EFFICACY OF ADDING INTRANASAL CALCITONIN TO ESTROGEN TREATMENT IN POSTMENOPAUSAL OSTEOPOROSIS

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SUMMARY

The purpose of the present study is to investigate the efficacy of adding intranasal calcitonin to estrogen replacement therapy on bone mass density in postmenopausal osteoporosis. Twenty posmenopausal women were randomized to receive either 100IU intranasal salmon calcitonin in addition to 0.625 mg conjugated estrogens and 2.5 mg medroxyprogesterone acetate or 0.625 mg conjugated estrogens and 2.5 mg medroxyprogesterone acetate alone. Women were assessed at 6 months for bone mass density at lumbar spine and femur neck. Both treatment groups not only stopped further bone loss, but had a small increase in bone mass density at the end of 6 months of treatment. In conclusion it appears that adding calcitonin to estrogen treatment in postmenopausal patients does not have an additive effect in inreasing bone mass density. However intranasal calcitonin, may be an alternative in patients suffering from pain due to postmenopausal osteoporosis.

Key Words: Calcitonin, Estrogen, Postmenopausal osteoporosis.

INTRODUCTION

The number of women sustaining postmenopausal osteoporotic fractures is increasing. This leads to an increase in morbidity and mortality from the condition (1). Prophylaxis for osteoporotic fractures has therefore assumed greater importance. Oral estrogen replacement is effective in preventing postmenopausal bone loss if it has been started within 5 years of the menopause (2-4). Similarly numerous controlled studies demonstrated the preventive and therapeutic effectiveness of calcitonin in the context of postmenopausal osteoporosis (5-9). In women with established osteoporosis, the main goal of treatment is to increase bone mass. Nevertheless the optimum treatment modality is not clear yet. The purpose of the present prospective randomized study is to investigate the efficacy of adding calcitonin to oral estrogen replacement therapy in postmenopausal osteoporosis.

METHODS

Twenty postmenopausal women were recruited from patients presenting to the Marmara University Hospital Menopause Clinic complaining of routine postmenopausal symptoms. Informed consent was obtained from each patient. True post menopausal status was confirmed in all cases by the measurement of gonadotropins and steroid hormones. All women included to the study were between 5 and 8 years postmenopausal. Women were excluded from entering the study, if they had been on sex steroids or calcitonin prior to the study.

They were also excluded if they suffered from various chronic diseases, from metabolic disorders or had evidence or history of neoplastic disease. None of the patients were smoking. All women were randomly assigned to one of two groups. Group A women received 0.625 mg conjugated estrogens (Premarin Ayerst New York NY) and 2,5 mg medroxyprogesterone acetate (Farlutal, Deva Istanbul) daily orally for 6 months. Group B women received 100 IU salmon Calcitonin (Miacalcic Sandoz Basel) intranasally in addition to 0.625 mg conjugated estrogens and 2.5 mg medroxyprogesterone acetate continuously daily orally for 6 months. All patients received 1 gram of elemental calcium orally. Women were assessed at baseline and at 6 months for bone mass density. Assessment of lumbar spine and femur neck was carried out using a dual beam photon absorptiometer (Norland) in a single blind manner. The error calculated in the method of assessing bone density at L2-L4 was 1% and at femur neck it was 2.5 % on the eguipment used.

Statistical Analyses:
The values were expressed as means ± SD. Comparisons of the means were performed by the paired t test and percent of changes in bone mass density between treatments were tested with one-way ANOVA.

RESULTS

Patient data on women at the initiation of the study are presented in table I. Age, age from menopause and baseline bone mass density were similar between the treatment groups. Bone mass density increased from a mean of 0.722 ± 0.13 to 0.793 ± 0.142 at femur neck and from 0.916 ± 0.178 to 0.965 ± 0.240 at lumbar site in estrogen and progesterone treatment group. Similarly in calcitonin plus estrogen and progesterone group, bone mass density increased from 0.670 ± 0.004 to 0.734 ± 0.07 at femur neck and from 0.815 ± 0.143 to 0.865 ± 0.153 at lumbar site.

Table II shows the percent of change of bone mass density in both treatment groups at the end of 6 months. There was a small increase in bone mass density in both treatment groups. The percent of change in bone mass density neither at femur neck nor at lumbar site showed a significant difference between the treatment groups.

Two patients (20%) in each group experienced uterine bleeding as spotting, in the first 3 months of treatment, which disappeared spontaneously. No side effects were reported due to intranasal calcitonin. Three patients in each group complained of severe bone pain prior to treatment. It appeared that 3 patients in the calcitonin treatment group had a better improvement of pain relief in comparison to 3 patients in estrogen treatment group.

DISCUSSION

Several studies have demonstrated that circulating calcitonin decreases with advancing age (10, 11). It has been suggested that deficiency of calcitonin could be responsible for the higher prevalance of osteoporosis among postmenopausal women (12). Recently Reginster et al (13) have shown that postmenopausal women have a significant reduction in serum calcitonin levels, suggesting that a reduction of the capacity to secrete calcitonin is a result of estrogen deficiency. Nevertheless several reports to the contrary suggest an apparent lack of consensus currently (14, 15). It has also been suggested that the protective effect of estrogens on the skeleton is mediated by the control of calcitonin synthesis (16).

As postmenopausal osteoporosis is characterized by bone resorption in excess of formation (17). Calcitonin is one of the promising agents for treatment as it is known to inhibit osteoclastic activity (18,19) and stimulate bone formation (5,20). It has been clearly demonstrated that estrogen treatment is effective in maintaining bone mass if started within 5 years of menopause (2-4). Numerous studies have evaluated the effect of calcitonin in women with established postmenopausal osteoporosis and reported that calcitonin stops further bone loss in those patients (5,6,21). A few studies have reported a significant increase in bone mass on calcitonin treatment (22). In an attempt to investigate the efficacy of adding calcitonin to estrogen replacement therapy in established osteoporosis; we compared

Table I- Patient data on women at the beginning of the study +

	Group A	Group B
Age (SD) years	53.3 ± 3.28	55.1 ± 4.69
Age from menapouse	8 ± 4.87	8.7 ± 6.34
Initial bone density at lumbar site	0.916 ± 0.178	0.815 ± 0.143
Initial bone density at femur neck	0.722 ± 0.13	0.670 ± 0.004

+ : No significant difference between the groups
Group A - Estrogen and Progesterone
Group B - Calcitonin + Estrogen and Progesterone

Table II- Percentage of change of bone mass density over 6 months

	% of Change in BMD at Femur neck	% of Change in BMD at Lumbar site
Group A	9.8 %	5.3 %
Group B	9.5 %	6.1 %
P Value	P > 0.05	P > 0.05

P : No significant difference between the groups
Group A- Estrogen and Progesterone
Group B- Calcitonin + Estrogen and Progesterone

calcitonin and estrogen with estrogen alone treatment in patients 5 to 8 years of the menopause.

The present study confirms that both treatment groups, estrogen with or without calcitonin, not only stopped further bone loss but caused a small increase in bone mass density at the end of 6 months as well. It appears that calcitonin treatment is more effective in improvement of pain relief which could be explained by the analgesic effect of calcitonin which is reported to be mediated by endogenous opiate system (23). It has been reported that intranasal calcitonin is more effective than parenteral calcitonin in improvement of pain relief (24).

Meschia et al (25) compared the effects of calcitonin alone estrogen alone, calcitonin estrogen combination and placebo on vertebral bone mass density in 2 years of treatment. They reported that both calcitonin and estrogen alone prevented bone loss. However only estrogen treatment caused a significant increase in bone mass. Combination of parenteral calcitonin and estrogen treatment not only prevented bone loss but led a significant and prominent gain. MacIntyre et al (26) in a similar designed study reported that both parenteral calcitonin and estrogen treatment reduced vertebral bone loss. However combination of calcitonin and estrogen treatment was more effective in reducing bone loss. The current study demonstrates that in established postmenopausal osteoporosis, estrogen alone is as effective as combination of calcitonin and estrogen treatment in preventing further bone loss.

As a conclusion, it appears that adding calcitonin to estrogen treatment in postmenopausal patients, does not have an additive effect in increasing bone mass density neither at femur neck nor at lumbar spine. However nasal spray calcitonin with its safety, lack of side effects and simple administration could be recommended to patients suffering from bone pain due to postmenopausal osteoporosis. Considering the small number of subjects of the present study, future studies with larger groups are needed to confirm these results.

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