PREVENTIVE EFFECT OF CALCITONIN ON HEMIOSTEOPOROSIS AFTER STROKE

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ABSTRACT

Aim: Osteoporosis-related fracture is one of the important complications that negatively affect the rehabilitation outcome after stroke. Preventing falls and hemiosteoporosis in stroke patients are the goals of rehabilitation programs. In this retrospective study, we investigated the effect of 100IU intramuscular salmon calcitonin treatment on the development of hemiosteoporosis in stroke patients.
Patients and Methods: Hospital records of 44 first-stroke inpatients with an average of 62.4 8.1 years were reviewed. Twelve patients received calcitonin treatment, whereas 32 patients did not receive any medication altering bone metabolism. The outcome measure was determined as the rate of bone mineral density (BMD) loss at lomber region, bilateral femoral neck and wrists, from admission to discharge from rehabilitation clinic.
Results: There was no difference regarding age, gender, time since stroke, side of lesion and motor impairment level. Calcitonin group showed significantly less percentage bone loss at all sides than those of the control group ($p<0.05$).
Conclusion: We suggested that 100IU salmon calcitonin may be an effective medication for preventing osteoporosis in patients with stroke. We believe that the therapeutic effects should be clarified by prospective, randomized, controlled studies.

Key words: Stroke, hemiplegia, bone mineral density, calcitonin, rehabilitation

ÖZET

Amaç: Osteoporoza bağlı gelişen kırık, inme sonrası rehabilitasyon sonuçlarını olumsuz etkileyen önemli komplikasyonlardan biridir. İnmeli hastalarda hemi-osteoporozu ve düşmeyi önlemek rehabilitasyon sürecinin hedefleri arasındadır. Bu retrospektif çalışmada, 100 IU intramüsküler salmon kalsitonin tedavisinin inmeli hastalarda hemi-osteoporozu önlemedeki etkinliği araştırılmıştır.
Hastalar ve Metod: İlk inme öyküsü olan 44 yatan hastanın verileri çalışmaya dahil edildi. Yaş ortalaması 62.4 8.1 idi. Oniki hasta refleks sempatik distrofisi nedeni ile kalsitonin tedavisi alırken, 32 hasta kemik metabolizmasını etkileyen herhangi bir ilaç almıyordu. Son durum ölçeği; yatıştan taburculuğa kadar olan süre içindeki lomber bölge, bilateral femur boynu ve elbileğinin kemik mineral yoğunluğu (KMY) kaybı oranı olarak belirlendi.
Sonuçlar: Gruplar arasında yaş, cinsiyet, inme sonrası geçen süre, lezyon tarafı, motor yetersizlik seviyesi açısından fark saptanmadı. Kalsitonin grubunda, kontrol grubuna göre tüm bölgelerde kemik kaybı oranı anlamlı olarak daha düşük saptandı ($p<0.005$).
Sonuç: 100 IU salmon kalsitoninin inmeli hastalarda osteoprozu önlemede etkin bir tedavi olduğunu düşündük. Töropatik etkileri, prospektif randomize kontrollü çalışmalarla netleştirilebilir kanaatindeyiz.

Anahtar kelimeler: İnme, hemipleji, kemik mineral yoğunluğu, kalsitonin, rehabilitasyon

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INTRODUCTION

Recent studies have shown that one of the most serious complication after stroke is osteoporosis-related fractures that usually occur on the paretic side (1). After stroke, the risk of hip fracture is increased 2 to 4 times relative to a reference population (2). The high frequency of fractures after stroke may result from disuse hemiosteopenia, hypovitaminosis D, and increasing risk of falls (3-5). Fracture in a patient with stroke makes rehabilitation more difficult and significantly decreases the level of the expected rehabilitation outcome. In order to prevent falls after stroke, assisstive device training, balance and coordination exersises, and training caregivers on environmental safety and supervision are suggested (6) Calcium supplements and 1 -hydoxyvitamin D3 (7), menatetrenone (8), ipriflavone (9), and etidronate (10) are the therapeutic agents used for the management of hemiosteoporosis after stroke.

In an earlier study, we have investigated the development of osteoporosis in stroke inpatients and found that stroke patients were at increased risk of osteoporosis on the paretic side especially at the wrist. In the same study, 12 patients had excluded from the study because they received 100IU salmon calcitonin for the treatment of reflex sympathetic dystrophy (RSD). Current retrospective study was planned to investigate the effects of calcitonin treatment on the bone loss rate of stroke patients. To our knowledge, calcitonin has not been used before for the management of hemiosteoporosis after stroke.

METHOD

Hospital records of 44 inpatients from the data of an earlier study, having unilateral first stroke and extensive extremity paresis or total paralysis, were reviewed retrospectively. Exclusion criteria were having previous osteoporotic fracture, or ongoing treatment with drugs known to alter bone metabolism like corticosteroids, thyroxin or anticonvulsants. None of the patients had persistent paresis from previous strokes, and all had been independent before the stroke. Among the data 12 patients with stroke who received 100 IU intramuscular calcitonin treatment every second day during 2 months for the treatment of reflex sympathetic dystrophy (RSD) were selected as calcitonin group. Other 32 patients did not receive any medication altering bone metabolism and named as control group.

Demographic and clinical characteristics of the patients were documented. Lumbar spine, bilateral femoral neck and distal radius bone mineral densities (BMD) of all patients was assessed using dual-energy X-ray absorbsiometrya at admission and discharge. Change in BMD was calculated as (BMDadmission - BMDdischarge)/ BMDadmission X 100. Mann-Whitney-U, Wilcoxon and chi-square tests were used for the statistical comparisons between the groups. Alpha levels were set at .05.

RESULTS

Table 1 presented the demographic and clinical characteristics of the groups. There were no significant differences between the groups in terms of demographic and initial clinical characteristics ($p>0.05$ for all variables). Table 2 showed the comparison of changes in BMD (percentage loss) of the groups. In the calcitonin group, in both paretic and nonparetic sides, 2-12% loss of BMD values at femoral neck and distal radius had been determined,. Calcitonin group showed significantly less bone loss in each of 5 sites than those of the control group and the difference between the groups was statistically significant ($p<0.05$).

DISCUSSION

Several studies have reported BMD loss on affected side after hemiplegic stroke (11-14). Bone loss from the paretic femoral neck of stroke patients has been reported up to 14% within one year in a previous study (15). The possible mechanisms underlying hemiosteoporosis after stroke have been investigated and listed as immobilization, vitamin D deficiency due to malnutrition, sunlight deprivation, immobilization induced hypercalcemia, compensatory hyperparathyroidism, degree of functional recovery, anticoagulation with warfarin and severity of hemiplegia (3,7,9,16-18). An increased bone resorption and enhanced osteoclast activity has been suggested after stroke (2,3,18).

Two studies with etidronate (10,19) and one study with risedronate sodium (20) have been published reporting beneficial effect of these drugs on

bone loss when administered after acute stroke. However, dysphagia or drowsiness after acute stroke may limit their use for those at most risk (21). Therefore, intravenous or intramuscular therapies may be more convenient in the prevention of bone loss after stroke. Intravenous bisphosphonate has been studied before. Poole et al showed the efficacy of a single infusion of zoledronate, an intravenous bisphosphonate, in preserving hip bone density after stroke (22). Intramuscular calcitonin therapy in prevention of osteoporosis in patients with stroke has not been studied yet.

Calcitonin is a peptide composed of 32 amino acids which binds to osteoclasts and inhibits bone resorption (23). Calcitonin is an effective inhibitor of osteoclastic bone resorption and has a direct central analgesic effect which may be mediated through increases in -endorphin secretion (24). Its ability to reduce vertebral fracture rates in postmenopausal osteoporosis has been demonstrated (25). Both intranasal and intramuscular calcitonin have been shown to be effective in postmenopausal osteoporosis (26). An observational study by Kanis et al. demonstrated a 30% reduction in hip fractures in patients treated with injectable calcitonin in postmenopausal women (27) .Calcitonin has also been used to control pain and restore bone in patients with reflex sympathetic dystrophy (RSD) (28,29). Depending on this literature knowledge and our clinical experience, we suggested that calcitonin might be effective in prevention and treatment of osteoporosis in stroke patients.

Uebelhart et al. has shown in a prospective randomized study that administration of 200IU intranasal calcitonin did not influence the levels of biochemical markers of bone and connective tissue metabolism (30). Although the mechanism of action and bone turnover have not been investigated in our study, 100IU intramuscular salmon calcitonin every second day for 2 months, is thought to reduce bone loss by inhibiting osteoclastic bone resorption in patients with stroke. Methodology of that study differ from ours in terms of application form and the study design. They have applied calcitonin via intranasal route. The bioavailability of nasal salmon calcitonin is only about 25 percent that of intramuscular calcitonin; thus, the biological effect of 50 IU of intramuscular salmon calcitonin is equivalent to that of 200 IU of nasal salmon calcitonin. The absorption of the nasal dose is delayed compared with the parenteral route (31). Moreover, they have not investigated the effect of intranasal calcitonin on the bone mineral density of patients with stroke.

Analgesic effects of calcitonin might have leaded the patients more active and the other possible mechanism might be the over encouragement of patients who had RSD to exercise more than before in our study.

As a conclusion, our observation convinced us that calcitonin is effective in preventing hemi-osteoporosis after stroke. However, this was a small sample, and there was no random assignment to calcitonin versus non-calcitonin groups. The therapeutic effects and dosages of calcitonin for this purpose should be clarified by prospective, randomized, controlled studies.

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