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Comparison between pulsed high intensity Nd: YAG laser and ultrasound in treatment of osteoporosis in Men

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Osteoporosis is a progressive disease characterized by low bone mass and micro architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. The aim of this study was to compare between pulsed high-intensity Nd: YAG laser (HILT) and pulsed ultrasound (PUS) in treatment of osteoporosis in men. Fifty five male patients were participated in this study, their age between 45- 55 years, the patients divided randomly into three groups. Laser group (LG, n=18), ultrasound group (USG, n=18) and control group (CG, n=19). Patients in Laser and ultrasound groups received treatment for 10 weeks on the lumbar spine according to designed protocol ten minutes five times per week plus exercise program but the control group receive exercise program only. Patients in the three groups evaluated at the beginning of the study and after 10 weeks using the DXA device for measuring the bone density and the results will be compared in the three groups. The result of our study showed that there was significant improvement in bone density in LG, USG and control group without significant difference between HILT and US. In conclusion, LASER and US was an effective physiotherapy modality in treatment of osteoporosis and improve bone mineral density.

Keywords: Osteoporosis, Laser, Pulsed Ultrasound, Bone density, Exercise.

INTRODUCTION

Osteoporosis is a progressive and disabling skeletal disorder characterized by decrease bone mass over time and deterioration of bone micro architecture, predisposing it to increased risk of fracture due to minor trauma. It affects about 200 million people all over the world (Lin and Lane. 2004) and associated with significant morbidity and mortality (Totosy de Zepetnek et al. 2009).

Osteoporosis and its-related fractures are an important public health concern; increasing in physical and psychological problems as chronic disabling pain, depression, fear and anxiety, difficulty of the activities of daily life (ADL) as well as decrease in functional mobility and thereby reduction in quality of life (QoL) (NIH Consensus Development Panel on Osteoporosis Prevention Diagnosis and Therapy 2001, Totosy de Zepetnek et al. 2009).The fractures resulted from osteoporosis exert a great impact on public health, life style, QoL as they are often associated to increased morbidity, mortality, loss of function and high economic costs which, only in the United States, may reach 15 billion dollars a year (NIH Consensus Development Panel on Osteoporosis Prevention Diagnosis and Therapy. 2001). There are many pharmacological interventions are widely used to treat and prevent osteoporosis and its related fracture clinically but it is associated with undesirable side effects as osteonecrosis of the jaw, venous thromboembolism, a syndrome of myalgias and arthralgias, induce osteoporosis in children and gastrointestinal problems (Lewiecki. 2010, Whyte et al. 2008, Nelson et al. 2002, Noller. 2002). Ultrasound is one of the therapeutic modality used for treating osteoporosis. The beneficial effect of ultrasound on bone healing is due to the piezo-electric phenomenon (Sheng et al. 2001). Bone is piezo-electric, which means that electric potentials are produced in bone when it is subjected to mechanical stress (Hadjiargyrou. 1998).Previous studies found that ultrasound stimulate osteoblasts to increase collagen production, stimulate osteogenesis in bone, (Rutten. 2008), stimulate vascularization (Trelles. 1987), organization of collagen fibers and ATP levels (Garavello-Freitas. 2003), inhibiting mature osteoclasts from resorbing bone and stimulating osteoblasts for bone formation (Doan. 1999). Laser therapy has the ability to stimulate the attachment and proliferation of the human osteoblasts like cells cultured on titanium implant material indicating that LLLT can modulate the activity of cells surrounding implant material (Khandra. 2008). The study conducted by (Márquez 2008) conclude that, laser application improve collagen fiber deposition at early stages of the healing and increased amount of well-organized bone trabeculae at the end of the experimental period on irradiated animals. Laser light affects the mitochondrial respiratory chain and consequently their selective permeability for sodium, potassium and calcium ions, or by increasing the activity of certain enzymes such as cytochrome oxidase and adenosine triphosphatase. It also increases DNA synthesis, collagen and pro-collagen production and may increase the cell proliferation or alter locomotory characteristics of cells (Loevschall 1994, Chrys et al. 2004, Khandra. 2008, Lan et al. 2006). There was no study evaluate the comparison between laser and US. So our study was conducted to compare between pulsed high intensity laser and pulsed ultrasound in treatment of osteoporosis.

Many studies indicate that physical exercises have beneficial effects on bone mass. Active exercises have significant osteogenic effects on bone structure (Burrows. 2007, Hind et al. 2008). It encourage calcium absorption in bone as a result of increased blood flow, which aids the deposition of vital nutrients and minerals such as calcium from general circulation in compressed sites and create piezoelectric forces that affect bone remodeling (Nikander et al. 2010), also; active exercises are one of the most important methods to prevent bone loss and to help maintain BMD (Marwaha. 2009, Burrows, 2007, Jessup et al. 2003).

MATERIALS AND METHODS

This was a 10-week randomized study with two measurement points' baseline and 10 weeks. Fifty five osteoporotic patients were enrolled in this study. Inclusion Criteria: Their age between 45 to 55 years (to avoid inclusion of older patients with multiple medical problems) with no history of cancer, renal disease, gastrectomy, metabolic bone disease or any condition (such as a neurogenic, myopathic or connective tissue disorder) that could cause secondary osteoporosis. The participants did not intake any medications associated with accelerated bone loss as steroids or any medications affected bone metabolism (calcium, vitamin D), nonsmoker, and led sedentary life style without participation at any exercise training during this study. All participants were given a full explanation of the treatment protocol and a written informed consent form giving agreement to participation and publication of results was signed by the patients.

Randomization

The participants in this study were randomly assigned by computer program into one of three groups (three randomized groups in a pretest-posttest design): Pulsed Nd: YAG laser group (LG, n=18), Low intensity ultrasound group (USG, n=18) and control group (CG, n=19). Subject characteristics (Mean ± SD) of all groups were listed in the table (1).

Pulsed high intensity laser therapy

Laser group received pulsed Nd: YAG laser on the lumbar region (L_{1-5}) plus exercise program, 5 times/week, 10 minutes for 10 weeks by Pulsed High Intensity Laser, High intensity laser machine by ASAsrl Company, Hilterapia, HIRO 3.0, Italy. High intensity laser (Nd:YAG), with pulsed emission (1064 nm). ,Very high peak powers (1-3 KW), Elevated energy content (150 - 350 mJ) ,High levels of fluence (energy density) (810-1780 mJ\ cm^2) ,Brief duration (120-150 µs),Low frequency (10-40 Hz) ,Duty Cycle of about 0.1%. The delivery technique for this group was automatic scanning with total energy of 4500 joule. HILT was delivered in two different phases, Initial phase and final phase. In initial phase, three sub-phases of fast manual scan (every10 cm scanned in about 1.5 second) was performed to lumber region with increasing fluences (710-910-1530 mj/cm^2) and decreasing frequencies (30-20-15Hz) with total energy of 2500 juels reached lumber region. In Final phase: 3 sub-phases of slow scanning (every 10 cm scanned in about three second) with increasing fluences (710-910-1530 mj/cm^2) and decreasing frequencies (30-20-15Hz) with total energy of 2000 juels reached lumber region. Scans can be longitudinal or transversal to the anatomical structure to be treated, ideally following a straight lines path**.** The irradiation was performed contact with the back and done in three phases (initial, intermediate and final phase) according to designed protocol for laser application.

Pulsed low intensity ultrasound

Ultrasound group received low intensity ultrasound on the lumbar region plus exercise program (L_{1-5}), 5 times/week, 10 minutes for 10 weeks. Low intensity ultrasound was composed of a pulse width of 200 µs containing 1.5MHz sine waves, with a repeated frequency of 1.0 kHz with a spatial-averaged temporal-averaged intensity of 30 mW/cm2 (Warden et al. 2001). Before the application of LIUS, its output characteristics were measured by hydrophonic scanning. The treatment procedure was explained to all subjects. Skin was cleaned with alcohol. During the irradiation, the position of the subjects was the same for both groups (prone lying position with a pillow under her abdomen).

Exercise program

The three groups in our study received the same exercise program during the study; exercise was performed for 40 minutes, 5 times per week for 10 weeks. The exercise-training program include weight bearing exercises on treadmill for 10 min, hip extension from quadri-bed for 10 minutes, closed kinetic chain exercises in form of leg press for 10 min lunges and cycling for 10 min with 5min rest between each exercises to avoid fatigue.

Outcome measures

include BMD assessed by DEXA (Dual x-ray Absorptiometry (DXA) (Model QDR-1000W, Hologic, Inc., Waltham, MA) was used for the qualitative assessment of BMD in the vertebral bodies of the lumbar spine for both groups. DEXA performs an imaging test that measures bone density by passing x-rays with two different energy levels through the bone. It is used to diagnose osteoporosis (decrease in bone mass and density). It is also called bone mineral density scan (BMD scan).

Statistical analysis

All data were assessed using SPSS version 16.0. Data were tested by Shapiro-Wilk test and were normally distributed. Data were statistically analyzed using repeated measures ANOVA to test hypothesis and to assess both within and between variabilities. Results are reported as means and standard deviations. For all procedures, significance was accepted at the alpha level of 0.05

RESULTS

Fifty five male subject participated in this study. Their age ranged from 45 to 55 years with a mean (51.46± 4.13). Their weight ranged from 59 to 87 kg with mean weight 77.6 ± 7.4 and their height ranged from 164 to 179 cm with a mean 173.05 ± 5.55 cm. Un paired t-test showed a non-significant difference between the subjects age, weight and height as p value was 0.56, 0.46 and 0.37 respectively, also; there was no significant difference between all groups at baseline values (p=0.4040), table 1.

There was a significant increase in T- score after 10-weeks in the laser, ultrasound and exercise group with the favor in laser and ultrasound groups as compared with baseline values. By comparing the two values after 10 weeks there no significant difference in T- score between laser and ultrasound groups (p=0. 8424 and t=0.2003) as shown in table 1 and figure 1

DISCUSSION

The result of our study showed that the HILT and PUS combined with exercise program was effective in improving the bone mineral density after 10 weeks of treatment and the effect of both modality nearly equal without significant difference in between, also exercise program was effective in increasing bone density but with significant differences between combination of therapeutic modalities.

One of nonpharmacological intervention for many people with an increased bone fracture risk due to osteoporosis is ultrasound (US) (Warden et al. 2001). US, refers to a high-frequency nonaudible acoustic energy that travels in the form of a mechanical wave, can be directed at osteoporotic sites to exert a mechanical stimulus. Recently, several studies have shown that low-intensity ultrasound (LIUS) with a 200 ls burst of 1.5 or 0.5 MHz sine waves, 1.0 kHz pulse repetition and 30 mW/cm2 intensity are capable of ameleorating bone strength, particularly its irregular geometry (Siffert and Kaufman 2007).

Table 1: The mean values of T- score for all groups at baseline and after 10 weeks.

	LG (n=18)	USG (n=18)	CG (n=19)	P value (between LG and USG)
Baseline	-2.7±0.35	-2.8±0.36	-2.8±0.48	0.4040**
10 weeks	0.70±1.34	0.80±1.64	-2.03±0.60	0.8424**
P value(withingroup)	<0.0001*	<0.0001*	0.0074*	
T value	6.433	5.820	2.836	

** Non-significant * Significant LG, Laser group USG, Ultrasound group CG, Control group

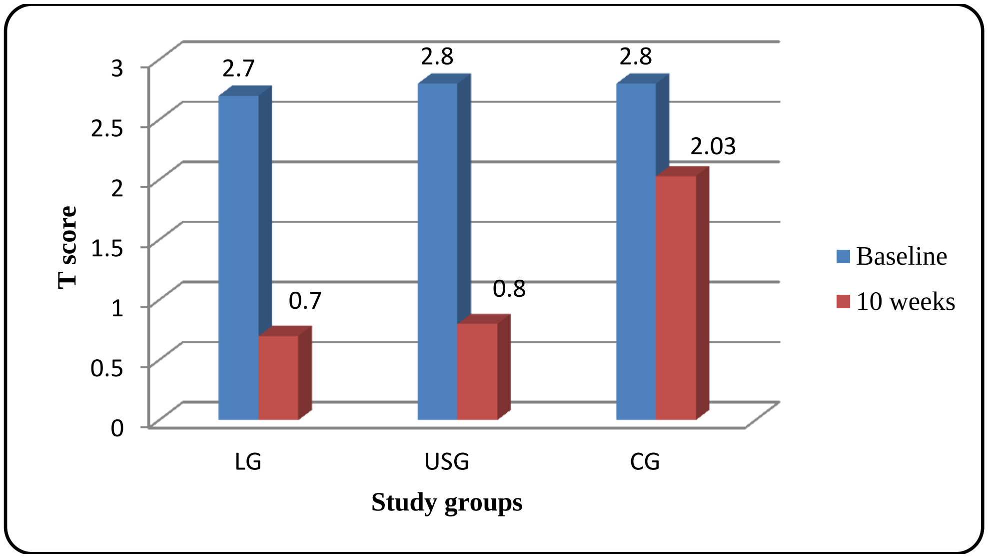

Figure 1:- Mean values of t-score for all groups at baseline and after 10 weeks.

Pilla. 2002 stated that signals generated by electromagnetic fields and ultrasound waves have a clinical significant effect upon bone repair directly by electromagnetic fields and indirectly via the piezoelectric effect of ultrasound.

There was many previous studies have examined possible treatments and preventive strategies to deal with the bone loss in osteoporosis. Results of previous study by Wing-Hoi et al. 2012 showed that low intensity pulsed ultrasound (LIPUS) was proven to improve healing of fractures effectively; and can be applied clinically to optimize both normal and osteoporotic fracture healing .

Bone is piezoelectric, which means that electric potentials are produced in bone when it is subjected to mechanical stress, the ultrasound showed worthwhile through the piezoelectric phenomenon on bone healing (Sheng et al. 2001). According to Wolff's law which stated that bone remodels according to functional demands, it is assumed that the stress generated potentials in bone serve as a signal which controls bone remodeling (Hadjiargyrou. 1998).

There was many physiological effect of low-intensity ultrasound (LIUS) on osteoporotic bones as it conserve bone microarchitecture ,decrease the risk of osteoporotic bone fracture by increasing the mechanical characteristics of osteoporotic bone via improvements in both its effective structural and elastic modulus and LIUS would be very effective clinically in preventing osteoporotic bone fracture (Dae-Gon et al. 2010).

Ultrasound stimulated osteogenesis in bone in vitro studies and stimulate osteoblasts to increase collagen production, increase the production of prostaglandin E2, an important bone-healing mediator that exert different effects on bone cells in the same microenvironments, such as inhibiting mature rat osteoclasts from resorbing bone and stimulating osteoblasts for bone formation (Rutten. 2000, Doan. 1999).The majority of studies conducted over the last thirty years in laser therapy have been carried out with medium and low intensity Laser devices (Low Level Laser Therapy: LLLT), with wavelengths in the infrared and near infrared 600 - 900 nm . Within this spectrum the laser beam is partially absorbed by the natural chromophores, like melanin, which withhold part of the energy irradiated. This study on the other hand is based on the use of Nd: YAG Pulsed High Intensity Laser Therapy (HILT), which characterized by a wavelength 1046 nm that allows it to penetrate and spread more easily through the tissue due to not having an endogenous chromophore (Parra et al. 1992). Nd:YAG lasers can produce new collagen formation in the papillary dermis (Chrys et al. 2004).

One promising treatment in physical therapy field is the use of the low level laser therapy (LLLT), which seems to induce osteogenesis and stimulate fracture healing (Gauthier et al. 2005). Its action is based on the absorption of the light by tissues, which will generate modifications in the cell metabolism. When the LLLT is applied on tissue, the light is absorbed by photoreceptors located in the cells, called chromophores. Once absorbed, the light can modulate cell chemical reactions and stimulate the mitochondrial respiration, the production of molecular oxygen and ATP synthesis, decrease inflammation process and improve angiogenesis (Stein et al. 2005, Lan et al. 2006). These effects can increase the synthesis of DNA, RNA and cell-cycle regulatory proteins, stimulating cell proliferation.Laser can modulate the activity of cells surrounding implant material due to its ability to stimulate the attachment and proliferation of the human osteoblasts like cells (Khandra. 2008). The study conducted on the effect of laser photo biomodulation on the repair of surgical defects on the femur of rats showed that there was increased amount of well-organized bone trabeculae at the end of the experimental period on irradiated animals and histological evidence of improved collagen fiber deposition at early stages of the healing (Márquez. 2008) indicating that, laser can enabling maximal photoactivation and stimulation of biological processes.In vitro studies using osteoblastic cells showed that LLLT is capable of increasing mitochondrial activity (Pires-Oliveira et al. 2008) osteoblast, DNA and RNA synthesis, bone nodule formation, osteocalcin and osteopontin gene expression and alkaline phosphatase activity. Also, the LLLT has demonstrated to be able to accelerate the process of fracture repair in rabbits and rats, increasing the callus volume and bone mineral density (BMD) (Liu et al. 2007, Rennó et al. 2007). The study conducted on osteoprotic rat using two fluence of laser doses by (Paulo Sérgio et al 2012) conclude that, LLLT improves bone repair as a result of stimulation of the newly formed bone, angiogenesis and fibrovascularization. Laser.

Laser application exert many physiological effect on living cells as increase mitochondrial respiratory chain by changing the electric potential of cell membranes and, consequently, improving permeability for sodium, potassium and calcium ions, or by increasing the activity of certain enzymes such as cytochrome oxidase and adenosine triphosphatase. It also increases DNA synthesis, collagen and pro-collagen production, and may increase the cell proliferation or alter locomotory characteristics of cells, accelerate bone formation by increasing osteoblastic activity, vascularization, organization of collagen fibers (Noble. 1992).Recent studies are suggesting the use of higher laser dosages stimulate bone metabolism (Rennó et al. 2006). In an in vitro study, comparing the effects of the 830 nm laser, at the dosages of 1, 5 and 10 J/cm2, showed that the higher dosage was more efficient to produce an increase of osteoblast proliferation and alkaline phosphatase activity. These findings further support the notion of cell/tissue, and dose/wavelength specificities. Also; the 830 nm laser irradiation, at 120 J/cm2, was able to increase the biomechanical properties and bone mineral density of osteopenic rats (Rennó et al. 2006).Many studies indicate the beneficial effects of physical training on bone. Active exercises have significant osteogenic effects on bone structure (Burrows. 2007, Hind et al. 2008). Active exercises encourage calcium absorption in bone as a result of increased blood flow, which aids the deposition of vital nutrients and minerals such as calcium from general circulation in compressed sites (Burrows, 2007, Jessup et al. 2003).

Weight-bearing exercises are low impact aerobic workouts and are suitable for the majority of elderly patients (Englund et al. 2005). Also; weight-bearing bones are maximally affected by gravitational forces and repetitive muscular actions during weight-bearing exercises, e.g. running and walking (Marwaha. 2009). It has been reported that the bone mass of physically active individuals is significantly higher than their nonactive counter parts and that muscular contraction during strengthening exercises and gravitational forces create piezoelectric forces that affect bone remodeling (Nikander et al. 2010). Accordingly, active exercises are one of the most important methods to prevent bone loss and to help maintain BMD (Marwaha. 2009).

In addition, they enhance aerobic capacity as well as increase muscle strength, flexibility and improve posture and balance performance (Ashe et al. 2004, Brentano et al. 2008, Jessup et al. 2003).

CONCLUSION

Pulsed high intensity Nd: YAG laser photostimulation and pulsed ultrasound accompanied by exercise program have favorable beneficial effects on bone mineral density in treatment of osteoporosis.

CONFLICT OF INTEREST

The present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

AAE and AAT designed the study and perform the treatment of laser protocol, ultrasound in both groups and exercise program in all groups. They wrote all parts of the manuscript. AE and AT performed data collection and statistical analysis of all variables measured in the study. AE and AT reviewed the manuscript, read and approved the final version of the manuscript.

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