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Serum osteocalcin as a specific marker of bone turnover in postmenopausal women

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Abstract

The field of bone turnover markers has developed considerably in the past decade. Biochemical monitoring of bone metabolism depends upon measurement of enzymes and proteins released during bone formation and of degradation products produced during bone resorption. The aim of this study was to use osteocalcin as a marker of bone formation that allow a specific and sensitive assessment of the rate of bone formation of the skeleton and study the correlation between serum osteocalcin level with bone mineral density (BMD) and age in postmenopausal women. A total of 60 postmenopausal Albanian women participated in the study. Subjects were divided into two groups: postmenopausal normal women and postmenopausal osteoporosis women. All subjects completed a questionnaire on life style factors. Height and weight were measured. Bone density was scanned using Quantitative Ultrasound (QUS). Serum samples were collected and osteocalcin levels were measured by electrochemioluminiscence (ECL) using Elecsys 2010. The Pearson correlation test indicated a negative correlation between osteocalcin levels and BMD. Serum osteocalcin levels was positively correlated with age which showed increase serum osteocalcin levels with aging. We observed significantly higher levels of serum osteocalcin in postmenopausal women with problems of osteoporosis compared to postmenopausal normal women ($P<0,05$).

Keywords: Serum osteocalcin, postmenopausal women, osteoporosis, bone mineral density.

Introduction

Osteoporosis is a complex heterogeneous disorder characterized by an imbalance in bone remodeling which culminates in reduced BMD, deterioration of microarchitectural integrity of the bone, and increased risk of fracture. It has a major economic [1] and health impact. Osteoporotic fractures are associated with increased morbidity [2] and mortality [3].

A lack of estrogen in postmenopausal women prevents the absorption and utilization of calcium and is the single most important factor in the development of osteoporosis in older women. Increase in life expectancy is another concept of formation of osteoporosis. Menopause and ageing is associated with accelerated loss of cortical bone.

Bone loss occurs when the balance between formation and resorption is upset and resorption is excessive resulting in a negative remodeling balance [4, 5].

Bone turnover may be assessed by the measurement of enzymes or matrix proteins produced by osteoblasts (which form bone) or osteoclast (which resorb bone) [6] . Osteocalcin also known as bone gamma-carboxy glutamic acid-containing protein (BGLAP) is a marker of bone formation.

Osteocalcin (OC) is 49 residue polypeptide with 5.8 –kDa. In humans, the osteocalcin is encoded by the BGLAP gene [7].

Osteocalcin is a non-collagenous protein synthesized and secreted by osteoblasts. Its main physiological functions are calcium ion homeostasis, maintain the normal bone mineralization rate, inhibit the abnormal formation of hydroxyapatite crystal, and to be involved in bone remodeling through a negative feedback mechanism [8]. Osteocalcin has a high affinity for calcium and exhibits a compact calcium dependent α helical conformation, in which the gamma-carboxy glutamic acid (Gla) residues binds and promote absorption to hydroxyapatite in bone matrix, in this way mineralization of bone takes place [9].

Materials and Methods

To evaluate the levels of osteocalcin we studied 60 postmenopausal women, who were divided in two groups: postmenopausal normal women and postmenopausal osteoporosis women.

Their mean age was 57 years (44-74) years. Height, weight, BMI, age at menarche, years since

menopause in case of postmenopausal women, history of disease, and fracture, if any, were recorded. BMD assessment was done using Quantitative Ultrasound

(QUS) and T-scores were calculated. According to World Health Organization (WHO) diagnostic guidelines:

•T-score -1.0 or greater is "normal".

•T-score between -1.0 and -2.5 is "osteopenia".

•T-score -2.5 or below is "osteoporosis" [10].

Serum osteocalcin (OC) were measured on the fasting sample. We use the electrochemiluminescence assay (ECL) on Elecsys 2010 from Roche Diagnostics.

For the statistical analysis we used SPSS. 19 programm. Differences between the two groups were analysed using student's unpaired t-test. Significance limits was $P<0.05$.

Results and Discussion

In this study there were 60 women meeting the inclusion criteria, for whom the major characteristics are shown in Table 1. The mean age of the subjects was 57 ± 6.67 years. Mean levels of serum osteocalcin was 23.70 ± 12.17.

Result of this study found that serum osteocalcin level was positively correlated with age ($r = 0.423$; $P = 0.001$), similar to other published studies [11-15]. Serum osteocalcin levels increase with age and women aged above 65 years have nearly 2 fold higher osteocalcin concentration as compared to those less than 44 years of age [13].

The results of the Pearson correlation test showed a significant inverse correlation between serum osteocalcin concentrations and BMD ($r = -0.271$; $P = 0.041$).

Table 1. Characteristics of the subjects (n=60)

	N	Minimum	Maximum	Mean	Std. Deviation
Calcium (ng/ml)	60	8.10	10.10	9.05	0.51
Age (years)	60	44.00	74.00	57.05	6.67
Osteocalcin (ng/ml)	60	6.26	63.61	23.70	12.17
BMD (T-score)	60	-3.00	-0.10	-1.84	0.68
BMI (kg/m^2)	60	18.36	39.43	27.84	4.02
Weight (kg)	60	45.00	102.00	70.83	11.05
Height (cm)	60	144.00	175.00	159.58	6.05

Since there is a complex relationship between bone turnover and bone mass, such that high bone turnover is associated with decreased bone mass,[16] it has been suggested that bone markers can predict fractures in elderly women, particularly those involving trabecular bone,[17] and that the use of a combination of BMD and bone markers can improve fracture prediction [9].

We divided the subjects into two groups: postmenopausal normal women and postmenopausal osteoporosis women. Defferences between the two groups are shown in Table 2.

Osteoporosis women are older than normal postmenopausal women.

Table 2. Differences between normal and osteoporosis postmenopausal women

	Normal postmenopausal women (n=48)	Osteoporosis postmenopausal women (n=12)
Age (years)	55.6 ± 6.11	62.6 ± 6.01
Weight (kg)	71.2 ± 10.1	69.2 ± 14.5
Height (cm)	159.5 ± 6.2	159.9 ± 9.4
BMI (kg/m^2)	28.06 ± 3.9	26.94 ± 4.3
BMD (T-score)	- 1.64 ± 0.6	-2.65 ± 0.1
Osteocalcin (ng/ml)	22.52 ± 10.5	28.42 ± 17.1

We observed significantly higher levels of serum osteocalcin in postmenopausal women with problems of osteoporosis compared to postmenopausal normal women (P=0.049).

Serum OC is considered a specific marker of osteoblast function, as its levels have been shown to correlate with bone formation rates.

However, since it is also released from bon matrix during bone resorption, it reflects the overall turnover of bone and is considered as a bone turnover marker. OC has a high affinity for calcium and has a compact á helical conformation that is calcium dependent.

The ã carboxyglutamic acid (Gla) residues of OC are capable of binding to bone matrix hydroxyapatite, thus leading to bone mineralization. Calcium- and phosphorus deficient osteoporotic women may have a decreased rate of bone mineralization due to a reduction in hydroxyapatite crystal formation.

In this condition, free OC may be present in the circulation, thus explaining the increased serum OC concentration in osteoporotic postmenopausal women [13, 18, 19].

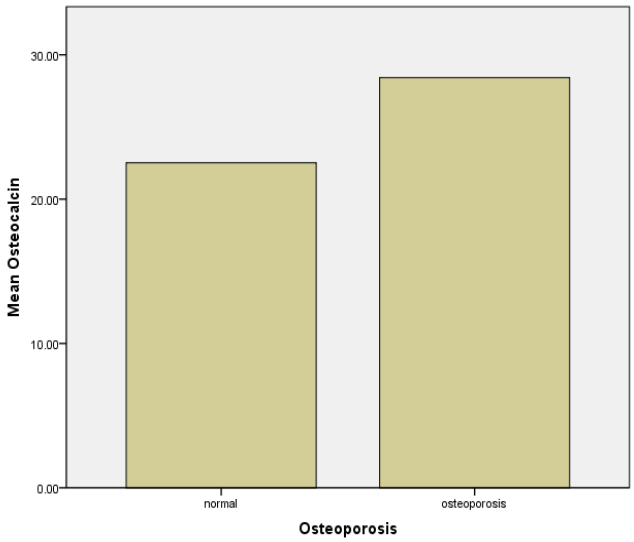

Figure 1. Osteocalcin levels in normal and osteoporosis women

The results of the study suggested that biochemical markers of bone turnover like osteocalcin may serve as indicator of altered bone metabolism and therefore can be used to monitor bone turnover in postmenopausal women subsequently helping in evaluating the risk of developing osteoporosis. With rapid advancement in technology, test for these marker will become more reliable, more widely available and cost effective as compared to the radiographic methods

References:

1. Burge R, Hughes BD, Solomon DH, Wong JB, King A, Tosteson A: **Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025.** Journal of Bone Mineral Research 2007, 22: 465-475
2. Adachi JD, Adami S, Gehlbach S, Boonen S, Chapurlat R, Compston JE, Cooper C, Silverman S, Nika G, Watts NB: **Impact of prevalent fractures on quality of life: baseline results from the global longitudinal study of osteoporosis in women.** Mayo Clincal Proceedings 2008.
3. Brauer CA, Coca-Perraillon M, Cutler DM, Rosen AB: **Incidence and mortality of hip fractures in the United States.** JAMA 2009, 302: 1573-1579
4. Sachdeva A, Seth S, Khosla AH, Sachdeva S. **Study of some common biochemical bone turnover markers in postmenopausal women.** Indian Journal of Clinical Biochemistry 2005;20(1):131–4.
5. Dogan E, Posaci C. **Monitoring hormone replacement therapy by biochemical marker of bone metabolism in menopausal women.** Post Graduate Medicine Journal 2002;78:727–31.
6. Eastell R, Blumsohn A. **The value of biochemical markers of bone turnover in osteoporosis.** Journal of Rheumatology 1997;24:1215–7
7. Cancela L, Hsieh CL, Francke U and Price PA. **Molecular structure, chromosome assignment, and promoter organization of the human matrix Gla protein gene.** Journal Biological Chemistry 1990; 265(25):15040–15048.
8. Lumachi F, Ermani M, Camozzi V, Tombolan V and Luisetto G. **Changes of bone formation markers osteocalcin and bone-specific alkaline phosphatase in postmenopausal women with osteoporosis.** Annual New Yourk Academic Sciences 2009; 1173Suppl 1:60–63.
9. Jagtap VR, Ganu JV and Nagane NS. BMD and Serum Intact **Osteocalcin in Postmenopausal Osteoporosis Women.** Indian Journal of Clinical Biochemistry 2011; 26(1):70–73.
10. WHO. **Assessment of fracture risk and its application to screening for postmenopausal osteoporosis.** Report of a WHO Study Group. World Health Organization technical report series, No. 843, 1994.
11. Pino JD, Gomez EM, Rodriguez MM, Sosa CL, Cordero M, Lanchares JL and Talavera JRG. **Influence of sex, age and menopause in serum**

osteocalcin (BGP) levels. Journal of Molecular Medicine 1991; 69(24):1135–1138.

12. Chailurkit LO, Pongchaiyakul C, Charoenkiatkul S, Kosulwat V, Rojroongwasinkul N and Rajatanavin R. **Different mechanism of bone loss in ageing women and men in Khon Kaen Province**. Journal of Medical Association Thai 2001; 84(8):1175–1182.
13. Filip RS and Zagorski J. **Age and BMD related differences in biochemical markers of bone metabolism in rural and urban women from Lublin region, Poland**. Annual Agriculture Environmental Medicine 2004; 11:255–259.
14. Soontrapa S and Bunyaratavej N. **Serum concentration of undercarboxylated osteocalcin and the risk of osteoporosis in thai elderly women**. Journal of Medical Association Thai 2005; 88 Suppl 5:29–32.
15. Susanto LT. **Serum osteocalcin and bone mineral density in postmenopausal women**. University medicine 2011; 30(3):155–161.
16. Hsu YH, Venners SA, Terwedow HA, Feng Y, Niu T, Li Z, et al. **Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women.** American Journal of Clinical Nutriation 2006;83:146-54.
17. Gerdhem P, Ivaska KK, Alatalo SL. **Biochemical markers of bone metabolism and prediction of fracture in elderly women.** Journal of Bone Mineral Research 2004;19:386-93.
18. Kanis JA. **Diagnosis of osteoporosis and assessment of fracture risk.** Lancet 2002;359:1929-36.
19. Ravn P, Fledelius C, Rosenquist C, Overgaard K, Christiansen C. **High bone turnover is associated with low bone mass in both pre and postmenopausal women.** Bone 1996;19:291-8.