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RESEARCH ARTICLE

Pulsed Nd: YAGLaser versus Ultrasound in Treatment of Osteoporosis.

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Abstract

Background: Osteoporosis characterized by low bone mass and micro architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. **Objective:** the aim of this study was to compare between pulsed high-intensity laser (HILT) and pulsed ultrasound (PUS) in treatment of osteoporosis in men. **Method**: Sixty male patients their age between 40- 65 years included in this study, the patients divided randomly into three equal groups. Laser group (LG,n=20), ultrasound group (USG,n=20), twenty patients and control group (CG,n=20). Patients in Laser and ultrasound groups received treatment for 12 weeks on the lumbar spine according to designed protocol ten minutes three times a week but the control groupdid not receive any treatment. Patients in the three groups evaluated at the beginning of the study and after completion using the DXA device for measuring the bone density and the results will be compared in the three groups.**Results**: The result of our study showed that there was significant improvement in bone density in LG and USG without significant difference between HILT and US. **Conclusion**: LASER and US was an effective physiotherapy modality in treatment of osteoporosis and improve bone mineral density.

Introduction:-

Osteoporosis is a progressive skeletal disorder characterized by decrease bone mass and deterioration of bone micro architecture, predisposing it to increased risk of fracture. Osteoporosis affects approximately 200 million people worldwide **Lin and Lane 2004.**

These fractures exert a great impact on public health, 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**.

Osteoporosis is associated with significant morbidity and mortality and its-related fractures are an important public health concern; increasing in physical and/or psychological problems as depression, chronic disabling pain, fear and anxiety as well as decrease in functional mobility and thereby reduction in quality of life (QOL) and difficulty of the

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activities of daily life **NIH Consensus Development Panel on Osteoporosis Prevention Diagnosis and Therapy 2001,Totosy de Zepetnek et al., 2009.**

Pharmacological interventions are widely used to treat and prevent osteoporosis and its related fracture clinically. However, such interventions can be accompanied with undesirable side effectsas venous thromboembolism, osteonecrosis of the jaw, a syndrome of myalgias and arthralgias, induce osteoporosis in children and gastrointestinal intolerance **Lewiecki 2010,Whyte et al., 2008, Nelson et al.,2002, Noller 2002**.

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 study found that ultrasound stimulate osteogenesisin bone, stimulate osteoblasts to increase collagen production**Rutten 2008**, inhibiting mature osteoclasts from resorbing bone and stimulating osteoblasts for bone formation **Doan 1999,**stimulate vascularization **Trelles 1987,**organization of collagen fibers and ATP levels **Garavello-Freitas 2003.**

Laser 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**. Also; laser improve collagen fiber deposition at early stages of the healing; increased amount of well-organized bone trabeculae at the end of the experimental period on irradiated animals **Márquez 2008**.

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**. There was no study evaluate the comparison between laser and US.So our study was conducted to compare between pulsed high intensity lase and pulsed ultrasound in treatment of osteoporosis.

Material and methods:-

This was a 12-week randomized study with two measurement points' baseline (pre) and 12 weeks (post). Sixty osteoporotic patients were enrolled in this study. **Inclusion Criteria:**Their age between 40 to 65 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 (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 into one of three groups (three randomized groups in a pretest-posttest design): Pulsed Nd: YAG laser group (LG, n=20), Low intensity ultrasound group (USG, n=20) and control group (CG, n=20). 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}), 3 times/weeks, 10 minutes for 12 weeks by Pulsed High Intensity Laser, High intensity laser machine byASAsrl 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 4000 joule.

HILT was delivered in two different phases, Initial phase and terminal 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 2000 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 (L_{1-5}), 3 times/weeks, 10 minutes for 12 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).

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:-
Sixty subject participated in this study. Their age ranged from 40 to 65 years with a mean (54.47± 5.17). Their weight ranged from 58 to 85 kg with mean weight 76.7 ± 7.4 and their height ranged from 162 to 178 cm with a mean 172.04 ± 5.46 cm. Un paired t-test showed a non-significant difference between the subjects age, weight and height as p value was 0.57, 0.45 and 0.36 respectively, also; there was no significant difference between all groups at baseline values (p=0.2289), table 1.

Table 1: The mean values of T- score for all groups at baseline and after 12 weeks.

	LG (n=20)	USG (n=20)	CG (n=20)	P value (between LG and USG)
Baseline	-2.8±0.35	-2.9±0.36	-2.7±0.38	0.2289**
12 weeks	0.80±1.34	0.700±1.84	-2.5±0.70	0.8453**
P value (within group)	<0.0001*	<0.0001*	0.2630**	

** Non-significant* SignificantLG, Laser groupUSG, Ultrasound group CG, Control group

There was a significant increase in T- score after 12-weeks in the laser and ultrasound groups as compared with baseline values. By comparing the two values after 12 weeks there no significant difference in T- score between laser and ultrasound groups (p=0.8453 and t=0.1965) as shown in table 1.

Discussion:-
The result of the this study showed that the HILT and PUS was effective in increasing the bone mineral density after 12 weeks of treatment and the effect of both modality nearly equal without significant difference in between.
Many studies have examined possible treatments and prevent ivestrategies to deal with the boneloss in osteoporosis**.** Low intensity pulsed ultrasound (LIPUS) was proven to enhance fracture healing effectively; also pulsed ultrasound can be applied clinically to enhance both normal and osteoporotic fracture healing **Wing-Hoi et al., 2012.**

The beneficialeffect of ultrasound on bonehealingis due to the piezoelectricphenomenon**Sheng et al., 2001**. Boneispiezoelectric, whichmeansthatelectricpotentials are produced in bonewhenitissubjected to mechanical stress. SinceWolff'slawbasically states thatboneremodelsaccording to functionaldemands, itisassumedthat the stress generatedpotentials in bone serve as a signal whichcontrolsboneremodeling**Hadjiargyrou 1998.**

Application of low-intensityultrasound (LIUS) to osteoporoticbonespreserved the bone microarchitecture. It effectivelydecrease the risk of osteoporoticbone fracture by increasing the mechanicalcharacteristics of osteoporoticbone via improvements in bothits effective structural and elasticmodulus and LIUS wouldbevery effective clinically in preventingosteoporoticbone fracture **Dae-Gon et al., 2010.**

Ultrasound (US) is a potentialnonpharmacological intervention for many people with an increasedbone fracture risk due to osteoporosis**Warden et al., 2001.** US, refers to a high-frequencynonaudibleacousticenergythattravels in the form of amechanicalwave, canbedirectedatosteoporotic sites to exert a mechanical stimulus. Recently, severalstudies have shownthatlow-intensityultrasound (LIUS) with a 200 lsburst of 1.5 or 0.5 MHz sine waves, 1.0 kHz pulse repetition and 30 mW/cm2 intensity are capable of augmentingbonestrength, particularlyitsirregulargeometry. **Siffert and Kaufman 2007**. Signals from electromagnetic fields and ultrasound have a clinically significant effect upon bone repair, since electrical fields can be directly induced by electromagnetic fields and indirectly induced via the piezoelectric effect by ultrasound**Pilla 2002.**

Previousstudiesfoundthatosteogenesisisstimulated by ultrasoundcanbefound in vitro studies. Osteoblastscanbestimulated to increasecollagen production **Rutten 2000** and increase the production of prostaglandin E2, an important bone-healingmediatorthatexertdifferenteffects on bonecells in the samemicroenvironments, such as inhibiting mature rat osteoclastsfromresorbingbone and stimulatingosteoblasts for bone formation **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**Parraetal., 1992**.Nd:YAG lasers canproduce new collagen formation in the papillarydermis**Chrys et al., 2004.**

Laser has the ability to stimulate the attachment and proliferation of the humanosteoblastslikecellscultured on titanium implant materialindicatingthat LLLT canmodulate the activity of cellssurrounding implant material**Khandra 2008.** The studyconducted on the effect of laser photo biomodulation on the repair of surgicaldefects on the femur of rats filledwithlyophilized bovine boneshowedthattherewashistologicalevidence of improvedcollagenfiberdepositionatearly stages of the healing; increasedamount of well-organizedbonetrabeculaeat the end of the experimentalperiod on irradiatedanimals**Márquez 2008indicating laser** enabling maximal photoactivation and stimulation of biological processes.

Many mechanisms of action have been proposed trying to explain the stimulatory effects of laser therapy on bone healing, as the effects of the laser on the inflammation process and angiogenesis **Lan et al., 2006.**

One promising treatment 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 reactionsand stimulate the mitochondrial respiration, the production of molecular oxygen and ATP synthesis **Stein et al., 2005**. These effects can increase the synthesis of DNA, RNA and cell-cycle regulatory proteins, stimulating cell proliferation.

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**.

A study conducted by **Paulo Sérgio et al 2012** on the effect of low level laser therapy (LLLT) on osteoprotic rat using two fluence of laser doses and the authors conclude that LLLT improves bone repair in the osteoporotic rats as a result of stimulation of the newly formed bone, fibrovascularization and angiogenesis.
Laser light affects the mitochondrial respiratory chain by changing the electric potential of cell membranes 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**Noble 1992.**

Some authors affirm that low laser light treatment can accelerate bone formation by increasing osteoblasticactivity,vascularization, organization of collagen fibers **Noble 1992**.Recent studies are suggesting the use of higher laser dosages to stimulate bone metabolism **Rennó et al., 2006**. In an in vitro study, our group 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**.

Conclusion:-

Pulsed high intensity Nd: YAG laser photostimulationand pulsed ultrasound have a favorable beneficial effects on bone mineral density in treatment of osteoporosis

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