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14. ABSTRACT The purpose of this study was to assess the potential for brief periods of low magnitude high frequency mechanical stimulation signals in the musculoskeletal system. The major findings were that short bouts of extremely low-level mechanical signals, several orders of magnitude below that associated with vigorous exercise, increased bone and muscle mass in the weight bearing skeleton of young adult females with low bone density. Ultimately, this information could be of great benefit to enhance musculoskeletal development and decrease the risk for stress fractures in military recruits. Moreover, should these musculoskeletal changes persist through adulthood, this intervention may prove a deterrent to osteoporosis in the elderly.					
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INTRODUCTION

The incidence of osteoporosis, a disease that manifests in the elderly, may be reduced by increasing peak bone mass in the young. Indeed, susceptibility for low bone mass is present early in life, the amount of bone gained during adolescence is a main contributor to peak bone mass in the young adult, and peak bone mass in the young adult is a likely determinant of osteoporosis in the elderly. While research continues to identify means of reversing osteoporosis in the elderly, these data from children, adolescents and young adults indicate that enhancing bone health early in life represents a viable means of deterring osteoporosis decades before it arises. However, the benefits of early pharmacological interventions to prevent a disease that will not manifest for decades must be weighed against the possible complications of extended treatment. Preliminary data indicate that extremely low-level mechanical signals are anabolic to bone tissue, and their ability to enhance bone and muscle mass in young women was investigated in this study.

BODY

This study was designed to establish if brief, daily exposure to extremely low-level mechanical stimuli is anabolic to musculoskeletal development in young males and females, 15-20 years of age, with low bone density, who had previously sustained a fracture.

The effects of two twelve-month interventions on musculoskeletal development in young men and women were longitudinally studied and the results compared to matched groups of subjects undergoing no intervention. The mechanical intervention consisted of brief exposure to low level (0.3g; 1g = earth gravitational field) high frequency (30-Hz) mechanical loading for 10 minutes every day. The resistance exercise intervention consisted of 30 minutes of weight-bearing and trunk stabilization exercises three times per week.

A twelve-month trial was conducted in 48 young women (15-20y) with low bone density and a history of at least one skeletal fracture. Half of the subjects underwent brief (10 minute requested), daily, low-level whole body vibration (30 Hz, 0.3g); the remaining women served as controls. Quantitative computed tomography (CT) performed at baseline and at the end of study was used to establish changes in muscle and bone mass in the weight-bearing skeleton.

Using an Intention to Treat (ITT) analysis, cancellous bone in the lumbar vertebrae and cortical bone in the femoral midshaft of the experimental group increased by 2.1% ($p=0.025$) and 3.4% ($p<0.001$), respectively, as compared to 0.1% ($p=0.74$) and 1.1% ($p=0.14$), in controls. Increases in cancellous and cortical bone were 2.0% ($p=0.06$) and 2.3% ($p=0.04$) greater, respectively, in the experimental group when compared with controls. Cross-sectional area of paraspinal musculature was 4.9% greater ($p=0.002$) in the experimental group versus controls. When a per protocol analysis was considered, gains in both muscle and bone were strongly correlated to a threshold in compliance, where the benefit of the mechanical intervention as compared to controls was realized once subjects used the device for at least two minutes per day ($n=18$), as reflected by a 3.9% increase in cancellous bone of the spine ($p=0.007$), 2.9% increase in cortical bone of the femur ($p=0.009$), and 7.2% increase in musculature of the spine ($p=0.001$), as compared to controls and low-compliers ($n=30$).

Additionally, 24 males were initially enrolled in each of the vibration intervention and control groups. During the course of the intervention, one participant in the vibration intervention group moved out of state and one was incarcerated, the remaining 22 completed the intervention. There was no obvious benefit of the intervention in this group of subjects. These measures included paraspinous musculature, spine cancellous bone mineral density, spine cross-sectional area, visceral fat, subcutaneous fat, total fat, vertebral height and vertebral volume in the axial skeleton, and quadriceps femoris area, femoral cross-sectional area, femoral cortical bone area, femoral bone mineral density and femoral fat in the appendicular skeleton. Unfortunately, males were less compliant than females, possibly accounting for the negative results of this study

Serum levels of IGF-I were examined prior to and following the mechanical intervention in both study subjects and controls. At the mid-shaft of the femurs, IGF-I did not correlate with the material density of cortical bone ($r = -0.08$), but did correlate significantly with cortical bone area ($r = 0.50$; $P < 0.0001$) and with the cross-sectional area ($r = 0.49$; $P < 0.0001$) of the bone. When using multiple regression analyses, IGF-I was associated with both the cross-sectional area ($P = 0.03$) and cortical bone area ($P = 0.04$), even after accounting for age, gender, weight and the length of the femur. Thus, in the appendicular skeleton of male and female teenagers and young adults in this study, IGF-I had no influence on the material density of the bone, but was found to be a major determinant of the cross-sectional properties of the bone.

KEY RESEARCH ACCOMPLISHMENT

Establishing that short bouts of a low-level mechanical signal increases bone and muscle mass in young adult females.

REPORTABLE OUTCOMES

Abstracts and Presentations

Liu, X., C. Rosen, S. Mora, D. Dong, P. Pitukcheewanont, and V. Gilsanz, Low DXA and CT bone measures in young adults with a simple sequence repeat in IGF-I gene. *J Bone Min Res*, 2004. 19: p. S248.

Shepherd, J.A., B. Fan, M. Sherman, et al., Pediatric DXA precision varies with age. *J Bone Min Res*, 2004. 19: p. S234.

Wren, T.A.L., V. Gilsanz, P. Pitukcheewanont, et al., The Bone Mineral Density in Childhood Study (BMDCS): Substudy Comparing DXA and CT Vertebral Bone Measurements in Healthy Children and Adolescents. *J Bone Min Res*, 2004. 19: p. S67.

10/2004 “Low DXA and CT Bone Measures in Young Adults with a Simple Sequence Repeat in IGF-I Gene”
26th Annual Meeting of the American Society for Bone and Mineral Research
Seattle, WA

- 03/2005 “Comparison of CT and DXA Measurements in Healthy Children”
Bone Mineral Density in Childhood Study (BMDCS) Meeting
National Institute of Child Health and Human Development
Bethesda, MD
- 09/2005 “Mechanical Intervention Enhances Bone and Muscle in Young Women with
Low Bone Density”
American Society of Bone and Mineral Research 27th Annual Meeting
- 06/2006 “Mechanical Intervention Enhances Bone and Muscle in Young Women with
Low Bone Density”
CHLA Saban Research Institute 11th Annual Poster Session
- 06/2006 “Fat Mass is Not Beneficial to Bone”
CHLA Saban Research Institute 11th Annual Poster Session
- 06/2006 “Assessment of Vertebral Peak Bone Mass by CT and DXA”
CHLA Saban Research Institute 11th Annual Poster Session
- 09/2006 “Good, Good, Good Vibrations: Evidence for the Therapeutic Potential of Low-
Magnitude, High Frequency Mechanical Signals”
American Society of Bone and Mineral Research 28th Annual Meeting

CONCLUSION

Short bouts of extremely low-level mechanical signals, several orders of magnitude below that associated with vigorous exercise, increased bone and muscle mass in the weight bearing skeleton of young adult females with low bone density. Should these musculoskeletal enhancements be preserved through adulthood, this intervention may prove a deterrent to osteoporosis in the elderly.

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