The role of trace minerals in the pathogenesis of postmenopausal osteoporosis and a new effect of calcitonin

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Introduction

Osteoporosis is a condition of bone fragility resulting from microarchitectural deterioration and decreased bone mass. Adult bone mass depends on the peak attained and the rate of subsequent loss. Each component depends on the interaction of genetic, hormonal, environmental, and nutritional factors [1]. Trace minerals may be important in maintaining bone quality through their role as metalloenzymes in the synthesis of collagen and other proteins that form the structure of bone [2].

The risk of nutritional disturbances, in particular, trace element and vitamin deficiencies, is high during menopause. The participation of trace minerals in normal development and maintenance of the skeleton is related to their catalytic functions in organic bone matrix synthesis [3,4]. Trace elements are essential for normal growth and development of the skeleton in humans and animals. Although they are minor building components in teeth and bone, they play important functional roles in bone metabolism and bone turnover. Magnesium (Mg) enhances bone turnover through the stimulation of osteoclastic function. It has been suggested that Mg deficiency may play a role in postmenopausal osteoporosis [5]. Zinc [Zn] regulates secretion of calcitonin from the thyroid gland and has an influence on bone turnover [6]. Copper (Cu) induces low bone turnover by suppression of both osteoblastic and osteoclastic functions [5].

Mg also has direct effects on the bone formation processes of resorption and mineral aggregation [9].
The adverse effect of trace mineral deprivation on bone metabolism in animals has been recognized for many years and is known to be related to specific defects in organic bone matrix synthesis. Zn deficiency causes a reduction in osteoblastic activity, collagen and chondroitin sulfate synthesis, and alkaline phosphatase (ALP) activity [10,11]. Cu, a cofactor for lysyl oxidase, is required in the cross-linking of collagen and elastin [12,13]. Zinc is essential for life and reproduction and is a component of the cell nucleus, mitochondria, cytoplasm, cell membranes, and cell walls [14]. Zinc is a constituent of about 300 enzymes, and Zn ions are located in the catalytic site as well as in the structural site of the enzyme complex [15,16]. ALP, an enzyme involved in bone metabolism, is in the family of Zn enzymes. Among the trace elements in bone and hair, significant differences were found between normal subjects and osteoporotic patients in Zn, Cu, and manganese (Mn) content. However, the exact involvement of the trace elements in osteoporosis has not yet been clarified [5].

The biological effects of calcitonin may be divided into those related to Ca and P homeostasis and those related to gastrointestinal function [6]. The administration of calcitonin decreases renal tubular resorption of Ca and P as well as that of sodium (Na), potassium (K), and Mg [17]. To our knowledge, despite the documented involvement of trace minerals in normal skeletal metabolism, there have been no previous longitudinal studies reporting the effects of calcitonin therapy on trace minerals in postmenopausal osteoporosis. Thus, this longitudinal study may present a new concept: that calcitonin treatment improves osteoporosis by modulating trace minerals as well as by the reduction of osteoclastic bone resorption. The present study was designed to determine whether the mineral profile differed between osteoporotic and nonosteoporotic postmenopausal women and to evaluate the efficacy of calcitonin therapy during 6 months on these trace minerals in postmenopausal osteoporotic women.

**Patients and methods**

All 75 patients in the study were postmenopausal osteoporotic women and were selected from the Department of Physical Therapy and Rehabilitation of Dicle University Hospital. Their ages varied from 54 to 73 years for the patients with postmenopausal osteoporosis and from 50 to 68 years for the controls (the mean ages of the groups were not significantly different). Women were eligible for our study if they were 50 years of age or older and in good general health as determined by medical history and routine clinical blood analysis (complete blood counts and differential count). Women were excluded if they (1) had used any drug or had any disease or condition known to affect bone or calcium metabolism; (2) had taken corticosteroid medications during the previous 6 months; (3) had a history of chronic renal, hepatic, or gastrointestinal disease or lumbar compression fracture; or (4) had evidence of collapsed or focal vertebral sclerosis. Based on these criteria, 75 postmenopausal osteoporotic and 30 postmenopausal nonosteoporotic women were included in the study. All procedures were approved by the Human Studies Research Committee of the University of Dicle, Diyarbakir, Turkey, and written informed consent was obtained from each patient and control before inclusion in the study. Two women left the study after baseline measurements, and 3 patients stopped calcitonin therapy and were excluded, resulting in 70 osteoporotic women for analysis. The medications administered were calcitonin (100IU i.m./daily for the first week, every other day for the second week, and three times weekly for the third week and there after) with daily 1000mg calcium supplements. Medications were not administered in the control group.

We measured bone mineral density (BMD) with posteroanterior projection, using standard techniques from dual-energy X-ray absorptiometry (Hologic QDR model 1000; Hologic, Waltham, MA, USA). The variation coefficient for consecutive determinations on spine and femur images in our laboratory was 1.8% at the lumbar spine and 1.5% at the femur region. All spinal scans were reviewed for evidence of vertebrae with collapse or focal sclerosis by an experienced radiologist.

Blood was obtained after overnight fasting, and precautions were taken to avoid contamination. Blood samples were collected in trace element-free vacutainer tubes. Serum was separated using acid-washed pipettes, diluted with distilled water, and stored in acid-cleaned microcentrifuge tubes at 4°C. Serum Cu, Mg, and Zn concentrations were determined using atomic absorption spectrophotometry (GE496623 UNICAM 929, England). Serum chemical estimations were performed using Beckman-Synchron CX-5 technology, USA. Zinc, Cu, Mg, Ca, phosphate, and ALP levels were measured in blood before calcitonin therapy and again after 1 week and 1, 3, and 6 months in postmenopausal osteoporotic women and at baseline in the control group. Statistical analysis was carried out using the STATISTICA program for Windows. A median and standard deviation were calculated for each variable measured. Data were analyzed for significance using the unpaired two-tailed t test. The effect of calcitonin therapy on the biochemical markers during the 6 months of treatment (after 1 week and after 1, 3, and 6 months) was evaluated by the paired t test comparing each time period with baseline (before treatment). The