An experience with Reosto in managing osteoporosis: A short communication

Sharma, V.D., Professor
Srivastava, R.N., Associate Professor,
Ashish Mahendra, Lecturer,
Rakesh Singh, Senior Resident,
Amit Singh, Senior Resident,
Department of Orthopedic Surgery, Chatrapati Shahuji Maharaj Medical University,
Upgraded King George’s Medical College, Lucknow, Uttar Pradesh, India
and
Kala Suhas Kulkarni
Medical Advisor, R&D Center, The Himalaya Drug Company, Makali, Bangalore, India.

INTRODUCTION

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 Indian system of medicine mentions several plants that are used to heal fractures and cure many metabolic bone disorders. Ayurvedic preparations contain natural forms of calcium, which prevent development of fractures in osteoporosis. *Withania somnifera* is 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. *Commiphora wightii* increases the mineralization of bones. *Sida cordifolia* contains phytosterol and potent phytoestrogens. *Vanda roxburghii* has anti-inflammatory activity, which is useful for relief of bone pains of osteoporosis. Godanti bhasma and Kukkutandatvak bhasmas are rich in natural calcium. The calcium present in this formulation is extracted in a traditional way that can be easily absorbed in the intestines.

The search for natural alternatives to estrogen has led to a tremendous interest among postmenopausal women in phytoestrogens. Some foods and protein sources demonstrate estrogenic activity. The three main classes of phytoestrogens are isoflavones, lignans and coumestans. They are found predominantly in plants and seeds. Isoflavones are found principally in legumes (soybeans, lentils, beans, and chickpeas), and soybean products. Two additional phytoestrogens are resveratrol, which is found in dark-skinned grapes and black cohosh, which is a popular herbal preparation. Direct evidence for a protective effect of phytoestrogens on bone mineral density in humans is sparse. Early evidence suggests that dietary phytoestrogens may have a beneficial effect on BMD. Phytoestrogens, or plant-source estrogens, raise interesting possibilities. The efficacy and safety of phytoestrogens was recently reviewed by the North American Menopause Society and the data published as a consensus opinion. In essence, it seems that phytoestrogens are largely safe.

Osteoporosis literally means *porous bones*. Bones that once were strong become fragile. Activities that once were done without a second thought, such as bending over to pick up a newspaper or lifting a grandchild, can cause bone fractures in people with osteoporosis. At this point, the disease is advanced. Osteoporosis is called the silent disease because one cannot feel bones becoming weaker. Bone loss usually occurs slowly over time without symptoms, until a bone breaks.
Fortunately, osteoporosis now can be diagnosed before fractures occur by measuring bone density, and fractures can be prevented by beginning treatment early.

Experts at the 1993 Osteoporosis Consensus Development Conference in Hong Kong defined osteoporosis as “a metabolic bone disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk”. In simpler terms, osteoporosis results from not having enough bone tissue, which is referred to as low bone density, or low bone mass, as well as from having bone with a weakened structure. The loss of bone density and structural weakness lead to bones that can break under the slightest strain.

MATERIAL AND METHODS

This study was planned to evaluate use of Reosto, in increasing bone mineral density. The bone mineral density was assessed by bone densitometry. The protocol along with the research methodology, brochures with consent forms were approved by the ethics committee of King George’s Medical College, Lucknow.

Fifty patients were divided into two groups, namely drug and placebo groups of 25 patients each. The drug group included 19 females and 6 males, and the placebo group had 16 females and 9 males with clinical symptoms of osteoporosis like low back pain, multiple joint pains, etc. The mean ages of the drug and placebo groups were 59.2 and 60.5 years respectively. All patients were subjected to baseline investigations, including hematological and biochemical investigations, which included serum calcium, bone specific alkaline phosphatase etc.

A detailed history was obtained from all the patients and they were subjected to a thorough clinical examination including informed consent. Radiological diagnosis of osteoporosis was done using x-rays of the lumbar sacral spine and bone density was measured to assess extent of bone loss. Drug group patients received Reosto at a dose of 2 tablets twice daily, and placebo group patients received a placebo at the same dose as per the trial design and randomization. The patients were monitored at monthly intervals for clinical examination and adverse effects, if any, were noted at each follow-up. At the end of 6 months, bone density was measured and all of them followed up for one year.

All patients whose mineral density was confirmed as either osteoporotic or osteopenic were included in the study. The bone mineral density was measured at the calcaneum bone.

The measurement is done using the calcaneum densitometer bone and this 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 their use in diagnosing osteoporosis. The instrument used in this study was used to analyse structural density of bone tissue by ultrasonography. It measures 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.

**Criteria of Exclusion:**
- Pregnancy
- Cardiac failure of Grade II or more
- Hepatic or renal failure
- Bone tumors
- Endocrine disorders: Hyperthyroidism, hypogonadism or Cushing’s Syndrome
- Congenital disorders: Dysosteogenesis, Marfan’s syndrome.
- Any other major systemic illness necessitating treatment as diabetes mellitus, rheumatoid arthritis, etc.
- Chronic drug intake, particularly corticosteroids, methotrexate and heparin

**RESULTS**
Fifty patients received treatment for a period of 6 months and followed up for one year duration. The patients showed clinical improvement at every months follow-up. Mean serum calcium in the drug group, which was 9.296 mg/dl improved to 9.488 mg/dl at the end of 6 months. Thus a 2.07% increase was seen at end of 6 months. In the placebo group, mean serum calcium improved from 9.22 mg/dl to 9.26 mg/dl. Thus, an increase of 0.43% was seen over a period of 6 months.

Serum alkaline phosphatase decreased in the drug group from 34.52 KA to 28.72 KA, a fall of 16.08% at the end of 6 months. Serum alkaline phosphatase in the placebo group was 32.06 KA, which decreased to 31.94 KA, showing 0.37% improvement at the end of 6 months.

The T score in the drug group prior to therapy was –1.501. This improved to –1.393, a gain of 7.19%. The mean T score in the placebo group was –1.07, which improved to –1.06 (0.93%). In the drug group, Z score improved from –1.578 to –1.448 (8.23% increase). In the placebo group mean Z score was –1.19, which improved by 3.3% to –1.15. Thus, Reosto is a safe preparation for use in patients with primary osteoporosis.

**DISCUSSION**
In terms of bone health, menopause, both natural and surgically induced is important to assess the risk for osteoporosis and subsequently to undertake corrective measures. In some women, bone loss is rapid and severe, however in some bone loss progresses gradually.

Significant numbers of women are recommended immediate hormone replacement therapy to relieve early symptoms. Women are also discouraged by the side effects of HRT, particularly the increased risk of breast cancer associated with long-term use. Thus, many women prefer to use herbal supplements or dietary modifications to try to manage the symptoms of menopause.

The consequences of osteoporosis are an increased risk of fractures at hip, spine and wrist. Hip fractures, which occur about twice as often in women as in men, are more serious than most people realize. More than half of those who survive will not be able to walk or move about easily, and a
quarter will need long-term nursing home care. Fractures of the spine, also called vertebral crush fractures or vertebral compression fractures also are disabling and painful complications of osteoporosis. One-third women over the age of 50 eventually will have a spinal fracture, and some younger people will suffer from them also. These fractures usually are painful, although sometimes they occur without any symptoms. When several vertebrae are fractured, the spinal column becomes shorter or compressed, resulting in a loss of height and a forward curvature of the spine called kyphosis (also known as Dowager’s hump). This deformity, along with fractures lower in the spine, can cause both acute and chronic pain. Quality of life is greatly impaired in persons with severe osteoporosis, not only because of pain and deformity, but also because of limited ability to move and be active and the fear of breaking more bones.

The primary goal should be prevention of osteoporosis. If one already has osteoporosis, treatment can prevent further bone loss, decrease the likelihood of fractures, improve ability to move and be active, and enhance the quality of life.

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. The drug group as compared to the placebo group had beneficial effect by improving the bone density. There was rapid alleviation of pain associated with osteoporosis. It showed rapid improvement of symptoms in female post-menopausal patients.

In this clinical study, low calcium and increased alkaline phosphatase probably due to hypocalcemia were observed before treatment. After 3 months of Reosto medication, there was a significant increase in the serum calcium and a considerable drop in serum alkaline phosphatase levels. This proves that Reosto helps in absorption of natural calcium. It was also observed that Reosto 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 Reosto could be 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 were present in some patients probably due to co-existing osteoarthritis also improved with treatment of Reosto.

Reosto consists of powerful powders of Commiphora wightii and others herbs are Terminalia arjuna, Withania somnifera, Sida cordifolia, Vanda roxburghii with Godanti and Kukkutandatvak bhasmas. The above mineral mixture is a rich source of calcium and phytoestrogen, which are required for inhibition of bone resorption. The rich levels of calcium in Reosto provide approximately 1362 mg calcium per day when recommended as 2 tablets, twice daily. Moreover, Commiphora and Withania together produce significant anti-inflammatory activity, which offer relief from chronic pain and muscle pain associated with osteoporosis. The antioxidant and lipid lowering properties of Terminalia are also beneficial in minimizing the role of coronary artery disease in menopausal women.

CONCLUSION
This study was conducted for 12 months and there was a statistically significant improvement in all the patients treated with Reosto. However, long-term studies involving 1-2 years of treatment may
be required to evaluate the efficacy in remodeling the bone to its normal architecture. All the biochemical and hematological parameters were normal after treatment indicating the safety of Reosto in the population of patients studied.