

# Zinc in Postmenopausal Bone Loss



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## Abstract

Osteoporosis is a systemic disease which is affecting one in six women over the age of fifty. Our review of literature supports the effect of zinc in postmenopausal bone loss.

## Introduction

The adverse effects of the medications for osteoporosis treatment may exclude their long-term use. A need for an alternative therapy that can improve bone health without inducing adverse effects would be appreciated. Postmenopausal bone loss is one alleviating human ills which is becoming more and more recognized in this country. Growing evidence of the benefits of natural foods for bone health presents alternatives for the prevention or treatment of osteoporosis. Besides, trace elements play a major role in the maintenance of health. Out of all the trace elements, zinc has been considered as an essential element pertaining to bone health. The application of existing knowledge of trace element nutrition to problems of postmenopausal bone loss will depend on the understanding of biophysical and biochemical mechanisms. Number of advantages of zinc and its importance in the bone structure and composition has made us to think that its supplementation can prevent bone loss.

## Osteoporosis

Bone is a dynamic organ with a well-regulated turnover to allow bone tissue functions such as growth, locomotion, organ protection or calcium/phosphate homeostasis. Bone modeling involves both growth and shaping of bones. Like bone modeling, bone remodeling is a surface phenomenon that serves to maintain the mechanical integrity of adult skeleton and provides a mechanism by which calcium and phosphate ions may be released from or conserved within the skeleton Compston [1]. Any change in the composition and microarchitecture of bone will lead to a decrease in the bone strength. The prevalence of osteoporosis and the number of hip fractures is increasing at an alarming rate. For example, a recent estimate of the number of hip fractures in women worldwide was 1.2 million. This number

is expected to grow up to 4.5 million by the year 2050 Cooper & Melton [2]; Breast Cancer Care and Royal College of Nursing [3]. In South Asian countries, both the population growth rate as well as life expectancy is high, which makes it even difficult to predict the number of persons likely to be suffering from osteoporosis.

## Factors affecting Bone Loss

Bone strength is affected by diverse factors including ageing, malabsorption of various micro and macro-elements, hereditary, nutrition and hormonal imbalances. Osteoporosis following estrogen deficiency is the most prevalent type of disturbance to the bone remodeling process. Following estrogen deficiency, there is a phase of rapid bone loss dominated by an increase in bone resorption and trabecular thinning, thereby leading to loss of connection between trabeculae Riggs et al. [4]; Bhardwaj et al. [5]. Evidences also indicate that estrogen deficiency increases oxidative stress which subsequently leads to bone loss Bai et al. [6]; Wittrant et al. [7]; Bhardwaj et al. [5]. Reactive oxygen species not only directly promote osteoclastogenesis but also support bone loss by inducing apoptosis and decreased differentiation and activities of osteoblasts while stimulating Receptor activator of nuclear factor kappa b ligand (RANKL) induced osteoclast formation.

Though there are many treatments available for osteoporosis but these treatments cannot be continued for a long time because of their severe side effects like gastrointestinal problems, malignant tumour formation etc. There is a need for alternative therapies that have lesser side effects and will be a part of our routine diet. A variety of bioactive compounds are currently being used for the treatment of osteoporosis. Many of these like tea Shen et al. [8], onion Huang et al. [9], Soy Taguchi et al. [10], safflower Jang et al. [11] etc. have been verified to counteract

the ovariectomy induced bone loss. There are trace elements as well that also play an essential role in the normal growth and development of skeletal system in humans and animals Heaney [12]. Among the trace elements zinc is of particular interest as number of evidences from the literature suggests that zinc supplementation improves bone growth.

### Zinc effects on Bone Tissue

Bone is a reservoir of minerals and of trace elements such as zinc, which accounts for 28% of total body zinc. Zinc occurs in the mineral component of bone, probably in hydroxyapatite Murray & Messer [13]; Sauer and Wuthier [14]. It may complex with F, and both zinc and the zinc-F complex may improve the crystallinity of apatite Lappalainen et al. [15]. Haumont [16] found bone zinc to be concentrated in the osteoid layer prior to calcification, which corresponds to the greatest concentration of alkaline phosphatase. It plays an integral role in numerous osteogenic enzymes, including alkaline phosphatase (ALP) Oner et al. [17], Type IV gelatinases Wilhelm et al. [18], carbonic anhydrase II Pocker & Sarkanen [19] and tartarate resistant acid phosphatase (TRAP) Susi et al. [20]. Zinc acts as a local regulator of an osteoblast to form the bony framework for organic matrix formation. Positive effects of zinc on bone tissue growth and mineralization in rats Becker and Hoekstra [21] along with the zinc-specific inhibition of osteoclast-mediated bone resorption in vitro Holloway et al. [22] provide evidence of an important role for nutritional zinc in bone tissue accumulation and retention. Bhardwaj et al. [23] have demonstrated zinc-related increases in the collagen and phosphate content of the femur and tibia bones in postmenopausal condition. Yamaguchi & Ozaki [24] showed that oral P-alanyl-L-histidinato Zn (AHZ) significantly increased the calcium and zinc content, DNA content and alkaline phosphatase activity of the femoral diaphysis in elderly rats. Zinc increases the activity of bone alkaline phosphatase and activates osteoblast tyrosine kinase and RNA synthetase. Deficiency in the zinc during postmenopausal condition leads to bone growth retardation and osteopenia which has also been demonstrated in our previous work Bhardwaj et al. [5]. The changes in cortical bone attributed to estrogen deficiency are arrested by zinc supplementation has been well documented in our studies Bhardwaj et al. [5,25].

Yamaguchi & Uchiyama [26] studied the direct effect of zinc on the proliferation activity of bone cells and found that it has stimulatory effect on the osteoblastic bone formation and inhibitory effect on the osteoclastic bone resorption. Positive effects of zinc on bone tissue growth and mineralization in rats Becker & Hoekstra [21], along with the zinc-specific inhibition of osteoclast-mediated bone resorption in vitro Holloway et al. [22]. provided ample evidence of an important role for zinc in bone tissue accumulation and retention. Zinc increases the activity of bone alkaline phosphatase and activates osteoblast tyrosine kinase and RNA synthetase. Many of the effects of zinc deficiency on bone metabolism may be related to a generalized

impairment of nucleic acid and protein metabolism. Deficiency in zinc will lead to bone growth retardation and osteopenia due to insufficient bone mineral mass Prasad [27,28]. Zinc has been shown to have an inhibitory effect on RANKL-induced osteoclast-like cell formation in mouse marrow culture Yamaguchi & Uchiyama [26] and also in in vivo condition as evident by the TRAP-5b measurement Bhardwaj et al. [5].

RANKL plays a pivotal role in the development of osteoclasts from preosteoclast. RANKL is secreted from osteoblasts. It is a member of the TNF superfamily and expressed in the activated T cells. It promotes the survival of dendritic cells by binding to its receptor RANK. RANKL/RANK pathway is essential for osteoclast differentiation. The effect of RANKL was completely abrogated by a natural antagonist of RANKL, osteoprotegerin (OPG), which is produced in osteoblastic cells. Zinc has been shown to have an inhibitory effect on RANKL-induced osteoclast-like cell formation in mouse marrow culture Yamaguchi & Uchiyama [26]. Zinc also inhibited TNF  $\alpha$  -induced osteoclastogenesis Zou et al. [29].

### Conclusion

Accumulating studies suggest that zinc plays a very important role in the maintenance of bone homeostasis. The number of biological functions and health implications pertaining to zinc indicates a need for further studies to evaluate the role of zinc in the maintenance of bone homeostasis.

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