.004	0.0001	0.0001	0.0001
Significance	NS	S	S	S	S

IQR: Interquartile range P-value: probability value NS: non-significant S: significant.

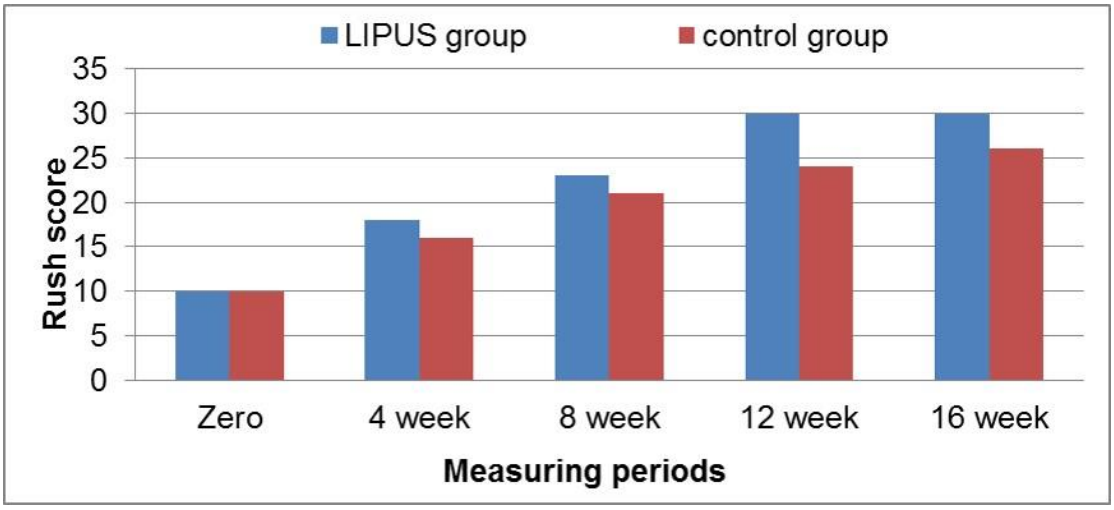

Figure (2): Show median values of Rush score between (LIPUS) and control group

Table (3): Comparison mean values of healing time in weeks between LIPUS and control group.

Items	Healing time in weeks	
	LIPUS group	Control group
Mean ±SD	11.45 ±0.51	15.75 ±0.44
t-value	12.418	
P-value (P<0.05)	0.0001	
Significance	S	

SD: standard deviation P-value: probability S: significant

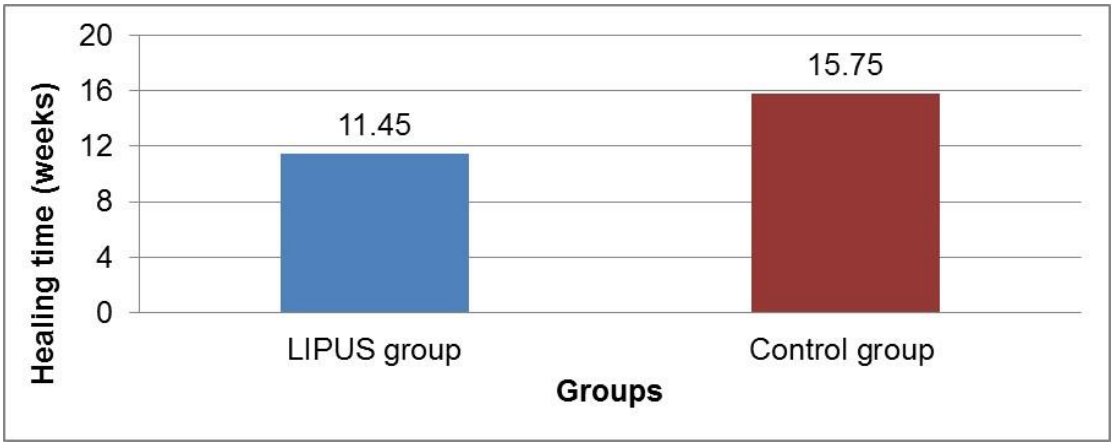

Figure (3): Show mean values of healing time in weeks between LIPUS and control group

DISCUSSION

Low-intensity pulsed ultrasound (LIPUS) has been reported, by various authors, to promote bone healing. Different literatures have been published describing the efficacy of (LIPUS) on bone healing .despite the variability of this studies there is heterogeneity among in-vitro, animal studies and their application to human studies. Moreover the quality of studies varied from one another in terms of treatment plan, bone healing assessment tools and outcome measures.

The aim of this study was to investigate the healing time response to (LIPUS) in hip fractured osteoporotic postmenopausal women.

The findings revealed that there were no significant differences in Rush score between both groups at zero time (P=1.000; P<0.05) which represent immediately post-operative time before starting the treatment, while there were significant differences at 4th weeks (P=0.004; P<0.05), 8th weeks (P=0.0001; P<0.05), 12th weeks (P=0.0001; P<0.05), and 16th weeks (P=0.0001; P<0.05), also there were significant differences on healing time (P=0.0001; P<0.05) between LIPUS and control group which reflect decrease the radiographic healing time in (LIPUS) group.

Our study results were consistent to the study of Kamath et al., (2015) which examined the effect of (LIPUS) on internally fixed fracture of both tibia and femur during the early stages of healing. Results revealed that there is significantly more callus formation in the LIPUS group compared to the control group, especially in the initial stages of fracture healing. The effect of LIPUS on the femur fracture is more compared to that on the tibial fractures, probably because of the good biological sleeve surrounding the femur.

Similarly, Lee et al., (2016) concluded that using of LIPUS considered a beneficial possible treatment approach for delayed union and non-union of displaced femoral neck fractures in young patients that was previously treated with internal fixation before considering second surgical intervention and the results confirmed by CT scan taken Eight weeks later which proved a good callus formation that was visible at the lateral and posterior fracture sites.

Moreover, a retrospective study conducted by Roussignol et al., (2012) examined the effect of LIPUS on 60 patients supports advocating the usage of LIPUS on treatment of non-union tibia and femur with inter-fragment gap less than 10mm with stable osteosynthesis as first-line implementation with 88% bone healing rate, which was higher than in traditional surgery and considered the LIPUS as non-invasive, cost effective treatment option, which also could be applied at home.

In addition Cheung et al., (2012) reported that LIPUS promoted not only normal fracture healing but also osteoporotic fracture healing, and the osteoporotic treatment group showed better results in callus width, stiffness measurement and response of endochondral ossification than normal group in closed femoral fracture rats.

Martinez de Albornoz et al., (2011) stated that due to the scarcity of previous literature examining the effect of (LIPUS) on fracture healing in human ,the evidence in vitro and animal studies suggests that (LIPUS) produces significant osteoinductive effects, accelerating the healing process and improving the bone-bending strength.

Lam et al., (2012) confirmed that daily ultrasound treatment significantly increased the rate of union

and the volumetric bone mineral density in rats.
Also, Numerous animal studies and clinical trials have shown that due to the positive effects of LIPUS on generation and activation of bone cells, the LIPUS capable of accelerating and augmenting the healing of osteoporosis, as LIPUS produces pressure waves, which induce biochemical and molecular events at the cellular level and whereby accelerated healing of osteoporosis (siska et al., 2008).
A study carried out by Hantes et al., (2004) proved that application of LIPUS significantly accelerated the fracture healing process, increased cortical bone mineral density and improved the lateral-bending strength of the healing fracture in a sheep osteotomy model.

Moreover, Lim et al., (2011) have showed that LIPUS may improve the micro architectural characteristics, material properties and mechanical strength in the osteoporotic bone, leading to decrease in bone fracture risks.
However, Simpson et al., (2017) demonstrated that LIPUS does not influence the rate of bone healing in adult patients, who undergo distraction osteogenesis for tibia, and the time needed for removing Ilizarov frame was the same in both treatment and placebo group, probably this is due to Smoking status of the patients which may influence bone healing.

The present study contradicts the study conducted by Emami et al., (1999) in which tibial fractures with a reamed intramedullary nail received active ultrasound (15patients) and placebo (17 patients) for 10 weeks. They concluded that there was no difference in the fracture healing time between the two groups. These results may be due to shorter treatment period and the fracture site, as most of studies support that LIPUS was more beneficial in fracture surrounded by soft tissue vascular sleeve as in femur.

CONCLUSION

In conclusion**,** these results showed that (LIPUS) could accelerate the process of fracture healing and decrease the time needed for radiological bone healing among osteoporotic postmenopausal women, also it could be considered as an effective, non-invasive therapeutic modality that could be added to the treatment protocol for patients with osteoporotic fractures as it proved to have clinical benefits.
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CONFLICT OF INTEREST

The Authors declare that there is no conflict of interest.

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AUTHOR CONTRIBUTIONS

All authors contributed equally in all parts of this study.

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