SERUM OSTEOCALCIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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SUMMARY : This study is aimed to get information about osteoblastic activity in female rheumatoid patients and female controls by measuring serum osteocalcin levels by radioimmunoassay. 20 female RA patients and 21 healthy female controls were included in the study. Mean disease duration was 7.65 years and mean age of menopause was 43.72 years in the rheumatoid group. Mean serum osteocalcin level was found to be a little higher in RA patients (4.6 ± 3.2 ng/ml) than controls (3.8 ± 1.43 ng/ml). But the difference was statistically insignificant. No significant difference was observed when the RA group was divided into two groups according to the menopausal state either. Stratifying RA group according to disease activity, functional class and disease duration also did not yield any significant difference in osteocalcin levels. Comparing the patients with high disease activity to the control group we again did not observe any significant difference. It is hard to support the idea that osteocalcin is a good marker of bone metabolism rate in RA patients.

***Key Words** : Rheumatoid Arthritis, Bone Metabolism, Osteocalcin, Bone GLA-Protein.*

INTRODUCTION

It is well known that patients with RA have lower bone mineral density than healthy people (Ekenstam, 1986; Magaro, 1989). The propensity for the development of osteoporosis in RA is still a poorly understood phenomenon, besides some obvious factors such as corticosteroid treatment and immobilization. Several studies investigating the bone metabolism in RA have yielded contradictory results indicating both increased or decreased turnover rate while some claim that no changes occur indeed (Ekenstam, 1986; Lian, 1988; Magaro, 1989; Pitschmann, 1989).

Osteocalcin (bone GLA-protein) is a non-collagenous bone matrix protein which is synthesized by osteoblasts and is known to reflect bone formation rate (Lian, 1988). Total bone metabolism rate can be assessed by measuring serum osteocalcin level in combination with urinary calcium and hydroxyproline excretion. In several studies investigating serum osteocalcin level in RA normal low or high values have been observed (Magaro, 1989; Sambrook, 1985; Pietschmann, 1989). Some authors suggest that disease activity is the factor elevating serum osteocalcin (Ekenstam, 1986; Magaro, 1989) while some others have showed that low levels are due to corticosteroid treatment (Als, 1986; Weisman, 1986). This study is aimed to get information about osteoblastic activity in RA patients and healthy controls and to investigate the validity of osteocalcin as a biochemical marker of bone me-

tabolism and its relationship with the parameters of the disease.

MATERIALS AND METHODS

Twenty female RA patients and 21 female healthy volunteers were included in the study. None of the female volunteers had any evidence of disease or drug administration known to interfere with bone metabolism. RA patients were selected according to ARA criteria with a disease duration of at least one vear. No alterations were made in drug therapy of RA patients and they continued taking nonsteroidal antinflammetory drugs (NSAID's) disease modifying anti-rheumatic drugs (DMARD's), and corticosteroids as they did before. The menoage, functional class and disease activity of the patients were recorded. Presence of at least six painful joints, at least three swollen joints, an erythrocyte sedimentation rate higher than 50 mm/h and early morning stiffness longer than 45 minuses were the criteria for active disease. Functional class of the patients were assessed according to Steinbrocker (Steinbrocker, 1949). Measurements of serum calcium, phosphorus and alkalene phosphatase were performed by routine laboratory procedures. Fasting venous blood samples were taken from each subject and sera were extracted and stored at -40 C until assay. Serum osteocalcin was determined by radioimmunoassay using a commercial kit manufactured by Incstar, Stillwater, Minnesota. The sensitivity of the assay was 0.2 ng/ml. Student's t test was used for statistical evaluation.

RESULTS

Clinical features of the patients and healthy controls are stated in Table 1. Mean age was 46.1 in patients group. and 48.1 in control group. Eleven subjects in each group were postmenopausal, and mean menoage was 43.7 and 47.9 in patient and control group respectively. No significant differences were found between two groups with regard to mean age and mean menoage ($p>0.05$). Serum Ca, P and alkalene phosphatase levels were in normal ranges in both groups. Mean serum osteocalcin level was found to be 4.6 ± 3.2 ng/ml in RA patients and 3.8 ± 1.4 ng/ml in controls. Despite being higher in RA group, serum osteocalcin levels showed no statistically significance between the two groups ($p>0.05$).

RA group was divided into two groups according to the menopausal state (premenopausal = 9. postmenopausal = 11) and no difference in serum osteocalcin level was encountered, either ($p>0.05$).

	Rheumatoid arthritis	Control
Number	20	21
Age (±SD)	46.1 ± 11.3	48.1 ± 9.9
(range)	(25-65)	(28-63)
Disease duration	7.6 ± 6.6	
(1-5 years)	11	
(6 years and over)	9	
Menoage	43.7 ± 45.4 (n=11)	47.9 ± 3.2 (n=11)
Functional class		
1-2	15 (% 75)	
3-4	5 (% 25)	
Corticosteroid*	3 (% 15)	
Activity**		
(-)	9 (% 45)	
(+)	11 (% 55)	
Osteocalcin (ng/ml)	4.6 ± 3.2	3.8 ± 1.4

Table - 1 : Clinical features and mean serum osteocalcin levels in RA patients and controls.
* < 10 mg/day methylprednisolone or equevalent for at least one year
** (+) activity : presences of at least six painful joints. at least three swollen joints, ESR > 50 mm/h, early morning stiffness of longer than 45 minutes.

Subgroupings of RA patients with regard to disease activity (active, inactive), functional class (class 1-2 versus class 3-4) and disease duration (1-5 years versus 6 years and above) yielded again no statistical significance in serum osteocalcin ($p>0.05$).

Statistical analysis was not performed according to corticosteroid administration since there were few patients using steroids (n=3). The comparison of serum osteocalcin in patients with active disease to healthy controls also was found to be insignificant ($p>0.05$).

DISCUSSION

In spite of the fact that bone metabolism is known to be impaired in patients with RA, it is hard to conclude that this impairment is attributable whether to increased bone resorption or decreased bone formation (Pietschmann, 1989). Serum osteocalcin is a matrix protein which is abundant in bone and reflects bone formation. Moreover, it also appears to be a sensitive marker of bone metabolism, because bone formation and resorption form a coupling process of total bone metabolism in which both components follow each other continuously (Ekenstam, 1986; Weisman, 1986; Pietschmann, 1989).

In this study, no significant difference in serum

osteocalcin levels between the RA group and the controls was encountered though the former was a little higher. Our results are consistent with those of Peretz and Pietschman (Peretz, 1989; Pietschmann, 1989). Magaro has found significant high levels or serum osteocalcin in rheumatoid patients compared to patients with psoriatic arthritis and he also disclosed that serum osteocalcin levels were higher in patients with high disease activity in another study of his (Magaro, 1989). Sambrook reported that serum osteocalcin level was in normal ranges in RA patients with recent onset and concluded that there was no alteration of bone metabolism in the beginning of the disease (Sambrook, 1985). Serum osteocalcin level was found to be decreased in both male and female rheumatoid patients by Weisman and the suppressive effect of steroids were demonstrated by this investigator. He also suggested osteocalcin to be a reliable marker of bone metabolism (Sambrook, 1985). Als and Ekenstam have got similar results in their studies.

This study investigates a rheumatoid female patient group which displays rather heterogeneous features with regard to disease duration and activity, type of drug administration and functional category. Range of disease duration is fairly wide (1-27 years) and most patients were on NSAID's, some got both NSAID's and DMARD's and only 3 of our patients were receiving steroids. Ideas about drug effect on serum osteocalcin are inadequate. NSAID's are known to have no effect of serum osteocalcin (Ekenstam, 1986) while the increasing effect of some DMARD's have been reported. This study could not make any evaluation in view of drug administiration since the petient group was small. However disease duration and activity and functional class seemed not to effect serum osteocalcin level. Pre and postmenopausal values were similar as well. However, on investigating the standard deviation of serum osteocalcin levels in RA group, it can clearly be recognized that the value is fairly higher which prompts us to think that some RA patients had very high levels while some had fairly low values, though no such deviation was the case with controls. Therefore it should be worth studying serum osteocalcin levels in RA, with larger number of patients and by stratifying them according to drug administration, disease duration and activity, physical activity and functional class.

Nevertheless, our results which displayed no significant differences in a small group of RA patients avoid us from supporting the idea that serum osteocalcin in solo, is a good biochemical marker of bone metabolism.

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