Serum and urinary zinc levels in cases with postmenopausal osteoporosis*

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Osteoporosis, currently considered a major health problem, is a mutifactorial diseas. The role of trace elements, particularly of zinc in osteoporosis has gained recent interest since the skeleton contains the major portion of total body zinc and zinc is indicated to be essential trace element in bone metabolism. This study was designed to evaluate the zinc status and its importance in diagnosis of osteoportic patients. The patient group consisted of 25 women with postmenopausal age between 4-11 years while the control groups comprised 18 healthy premenopausal women with a regular period of menstuation and 10 healthy postmenopausal women. Bone mineral density (BMD) (g/cm2) of L2-L4 lumbar vertebrae at anterior-posterior position and L2-L3 lumbar vertebrae at lateral position, along with proximal femur (femoral neck, the greater trochanter and Ward's triangle) were measured using a dual photon absorptiometer (DPA) . BMD was determined to be significantly lower in postmenopausal women with osteoporosis in comparison to both the premenopausal and postmenopausal control group($p<0.01$). Zinc levels in serum and 24 h urine in addition to routine biochemical parameters including alkaline phosphotase, calcium (in serum and 24 h urine), inorganic phosphorus, magnesium along with parathormone, thyroid stimulating hormone and osteocalcin were estimated in all of the cases to eliminate the causes for secondary osteoprosis. The only parameter that showed significant variation was zinc in 24 h urine which increased both in patients with postmenopausal osteoporosis and in postmenopausal healthy women in comparison to the premenopausal healthy controls ($p<0.01$). The elevation in zinc excretion in postmenopausal osteoporotic patients was significant also compared to the age matched postmenopausal healthy group ($p<0.01$) implying hyperzincuria as a marker of osteoporosis. [Turk J Med Res 1995, 13(5): 187-190]

Key Words: Zinc, Osteoporosis

Osteporosis, characterized by decrease in BMD, is multifactorial disease in which genetics, exercise, obesity, dietary and hormonal factors have been implicated (1-4). In some of the studies on osteoporosis, the role of trace elements on its pathogenesis has been investigated. Of the essential trace elements, zinc (Zn) is the most extensively studied one (5). Over a hundred Zn metalloenzyme complexes are recognized (2,6,7). The importance of Zn for life and reproduction is mainly due to its involvement in RNA and protein synthesis (8) . Although the major portion of the totalbody Zn is in skeleton, little is known about the role of Zn in bone metabolism (5). The importance of Zn in bone matrix development and bone density sustenance have been stressed considering that the osteoblastic activity, the synthesis of collagen and chondroitin sulfate, and the activity of alkaline phosphotase decrease as a result of Zn deficiency (2). The effects of disturbances in zinc metabolism of bones of adults and aged humans in health and disease has recently gained interest.

In the postmenopausal period, bone mass decreases due to estrogen deficiency which give rise to an increase in bone-turnover. For sensitive and reliable measurment of bone mineral density and bone mineral content DPA has been'extensively applied in the last 10 years as a noninvasive diagnostic tool (9-13). in this study we aimed to evaluate the importance of Zn as a biochemical marker for osteoporosis by measuring serum and urinary levels of Zn in postmenopausal women with osteoporosis diagnosed by DPA in comparison to the control groups of premenopausal and postmenopausal healthy women.

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Table 1. BMD (g/cm²) values of the lumbar vertebrae L2-L4 at anterior-posterior, L2-L3 at lateral position and the proximal femur in premenopausal and postmenopausal healthy and postmenopausal osteoporotic group.

	I. Premenopausal Healthy Group (CONTROL GROUP)	II. Postmenopausal Healthy Group	III. Postmenopausal Osteoporotic Group	p
L2-L4 *(P-A)	1.045*0.02	0.954±0.02	0.794±0.01	HI: NS II-III: <0.01 I-III: <0.01
L2-L3 "(Laf)	0.685±0.01	0.647±0.01	0.494±0.01	I-II: NS II-II: <0.01 I-III: <0.01
Femur Neck	0.838±0.02	0.782±0.04	0.671 ±0.02	I-II:NS II-III: <0.01 I-II: <0.01
Trochauter Major	0.689+0.01	0.667±0.01	0.605±0.01	I-II: NS II-III: <0.01 I-III: <0.01
Ward's Triangle	0.598+0.02	0.562±0.02	0.473±0.02	I-II: NS II-III: <0.01 I-III: <0.01

*P-A: Posterior-anterior position, "Lat: Lateral position, N.S: No significant

MATERIALS AND METHODS

The patient group consisted of 25 women with postmenopausal ages of 4 to 11 years who attended the Osteoporosis Unit of the Department of Endocrinology in Medical School Hospital of Ege University, between September 1993 and February 1994. None of the patients had recieved any long term medication known to affect bone metabolism and / or to prevent against osteoporosis. Eighteen premenopausal and 10 postmenopausal healthy women without any systemic disease constituted the control groups. The mean age of the patient and control groups were 60.72±1.84 yrs and 42.55±1.49 yrs (premenopausal), 58.83±1.76 yrs (postmenopausal) respectively.

BMD (g/ cm2) measurements were performed by DPA (XR- 26 Norland). The sites of measurements were chosen as L2-L4 lumbar vertebrae at antero-posterior position and L2-L3 lumbar vertebrae at lateral position. In proximal femur three sites were measured: the femoral neck, the greater trochanter and Ward's triangle.

Early morning fasting blood was obtained and serum was separated by centrifugation at 1500 g for 10 minutes. Alkalen phosphatase (ALP), calcium (Ca), inorganic phosphorus (IP),magnesium (Mg) levels in serum and Ca level in 24 h urine were measured by autoanalyzer (Hitachi-705). A colorimetric method was applied to determine Zn level in serum. For the estimation of urinary Zn, 24 h urine samples were collected in acid washed (5N HN03) polypropylene bottles. The pH of urine was adjusted to <2 with concentrated HCI and then mixed for two hours using a magnetic stirrer. Total volume was measured and aliquots were stored at -20 C until analysis. Following 1/2 dilution with 20 ml/ L HN03, measurement of Zn was performed by jobin Youn JY 24 ICP-AES (inductively Coupled Plasma-Atomic Emisson Spectrometer). The results were expressed as mg/ g creatinine. The disease states which might cause secondary osteoporosis were eliminated by determining thyroid stimulating hormone (TSH), parathormon (PTH) and osteocalcin (OC) applying the IRMA and RIA methods. For statistical analysis Student's t- test was applied. Correlation between urinary Zn and Ca excretion was investigated by the regression analysis.

RESULTS

BMD values of L2- L4 at anterior- posterior position and L2-L3 at lateral position were detected to be significantly decreased in postmenopausal osteoporosis (p<0.01) (Table 1) . BMD values of the proximal femur also showed a significant decrease in the postmenopausal group (p<0.01) (Table 1). As to biochemical parameters, there was no significant difference between the three groups except for urinary zinc excretion. 24 h urinary zinc levels were significantly high in postmenopausal osteoporotic cases (p<0.01) and in postmenopausal healthy women (p<0.01) compared to the premenopausal healthy women. There was also a significant difference between postmenopausal osteoporotic patients and the age matched postmenopausal healthy group (p<0.01).

DISCUSSION

The disturbances in zinc status with respect to aging and osteoporosis were investigated by several authors. Atik et al., who studied serum and bone tissue zinc content in 10 senile osteoporotic patients and 10 healthy controls observed that serum zinc levels are lower in senil osteoporotic group(14). Deviating from this

Table 2. Comparison of biochemical parameters between the postmenopausal osteoporosis and premenopausal healthy and premenopausal healthy group.

	I. Premenopausal Healthy Group (CONTROL GROUP)	• II. Postmenopausal Healthy Group	III. Postmenopausal Osteoporotic Group	
Age	42.55+1.49	58.83±1.76	60.72+1.84	I- II: <0.01 II- III: NS MiI: <o.oı
ALP (Ul/ml)	199.55±7.04	198.72±7.51	196.80+7.73	MI: NS İMİM NS MiI: NS
Ca++ (mg/dl)	10.03+0.11	9.86±0.15	9.74+0.16	I- II: NS II- III: NS MiI: NS
UP* (mg/dl)	3.03±0.10	3.25±0.09	3.48±0.07	I- II: NS II- II: NS İ-İİİ: NS
Zn (mg/dl)	121.45±2.73	118.36±2.47	114.56±2.98	I- II: NS II- II: NS MiI; NS
Mg (mg/dl)	1.92+0.8	1.87±0.78	1.83±0.87	I- II: NS II- III: NS MiI: NS
OC* (mg/dl)	11.45±0.6	11.20±0.52	10.73±0.41	I- II: NS II- III: NS MiI: NS
TSH[1] (mlU/ml)	0.97±0.08	1.15±0.10	1.37±0.14	I- II: NS II- III: NS MiI: NS
PTH[x] (pg/mi)	48.09±2.36	46.26+2.94	45.44±3.60	I- II: NS II- III: NS MiI: NS
Ca++ (Urine) (mg/g Creatinine)	181.70±20.9	193.6+18.8	201.0±16.2	I- II: NS II- III: NS MiI: NS
Zn (Urine) / (mg/g creatinine)	399.70+42.5	518.65±75.6	789.65±99.6	I- II: <0.01 II- III: <0.01 UIIi: <o.oı

* Alkaline phospholase t Inorganic phosptorus ± Osteocalcin
1 Throrol stimulating hormon X parathormon

finding, in this study serum Zn levels in the postmenopausal osteoporotic group (III) were not significantly different from the age matched postmenopausal healthy group (II). In addition, no significant differences were observed between serum Zn levels of pre and postmenopausal healthy groups which differed significantly with respect to age (Table 2). Lindeman et al. reported decreased plasma Zn levels with advancing age in both men and women (15). On the other hand, Weiss investigated 50 subjects over 60 years of age and concluded that serum zinc levels were in the normal range for the elderly. Besides, Weiss determined elevated Zn levels in urine, a finding also confirmed by Herzberg (5). Similarly in this study, significant differences in urinary Zn levels were observed between groups I and II indicating a relationship between urinary zinc excretion and age. Furthermore in accordance with Szatman et al. (16) the elevation in urinary zinc levels in group III was significant compared to group II as well as to group I implying that osteoporosis alone is also a factor in hyperzincuria.

The mechanism for renal excretion of zinc has not been fully understood yet. The urinary excretion of zinc in normal adult human was determined to be fairly constant and almost independent of dietary factors (17). According to Steele (18) and Abu Hamdan (19) zinc excretion is different from other divalent cations and discrepancy exists beetween calcium and zinc excretion. In accordance with these findings, no correlation was observed between 24 h urinary zinc and calcium in this study.

In most of the clinical conditions accompanied by hyperzincuria, such as hormonal disorders, systemic diseases and total parenteral nutrition bone involvement is observed (20). Although the mechanism of

zinc release from skeleton is still obscure the results of the experimental studies indicate that the skeleton does not serve as a reservoir of readily available zinc. However in states of net bone loss, especially those associated with high turn-over, such as hyperthroidism or thyrotoxicosis Zn may be released together with other bone minerals and collagen products and may be excreted in urine (5). Thus, the hyperzincuria observed in osteoporosis is possibly the result of increase in bone resorption due to high turn-over.

In conclusion, hyperzincuria is potentially a valuable biochemical marker of osteoporosis and may identify high turn-over bone loss in postmenopausal osteoporotic patients. Further studies are necessary to elucidate the role of zinc in pathogenesis of postmenopausal osteoporosis.

Postmenopozal osteoporozlu vakalarda serum ve idrar çinko düzeyleri

Güncel olarak, majör sağlık problemi olarak dikkate alınan osteoporosis multifaktoriyal bir hastalıktır. İskelet sisteminin total vücut çinko statüsünün önemli bir bölümünü içermesi ve kemik metabolizmasında çinkonun temel eser element olmasından dolayı, eser elementler ve özellikle çinko düzeyi osteoporozda son zamanlarda ilgi çekmeye başlamıştır. Bu çalışma osteoporotik hastaların tanısında çinko oluşumunu ve önemini değerlendirmek için düzenlendi. Hasta grubu postmenapozal yaşı 4-11 yıllar arasında değişen 25 kadından oluşurken, kontrol grubları düzenli menstrüel siklusu olan 18 premenapozal ve sağlıklı 10 postmenapozal kadından oluşmaktaydı. L2-L4 lumbar vertebra'nın anterior-posterior pozisyonda ve L2-L3 lumbar vertebranın lateral pozisyonda, proximal femur boyunca (femur boynu, büyük torakauter ve ward üçgen) kemik mineral dansitesi (KMD) (g/cm^2) dual foton apsorptiyometre (DFA) kullanılarak ölçüldü. KMD, postmenapozal kontrol ve premenapozal kadınlarda karşılaştırıldığında, osteoporozlu postmenapozal kadınlarda ciddi olarak düşüktü (p<0.01). Alkalen fosfataz, kalsiyum (serum ve 2 saatlik idrarda), inorganik fosfor, magnesiyum, parathormon, tiroid stimüle edici hormon ve osteokalsin sekonder osteoporozu belirlemek için ölçüldü. Bu parametrelere ilaveten serum ve 24 saatlik idrar çinko düzeyi ölçüldü. Osteoporozlu post-menapozal hastalarda, premenapozal ve postmenapozal sağlıklı kontrol grubunda değişiklik gösteren tek parametre 24 saatlik idrar çinko düzeyiydi. Postmenopozal osteoporozlu kadınlarda ve premenapozal kadınlarda 24 saatlik idrar çinko düzeyi postmenapozal sağlıklı kontrollere göre artmış bulundu (p<0.01). Postmenapozal osteoporotik hastalardaki çinko eksresyonu, yaşa göre uyarlanmış post menopoza! kontrol grubuyla karşılaştırıldığında anlamlı olarak fazla bulundu (p<0.01) ve bu çinko atılımının artması osteoporozun birmarkırı olduğuna işaret edebileceğini düşündürmektedir. [TurkJMedRes, 1995(5);!87-190]

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