THE EFFECT OF SALMON CALCITONIN ON BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS

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SUMMARY : This study aimed to investigate the annual bone loss and the efficacy of salmon calcitonin treatment on spinal osteoporosis in patients with rheumatoid arthritis. 22 patients with rheumatoid arthritis (17 females, 5 males) entered the study. 13 patients were administered salmon calcitonin for a mean period of 7.7 (range 6-13) months. 6 of these patients were investigated again after a period without treatment. 9 patients who were not administered calcitonin were assessed twice within a mean period of 16.4 (range 6-28) months. The spinal bone mineral density was measured by dual photon absorbtiometry. Patients treated with salmon calcitonin gained 0.9 % in bone mineral density ($p<0.005$), while the mean bone loss in the untreated group was 8.4 % ($p<0.01$). Salmon calcitonin treatment was suggested to be beneficial in treatment of generalized osteoporosis in rheumatoid arthritis, especially in cases with concomittant risk factors.

***Key Words** : Rheumatoid Arthritis, Bone Mineral Density, Osteoporosis, Treatment, Calcitonin.*

INTRODUCTION

Bone loss has been recognized as a complication of rheumatoid arthritis (RA) for more than a century (1). Loss is accelerated in the peripheral skeleton in early stages of the disease which is termed as "juxtaarticular osteoporosis", however generalized osteoporosis is also known to be associated with RA, as the disease advances. Although some metabolic, immunologic and drug-mediated mechanisms as well as immobilization and disease activity are blamed, the pathogenesis of generalized osteoporosis still remains unresolved (2, 3). Whatever the etiological explanation is, the fact that rheumatoid patients are prone to increased risk of fracture with loss of bone mass is generally neglected by clinicans dealing with this disease. Numerous studies have investigated the dimensions of generalized bone loss in RA (4, 5), but studies proposing a treatment regimen or assessing the efficacy of a therapy for improving bone density or preventing excess bone loss are few. Intranasal calcitonin (6) and biphosphonates (7) have been used for osteoporosis in RA, however the effect of hormone replacement therapy remains to be assessed.

Calcitonin is a hormone that inhibits bone resorption by suppressing the osteoclastic activity and is known to have analgesic activity via central neurogenic mechanisms (8). Therefore it is used for treatment of osteoporosis especially during phases of increased bone turn-over (6).

The aim of this study was to evaluate the annual bone loss in patients with RA and to investigate the efficacy of synthetic salmon calcitonin on bone

mass by quantitative bone mineral density analysis in a prospective clinical trial.

MATERIALS AND METHODS

The study population consisted of 22 patients (17 females, 5 males) with RA who fulfilled the ARA criteria for classical or definite RA (9). The mean age was 56.8 (range 46-70) in males and 45.3 (range 25-64) in females. Patient characteristics are shown in Table 1. Patients who received corticosteroids (8 mg/day prednisolone or equivalent) for at least one year were noted. One patient has been taking anticonvulsant therapy for epileptic seizures for years. Functional staging was made according to Steinbrocker (10).

	Females	Males
Number	17	5
Age	45.3	56.8
(range)	(25-64)	(46-70)
Disease duration (years)	10.8	12.2
Functional stage		
I	4	1
II	5	1
III	4	-
IV	4	3
Menopausal state		
premenopausal	8	
postmenopausal	9	
Steroid treatment	6	3

Table 1 : Patient characteristics.

13 patients (10 females and 3 males) received synthetic salmon calcitonin for a mean period of 7.7 (range 6-13) months. The calcitonin dose was 100 MRCU-subcutaneously-per day for 7 consecutive days, every other day for the next week and three times a week thereafter. Bone mineral density (BMD) of lumbar second, third and fourth vertebrae was measured and the average density (g/cm^2) was assessed prior to and after the treatment period by dual photon absorbtiometry (DPA-Norland 2600) using a source of Gadolinium 153. Six of these 13 patients (all females) served as their own controls and were investigated both after a treatment period and after an interval without treatment. The remaining 9 patients (7 females, 2 males) who were not administered calcitonin were investigated for bone mineral density twice with a mean interval of 16.4 (range 6-28) months. No alterations were made in the type of drug administration during the trial.

Wilcoxon signed rank test was used for evaluating bone mineral density differences between the measurement periods.

RESULTS

The percentage of changes in BMD results for treated and nontreated patients are demonstrated in Figure 1. BMD increased in 7 patients among 13 patients who received calcitonin within a range of 0.41 % - 22.67 %. A bone density increase of 0.41 % shuld be neglected since it stands within the precision of DPA which is approximately ± 3 % (11). The remaining 6 patients displayed remarkable increments in bone density. Two of these patients who showed an improvement in bone density by 8 %, and 22.56 % were taking steroids during the trial. 5 patients lost bone mass in a range of 1.53 % - 19.72 %. Similarly, the slight bone loss in one patient (1.53%) was negligible; which means 4 patients who were administered calcitonin had remarkeble

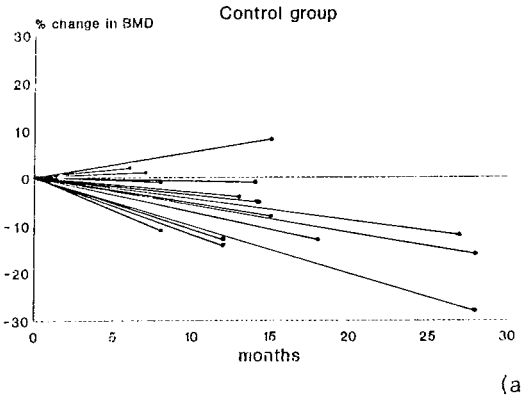

Fig - 1a : Percentage of changes in spinal BMD in rheumatoid arthritis patients without treatment with calcitonin.

bone loss during the trial. One of these 4 patients was taking steroids. The overall evaluation of bone mineral density revealed % 0.9 gain in patients treated with calcitonin.

Among the group of 15 patients who were investigated without calcitonin treatment, 12 patients

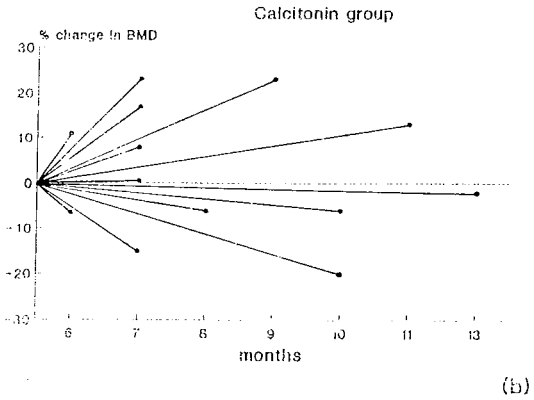

Fig - 1b : Percentage of changes in spinal BMD in rheumatoid arthritis patients with calcitonin treatment.

lost bone mineral. 3 of these were negligible (1 %) and the percentage of BMD loss ranged between 4.82 % - 27.9% in the rest. 3 patients seemed to gain BMD, but the improvements were again negligible (1.25 % and 1.64 %) in 2 patients. The third patient displayed a BMD increase of 7.95 % after a period of 15 months which may be attributable to her age (27) when the peak bone mass might not be accomplished yet. This patient had a disease duration of 5 years. The overall change in BMD in the untreated group revealed 8.4 % reduction of bone mineral.

The overall statistical comparison of BMD values in patients with or without calcitonin treatment is shown in Table 2. The BMD in patients treated with calcitonin significantly increased ($p<0.005$), where patients who did not get calcitonin had significant bone loss ($p<0.01$).

	BMD 1	BMD 2	P
Calcitonin + (n=13)	0.875 ± 0.153	0.893 ± 0.146	< 0.005
Calcitonin - (n=15)	0.979 ± 0.155	0.903 ± 0.156	< 0.01

Table 2 : Statistical analysis of BMD differences in patients with and without calcitonin treatment (Wilcoxon signed rank test).

DISCUSSION

Although generalised osteoporosis is accepted as a complication of RA, current management of bone involvement in this disease is unsatisfactory, as disease modifying antirheumatic drugs do not protect against the development of bone loss (12). Ralston et al, found that bone resorption was decreased biochemically after administering aminohydroxypropylidene biphosphonate, but they did not assess the lumbar bone mineral density changes (7). They concluded that biphosphonates might be of value in the prevention and management of osteopenia associated with RA. In a case presentation by Duell and Chestnut where they attempted to treat extensive vertebral osteoporosis in a patient with RA with sodium fluoride therapy, a repeated exacerbation of arthritis on three occasions of the same treatment was reported (13). Verstraeten et al reported that 1 alpha hydroxyvitamin D, calcium and lynesterol combination proved to be beneficial in postmenopausal rheumatoid arthritis patients from the aspect of bone metabolism (14). The only study with salmon calcitonin conducted by Sileghem et al revealed that morning stiffness was reduced and bone density increased by 1 % in the spine and no loss occured at the distal end of the radius. They did not observe a significant effect on erosion progression by calcitonin (6).

This study did not aim to investigate the effect of salmon calcitonin on clinical parameters of RA. Our aim was to assess the efficacy of calcitonin on spinal osteoporosis associated with RA. The results of the untreated group yielded an average bone loss of 8.4 % while administration of salmon calcitonin produced a slight increment of 0.9 % in bone mass in the treated group. The increments of bone density were remarkable especially in patients treated with steroids and in the particular patient who was taking anticonvulsant therapy and had hysterectomy at age 42 because of myoma uteri. The same patient had significant bone loss after discontinuing the calcitonin treatment. Although no correlation analysis was performed between disease activity and bone density differences, more pronounced bone loss was observed in patients with severely active disease in spite of calcitonin treatment.

Management of RA should also cover measures of treating or preventing excess bone loss, as well as controlling inflammation, since these patients already have less bone mass when compared to healthy subjects (1, 4). Improvement of nutritional state and encouraging physical exercise to maintain adequate bone mass should certainly be the first-line measures in preventing generalized osteoporosis in RA. Besides, we believe that synthetic salmon calcito-

nin may be helpful in decreasing the bone resorbing activity especially in patients having lower baseline values for bone mass with concommitant risk factors for osteoporosis, in RA.

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