The Efficacy of OST-6, A Polyherbal Formulation in the Management of Primary Osteoporosis: A Pilot Study

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ABSTRACT

This was an open clinical trial carried out to investigate the effect of an herbal preparation OST-6 on bone loss in primary osteoporotic patients. Fifty patients (13 male and 37 female) aged between 40-80 years, with clinical symptoms of osteoporosis such as low back pain were included in the study. After confirming the measurement of bone mineral density, at right heel, patients diagnosed with either osteoporosis or osteopenia were included in the study. Among them, 6 male and 13 female patients had osteopenia, and 7 male and 24 female patients had osteoporosis. Additional measures also included the estimation of serum calcium and phosphorous levels. All the patients were administered OST-6 at a dose of 2 tablets, twice daily for 6 months. In this trial, all the patients served as self-control. Symptom relief and bone densitometry was evaluated before and after treatment. Results indicated that after 6 months, there was an increase in bone mineral content by 1%. The bone loss in male patients when compared to healthy young adults of 25 years was 36.83% pre-treatment and 35.83% post-treatment. When matched for age, it was 20.75% and 19.58% at pre- and post-treatment respectively. In female patients, bone loss when compared to a young adult decreased from 25.27% to 24.61% and when matched for age, decreased from 12.51% to 11.86%. The ‘T’ score decreased by –0.06 in males and –0.12 in females. Serum calcium increased by 3% and serum phosphorous decreased by 3%. Biochemical parameters were within the normal limits before and after treatment, thereby indicating that OST-6 can be safely recommended for management of osteoporosis.

INTRODUCTION

Osteoporosis is a major public health problem and has been increasingly recognized that maximizing peak bone mass at skeletal maturity may provide important protection against risk of fracture in later life. Ninety to ninety five percent of total body peak bone mass is attained by the end of the second decade, with bone growth in adolescence accounting for about half of this figure. Peak bone mass is determined by a combination of endogenous (genetic, hormonal) and exogenous (nutritional, physical activity) factors. These exogenous factors are amenable to intervention and could thus provide a base for public health strategies for preventing osteoporosis.

The aetiology of osteoporosis is multifactorial and its characteristic features are uncoupling of the osteoblastic and osteoclastic processes of bone turnover and bone loss in adults. Approximately 3% of cortical bone is replaced each year and approximately 25% of trabecular bone is reabsorbed and replaced every year. The trabecular bone has high surface-to-volume ratio and 70-85% of the surface of the bone is in contact with bone marrow. After the mid thirties, there is 0.3 to 0.5% bone
loss per year. In early osteoporosis, there will be bone loss of 2-3% per year and it mostly occurs in cancellous bone. The total bone loss at a later stage may exceed 30-40%. After 50 years, there will be a 40% chance of developing osteoporotic fracture during a person’s remaining lifetime.\textsuperscript{5}

A specific cause of osteoporosis in most women is a rapid increase in bone loss after menopause, primarily due to loss of estrogen. However, whenever estrogen is taken, the patients should be cautioned about the development of breast cancer. Another fact is that not all postmenopausal women who have lost estrogen develop postmenopausal osteoporosis. A weaker association was found between calcium intake during adulthood and bone mass.\textsuperscript{6} Some women with very low calcium intakes do not develop osteoporosis. Treatment with Vitamin-D and calcium supplements will prevent some degree of loss of skeleton and decrease the likelihood of fractures. Calcium and calcitonin supplements act by decreasing bone resorption. Calcium acts mainly by decreasing activation of new bone remodeling units (not by decreasing action of existing osteoclasts). Postmenopausal women who are not treated with estrogen require about 1,500 mg daily for calcium balance. High dietary calcium suppresses age-related bone loss and reduces fracture rate in patients with osteoporosis. Calcitonin has recently shown to be an effective agent in management of patients with osteoporosis, but the drug is expensive and difficult to administer.

The ancient system of Indian medicine mentions several plants that are used to heal fractures and cure many bone metabolic disorders. Ayurvedic preparations contain natural forms of calcium, which prevent development of fractures in osteoporosis. One such preparation known as OST-6 consisting of \textit{Terminalia arjuna}, which has been extensively used in the treatment of many osteodystrophic conditions\textsuperscript{7}, \textit{Withania somnifera}, a rejuvenator that helps in relieving pain associated with osteodystrophic conditions and is also useful in people with general debility, nervous problems and muscular pain\textsuperscript{8}. \textit{Commiphora wightii}, increases the mineralization of the bones\textsuperscript{9}. \textit{Sida cordifolia} contains phytosterol and potent phytoestrogens. \textit{Vanda roxburghii} has anti-inflammatory activity, which is useful for relief of bony pains of osteoporosis. Godanti bhasma and Kukkutandatvak bhasma are the rich natural sources of calcium. The calcium present in this formulation is extracted in a traditional way that can be easily absorbed in the intestines.\textsuperscript{10} Experimental evaluation of OST-6 in animal models showed inhibition of bone reabsorption. It also stimulated new bone formation, thereby proving that it has a potential to be used as an anti-osteoporotic agent.\textsuperscript{11} This study was planned to evaluate OST-6 in increasing the serum calcium levels. The patients’ bone density was also indirectly assessed by ultrasound bone densitometry to evaluate if OST-6 increases the bone mineral content by measuring the bone loss. Since this was a pilot study involving a small group of patients and also to minimize the fracture risk, there was no control group. The protocol, which included the research methodology, investigators brochures and the patients’ consent forms was approved by the ethics committee of Kempe Gowda Institute of Medical Sciences Hospital and Research Centre, Bangalore, India.

**MATERIALS AND METHODS**

Fifty patients (13 male and 37 female) aged between 30-80 years, with clinical symptoms of osteoporosis such as low back pain were included in the study. After confirming the measurement of bone mineral density, at right heel, the patients were confirmed as either osteoporosis or osteopenia were included in the study. Among them, 6 male patients had osteopenia and 7 patients had osteoporosis. Thirteen female patients had osteopenia and 24 patients had osteoporosis. The
exclusion criteria included pregnant women, evidence of malignancy, hyperthyroidism, hypogonadism, and patients receiving long-term corticosteroids, methotrexate and heparin. All patients were subjected to bone densitometry using lunar calcaneum bone densitometry and were included only if they had more than 10% bone loss when compared to others of their age group and/or to a young adult of 25 years. Complete hematological and biochemical investigations were done including serum calcium and phosphorous.

Bone Densitometry Instrument:
New methods of measuring osteoporosis using ultrasound have also been developed. One such ultrasound system measures the fracture risk and also measures the percentage of bone mineral density loss for that particular age when compared to a young adult. The measurement is done using the calcaneum bone and takes about a minute. This instrument is useful as a screening test since it is simple and inexpensive and it has good reproducibility (1-3%). As bone density of the calcaneum reflects total body calcium, any thickening in the calcaneum may be used to predict fractures at other sites. These ultrasound systems for testing osteoporosis are smaller and less expensive than traditional DEXA systems. These systems have recently received US Food and Drug Administration (FDA) clearance for its use in diagnosing osteoporosis. The instrument used in this study is LUNAR ACHILLES PLUS DENSITOMETER QUS manufactured by General Electricals Medical Equipment, Bangalore, India. This instrument measures the stiffness, which is a clinical index developed by the Lunar Company and is a combination of BUA (Broad base Ultrasound Attenuation) and SOS (Speed of Sound). It also measures the bone loss for the corresponding age when compared to a healthy young adult of 25 years of the same sex. The T-Score, which is the standard deviation (SD) when compared to a 25-year-old young healthy individual of the same sex and the Z-Score is the SD for that corresponding age. These measurements were done using the right heel of the patients. The fragile fracture risk directly corresponds to the bone mineral density.

All the patients were recommended OST-6 at a dose of 2 tablets, twice daily for six months. These patients did not receive any supplementary calcium. The calcium content of OST-6 was measured and analyzed as 250 mg of calcium per tablet. Hence, the total calcium administered to the patient was 1000 mg/day. They were evaluated every month for improvement in the symptoms. At the end of 6 months, the patients underwent complete hematological and biochemical analysis, with bone densitometry. All these patients served as the self-control, because the efficacy of OST-6 was evaluated on symptomatology and calcaneous bone density after the treatment.

Statistical Analysis
The statistical analysis was done using repeated ANOVA measures using Graph Pad Prism 3.0 software.

RESULTS
Forty nine patients completed the 6 month study. One male patient was lost for follow up. The patients on being clinically evaluated showed an improvement in the symptoms from the first month onwards. The serum calcium, which was 9.24 ± 0.53, improved to 9.54 ± 0.54, which showed a 3% improvement during the 6 month study (p<0.0001). However, the drug was continued in these
patients till the bone mineral content was within normal limits. The phosphorous content, which was increased to $3.8 \pm 0.53$ due to osteoporotic changes, reduced to $3.5 \pm 0.51$ after treatment, which displayed a 3% decrease within a span of 6 months ($p<0.0001$) (Fig. 1). In the male patients, the bone density when compared to young adults increased by 1% and the bone density, when matched to age, increased by 1.17% ($p<0.0001$). The T score which was $-3.27 \pm 0.79$ reduced to $-3.21 \pm 0.98$ ($p<0.0001$). The bone loss decreased from 36.83 $\pm$ 11.68 to 35.83 $\pm$ 12.58 in 6 months ($p<0.0001$). Among female patients, the bone density when compared to a young adult female, also increased by 0.66% and the bone density, when matched to age, increased by 0.65% ($p<0.0001$). The T score, which was $-2.33 \pm 1.33$ reduced to $-2.21 \pm 1.41$ ($p<0.04932$) (Fig. 2). The bone loss decreased from 26.22 $\pm$ 13.20 to 25.22 $\pm$ 13.38 in just 6 months ($p<0.0001$) (Fig. 3). Hematological and biochemical parameters showed no difference before and after treatment (Table). This proves that OST-6 is a safe herbal preparation for use in patients with primary osteoporosis.

**DISCUSSION**

Osteoporosis is characterized by low bone mass and disruption of bone architecture resulting in reduced bone strength and increased risk of fracture. After the attainment of peak bone mass, bone loss in women begins, at or shortly before, menopause, in the spine and possibly as early as the mid-30s in the

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Fig. 1. Effect of OST-6 on Serum Calcium and Phosphorus

Fig. 2. Effect of OST-6 on T-score

Fig. 3: Effect of OST-6 on bone loss
femoral neck. Bone mass is a major determinant of bone strength, and prospective studies have shown an increasing gradient risk of fracture with decreasing bone density, a decrease in the latter of 1 SD being associated with a 1.5-fold to 3.0-fold increase in risk of fracture.\textsuperscript{13-16} The strength of this relation is similar to that between blood pressure and stroke and is equivalent to an eightfold to 12-fold difference in risk of fracture across the four quartiles of the distribution of bone density. Though measurement of bone mass at any of the skeletal sites commonly assessed is of value in defining risk of fracture, there is evidence that measurement of the site of potential fracture may provide the best prediction, at least in the case of fracture of the hip.\textsuperscript{17,18}

Bone fractures are an important cause of morbidity and mortality among the elderly even in western countries\textsuperscript{19} The annual occurrence of osteoporotic bone fractures is estimated at 1.3 million.\textsuperscript{20} Although a large majority of these occur among women, fracture rates among men are not trivial. For example, men at age 50 have a 5\% lifetime risk of sustaining a hip fracture.\textsuperscript{21} A low calcium intake has been postulated to be an important predictor of fractures because bones are largely composed of calcium phosphate and a combination of calcium phosphate and calcium hydroxide called hydroxyapatite. There is evidence of an association between dietary calcium intake and peak bone density,\textsuperscript{22-25} and conversely, calcium deficiency can lead to osteoporosis as a result of continued calcium loss through feces and urine.\textsuperscript{26}

Type I ("Postmenopausal") osteoporosis is due to loss of estrogen, which affects postmenopausal women. There is 2-3\% accelerated loss for 6-10 years, which then returns to basal loss of 0.3-0.5 \% per year. There is primarily loss of trabecular bone. It is associated with greater decline in medullary bone with preservation of cortical bone. The trabecular bone loss is three times more than the accelerated bone loss. There is decreased secretion of parathyroid hormone and increased secretion of calcitonin. There is also functional impairment in 25-Vitamin D hydroxylase activity with decreases in production of 1,25(OH)(sub 2) D and therefore decreases in calcium absorption. Any defect in calcium absorption may aggravate bone loss. Fractures in type I osteoporosis occur most frequently in vertebrae, distal aspect of radius and intertrochanteric region of the femur. The spine in type I osteoporosis shows loss of structural trabeculae, and weakened vertebrae and may predispose to acute collapse. The vertebral bodies are prone for fracture in osteoporosis. The vertebral fractures are usually of the "crush" type associated with large deformation and pain. The main reason for fractures of the vertebral body and distal radius is due to the fact that they contain large amounts of trabecular bone. The other most common fracture of the radius is the Colles’ fracture. Since there is great concern about the development of breast and endometrial hyperplasia, the treatment for all patients with type I osteoporosis is supplementation with calcium preparations.

Type II ("Senile") osteoporosis is caused due to long-term calcium deficiency. There is an age related decline in renal production of 1,25 Vitamin D with subsequent hyperparathyroidism and bone loss, which affects patients over the age of 75. There is an equal loss of cortical and trabecular bone with low bone turnover. In type II osteoporosis, fractures occur most often in vertebrae and the femoral neck, followed by fractures of pelvis, humerus and tibia.

In this clinical study, low calcium and increased phosphorus probably due to hypocalcemia were observed before treatment. After 6 months of OST-6 medication, there was a significant increase in the serum calcium and a considerable drop in serum phosphorus levels. This proves that OST-6 helps in absorption of natural calcium. It was also observed that OST-6 produced increased bone
density within a span of 6 months with reduction in bone loss. There was improvement in the ‘T’ score, which showed that OST-6 could be a useful therapy in patients who have osteopenia or osteoporosis. There was also improvement in the clinical signs and symptoms of osteoporosis. The joint swelling, pain and stiffness, which was present in some patients probably due to co-existing osteoarthritis also improved. This could be due to the presence of a plant resin named *Commiphora wightii*, which has both anti-osteoporotic and anti-arthritic properties.

**CONCLUSION**

This study was conducted for 6 months and there was a statistically significant improvement in all the patients. However, long-term studies involving 1-2 years of treatment may be required to see the efficacy in remodeling the bone to its normal architecture. All the biochemical and hematological parameters were normal indicating the safety of OST-6 in the population of patients studied.

**REFERENCES**


