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The Effect of Early Therapeutic Electrical Stimulation on Bone Mineral Density in the Paralyzed Limbs of the Rabbit

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The purpose of this animal experiment was to evaluate the changes of bone mineral density in paralyzed limbs, and to assess the effects of electrically stimulating muscle contraction upon bone mineral density (BMD) in paralyzed limbs during the four week period immediately following spinal cord injury (SCI).

Ten rabbits were used for the study, spinal cords were totally transected at the T11 spine level. The paralyzed quadriceps femoris of one limb was contracted by electrical stimulation for 60-minutes daily, while the other side was not stimulated as a control. The BMD of each lower limb was measured by Dual Photon Absorptiometry before and four weeks after acute SCI. BMD of both limbs decreased in all rabbits four weeks after SCI. The decrease in BMD for stimulated and non-stimulated limbs was 6.130 ± 3.212% and 9.098 ± 3.831%, respectively during the four-week period after SCI. The BMD of stimulated limbs decreased significantly less than that of the non-stimulated limbs. Electrically induced muscular contraction reduced bone mineral loss in the paralyzed limb during the early stage of SCI in the rabbit.

Key Words: Spinal cord injury, osteoporosis, electrical stimulation, bone mineral density

INTRODUCTION

Weight bearing and stress on the bone caused by muscle contraction play an important role in bone mineralization. It is well known that a marked reduction of bone mass progresses rapidly during prolonged periods of immobilization or in the gravity free state.[1,2] As an inevitable sequela of spinal cord injury (SCI), osteoporosis is related to a high prevalence of fracture and is one of the most difficult problems in the rehabilitation of SCI patients.[3,4] Bone mass homeostasis is difficult to assess precisely but most authors agree that major bone loss occurs during the 6 month period following spinal cord injury, and the stabilizes within 12-16 months.[5,6] This may be related to a decrease in muscle tone during the period of spinal shock and to immobilization during the acute stage following this type of injury.

Functional electrical stimulation (FES) has been used to produce contractions of upper-motor-neuron paralyzed skeletal muscle in patients with SCI as an electrical therapy.[7] These contractions can be used to produce functional movements in the extremities. Several studies have shown the usefulness of FES for the prevention or treatment of complications resulting from SCI, such as the prevention of, pressure sores, deep vein thrombosis, joint contracture, deconditioning due to lack of exercise and muscle atrophy.[8,9] On considering the results from several studies which have shown that muscle contraction places stress on the bone, and may prevent disuse osteoporosis,[10] FES may help prevent osteoporosis. However, FES in SCI is usually applied several months after the injury for various reasons, such as, an unstable medical condition, operations, or bladder and bowel management programs.

If muscular contractions by electrical stimulation were to be started in the early stage, when the majority of bone mineral loss occurs, osteoporotic changes, and complications such as fractures and so forth might be reduced.

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electrically stimulated early muscle contraction upon bone mineral density (BMD) in paralyzed limbs in the period immediately following SCI.

MATERIALS AND METHODS

Animal and surgical procedure

Ten healthy and well-matured male rabbits, weighing between 2.0 and 4.5Kg were used for this study. Pentobarbital sodium at 20 mg per Kg was injected intravenously for anesthesia during the scanning for BMD measurements and the operation. After confirming the location of the T11 vertebra by radiography, the T11 lamina was removed bilaterally, and the spinal cord totally transected. Each end of transected cord was tied using 5.0 surgical silk. Animals were kept in a climate-controlled room. The urinary bladder was evacuated by manual pressure during the spinal shock period. As the spinal shock subsided, spontaneous voiding returned with a variable post-void residual volume.

Electrical stimulation

The experimental group underwent electrical stimulation of the left quadriceps femoris muscle. The middle third of the anterior thigh were shaved and cleaned with alcohol. A 2 × 2 cm cathode was placed on the skin over the mid-portion of muscle belly and the anode was placed 2 cm distal to the active electrode. Gel was used to diminish impedance. The day after SCI, electrical stimulation was provided with a Mettler Electronics Stimulator (1333 South Claudina St., Anheim, CA 92805, USA) for 60 minutes daily. Each contraction lasted for 10 seconds (on time) followed by a resting period of 10 seconds (off time). The stimulus delivered (24Hz, 250 microseconds pulse duration, and 30-100 mA) was sufficient to provoke tetanic contraction. The quadriceps femoris of the right limb was not stimulated in the control group.

BMD measurement and data analysis

LUNAR DPX-L dual photon absorptiometry (DPA) and LUNAR Small Animal Software version 1.0 (Lunar Corporation, 313 West Beltline, Madison, WI 53713, USA) were used to measure the bone mineral density (g/cm^2) of both lower extremities. After scanning both lower limbs, the area of analysis from the neck of the femur to the ankle was adjusted using Animal Software, and the BMD of this area measured on each limb. BMD was measured before and after SCI with an interval of two weeks as long as the rabbits survived. The decrease in BMD 4 weeks after injury was calculated using the following equation to evaluate the effect of electrical stimulation.

Decrease rate of BMD (%) =
(BMD before injury - BMD 4weeks after injury) × 100/BMD before injury

Data analyses were conducted to compare the differences between the BMDs measured before and 4 weeks after SCI, and to compare the decrease of BMD in experimental and control groups. Two-way ANOVA was used for statistical analysis. The level of statistical significance was set at .05.

RESULTS

All rabbits were kept alive for four weeks after the SCI. No significant differences were found in the mean bone mineral densities of the experimental ($0.475 \pm 0.053 g/cm^2$) and control ($0.476 \pm 0.058 g/cm^2$) groups before injury (Table 1). The BMD decreased gradually after SCI in both lower limbs. Fig. 1 shows a typical pattern of changes

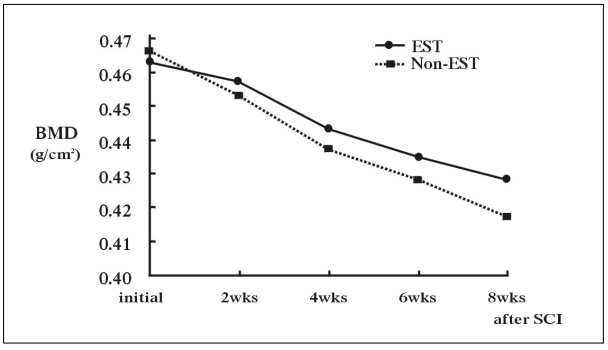

Fig. 1. Changes of the BMD of paralyzed limbs in one of the SCI rabbits. BMD, bone mineral density; EST, electrically stimulated; SCI, spinal cord injury.

in BMD after SCI. The BMD was significantly ower than the pre-injury value in both side four weeks after injury (Fig. 2). However, the BMD loss of the electrically stimulated limbs was less than the non-stimulated control limb loss in all rabbits. The BMD of the electrically stimulated limb was $0.445 \pm 0.046 g/cm^2$ four weeks after SCI, which was significantly greater than that of non-stimulated control side ($0.431 \pm 0.045 g/cm^2$), and the decrease in BMD over the four weeks following injury was $6.130 \pm 3.212\%$ and $9.098 \pm 3.831\%$, respectively (Table 1), and this difference was statistically significant ($p < 0.001$).

DISCUSSION

Decreased bone mineral density in paralyzed

Table 1. Changes of the BMD in the Paralyzed Limbs of Rabbit (n=10) after Spinal Cord Injury

	EST limbs (Mean ± SD)	Non-EST limbs (Mean ± SD)	p value
BMD (g/cm^2)			
Initial	0.475 ± 0.053	0.476 ± 0.058	> 0.05
4 weeks after SCI	0.445 ± 0.046	0.431 ± 0.045	0.01
p value	0.0001	0.0001	0.0005
BMD decrement for 4 weeks (%)	6.130 ± 3.212	9.098 ± 3.831	

BMD, bone mineral density; EST, electrically stimulated; SCI, spinal cord injury; SD, standard deviation.

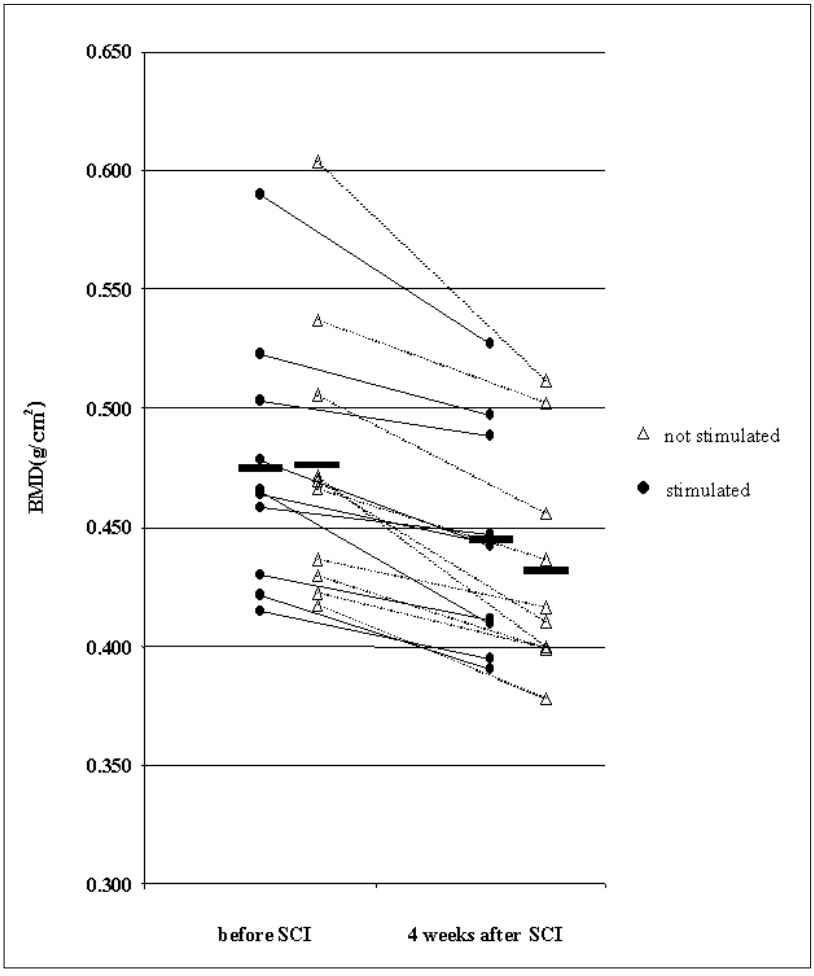

Fig. 2. BMD of paralyzed limbs before and 4 weeks after SCI. Solid bars represent mean values. BMD, bone mineral density; SCI, spinal cord injury.

limbs is a well-known sequela of spinal cord injuries. Using non-invasive techniques, such as DPA, make it possible to quantify bone loss very accurately. Many studies have used DPA to identify the changes of bone mass after SCI.[4,6,11] After an acute spinal cord injury, calcium metabolism is disturbed due in part to a loss of weight and the lack of voluntary muscle contractions.[2,4] This causes bones to become more fragile and increases the risk of fracture. Fractures of paralyzed limbs are a frequently occurring event in paraplegic patients undergoing rehabilitation programs.[12,13]

Because one of the mechanisms, which is believed to contribute to this profound bone loss, is the lack of muscle contraction and mechanical loading in the SCI patient, attention has been focused on the use of therapeutic neuromuscular electrical stimulation to reduce immobilization, and increase biomechanical strain, and thereby, to improve bone mass at localized skeletal regions.[8,11,14] Functional neuromuscular stimulation exercise studies in long standing SCI patients have shown rapid redevelopment of muscle tissue, but not bone recalcification.[14]

Leeds and associates[11] and Pacy and colleagues[14] reported no benefit of FES-induced bicycle ergometry on the bone mass of the proximal femur or lumbar spine in individuals with SCI, but the subjects of their study were chronic patients that had sustained injury two years previously. More recent reports have suggested that FES-induced bicycle ergometry can produce small increases of bone mass in patients with chronic SCI, but these benefits are localized to the skeletal regions receiving the greatest mechanical strain from the exercise regimen.[9]

Most authors agree that major bone mineral loss occurs during the period immediately following SCI,[5,15] and have reported that there is an increased, but an nevertheless, and unbalanced rate of bone remodeling, with bone resorption occurring at a faster rate than bone formation during this immediate post-SCI period. There is also general agreement that remobilization will not repair mineral loss after the first 6 months of immobilization, when the osteoporosis has become inactive and established.[16] Recently de Bruin et al, demonstrated that there was no or only insignificant loss of trabecular bone in early mobilized SCI subjects, whereas a marked decrease of trabecular bone was observed in the non-intervention subjects.[17] These findings could reconfirm the hypothesis that intervention must occur before the lower homeostatic level is obtained. Several recent studies have reported the effect of functional electrical stimulation on the rate of calcium loss, which was applied during the immediate post-SCI period. Wilmet and associates[6] observed a rapid decrease of bone mineral content in paralyzed areas, of 2 to 4% of the initial value/month during the first year, which supports the idea of trying to prevent bone loss early in the course of the disease. In a recent human experiment, early intervention with FES-induced bicycle ergometry following acute SCI was reported to significantly decrease hypercalciuria, however, no dramatic effect amelioration of osteopenia found.[18] On the contrary, Sipski et al.[19] reported that the prevention of osteoporosis is possible using electrical stimulation after SCI, and that the effect is specific to the muscle groups stimulated.

Our animal experiment also showed that electrically induced muscular contraction reduces bone mineral loss, when applied in the stage immediately following SCI. We chose to use each lower limb of the same animal in the experimental and control group, which could helpfully eliminate other factors influencing bone mineralization, such as nutritional or hormonal effects.

However, we did not determine whether our efforts to lessen BMD reduction were sufficient to prevent complications of osteoporosis. More extensive studies and data from human subjects are required to determine if muscular contraction or gait induced by FES can modify osteoporosis and osteopenia associated with SCI.

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