J Bone Miner Metab (2006) 24:505–507
DOI 10.1007/s00774-006-0717-9

SHORT COMMUNICATION

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Novel, high-frequency, low-strain mechanical loading for premenopausal women with low bone mass: early findings

Received: May 8, 2006 / Accepted: June 7, 2006

Abstract Universally safe and effective methods of mechanically loading the skeleton to improve strength and prevent fracture have yet to be identified. To be osteogenic, mechanical strains must either be of substantial magnitude or applied at high frequency (>15 Hz). High-magnitude loads place frail bones at risk of fracture. Active loading can rarely be achieved at a frequency faster than 2–3 Hz. A 12-month, uncontrolled, prospective, pilot intervention trial was conducted with five premenopausal Caucasian women with low bone mass. Subjects stood on a vibrating platform (Optimass model 1000 Mechanical Strain Device) and received a 0.2-g stimulus at 30 Hz, 2 × 10 min/day, for 12 months. Bone mineral density (BMD) was measured at the whole body, lumbar spine, proximal femora (PF), and distal radius at baseline and 6 and 12 months by DXA (Hologic QDR-1000/W). Blood and urine were collected at baseline and 3, 6, 9 and 12 months for markers of bone resorption and formation. A mean percent BMD increase of 2.03% ± 0.33% ($P < 0.02$) was detected at the non-dominant PF after 12 months. Trends for increases were observed at all other sites with the exception of the dominant PF. No uniform trends were observed in bone resorption and formation markers. One subject, on Fosamax, increased BMD by 6% at the lumbar spine and 4.4% at the distal radius. Preliminary findings provide evidence of a possible positive response of regions of low bone mass to brief daily bouts of in-home, passive, noninvasive, low-strain, high-frequency, mechanical loading.

Key words whole-body vibration · bone mass · osteoporosis

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Introduction

Bone is known to respond to altered habitual mechanical loading with changes in size and shape to best withstand future applications of similar loading. Some recommend exercise as a preventative measure for osteoporosis. Unfortunately, only certain forms of exercise (predominantly high impact) appear to stimulate bone, and gains are typically modest and specific only to loaded sites rather than generalized to the whole skeleton. Furthermore, the effect exhibits diminishing returns with time and, if the exercise is discontinued, the effect is quite rapidly lost in adults. Further detracting from the notion of exercise as a panacea for bone is its lack of universal practicality. The performance of high-intensity activity such as jumping and running is neither feasible nor safe for frail individuals susceptible to low-trauma fracture and falls. More novel approaches to harnessing the effect of mechanical loading than high-impact exercise are needed.

Although it was originally thought that large bone strains were necessary to stimulate the adaptive response, observations from animals have indicated that very low strains can be osteogenic if applied at sufficiently high frequency (between 15 and 40 Hz) [1]. Loads to the skeleton derived from typical locomotor forms of exercise are in the order of 1–2 Hz. While muscle loading occurs at frequencies up to 30 Hz [2], it is difficult to deliver such loading in any predictable or systematic way. Passive vibrational loading may be a method of delivering both direct mechanical and muscle-related strains to the skeleton.

Although whole-body vibration has not been found to improve parameters of bone strength in young healthy adults [3], an increase in hip bone mineral density (BMD) and a reduction in age-related bone loss has been observed

in postmenopausal women who complied well with the intervention [4,5]. The effect of whole-body vibration on premenopausal women with low bone mass has not previously been examined. The purpose of the current pilot investigation was to observe the effect of 12 months of 2×10 min/day whole-body vibration at 30 Hz on BMD at clinically relevant sites in skeletally compromised, but otherwise healthy, premenopausal women.

Materials and methods

All procedures were carried out in accordance with approval guidelines of the Stanford Research Compliance Panel (Stanford University, CA, USA) for the use of human subjects in medical research.

The study was a 12-month, uncontrolled, prospective, pilot intervention trial.

Women between the ages of 18 and 45 years of known low BMD at the proximal femur (*t*- and *z* score, less than –1.0) were recruited from the San Francisco Bay Area. Exclusion criteria included any condition or habitual behavior known to influence bone metabolism. One subject had been taking a stable dose of Fosamax for 12 months before enrolling in the study and continued to do so during the study intervention. Her data were evaluated independently of the remainder of the sample.

An Optimass model 1000 Mechanical Strain Device (Exogen, Piscataway, NJ, USA) was installed in the home of each subject. The device applied vertical whole-body vibration amounting to a 0.2-g mechanical stimulus at a frequency of 30 Hz via a floor-mounted platform. The stimulus is known to transfer to the skeleton of a standing individual [6]. Subjects were instructed to stand on the platform for 10 min morning and night. A record of compliance was uploaded from the machine every 6 months. Devices were checked every 3 months for actuator drive voltage (RMS) and frequency (peak to peak).

BMD was measured at the whole body (WB), lumbar spine (LS), both proximal femora (PF), and nondominant (nonwriting hand) distal radius (DR) at baseline and at 6 and 12 months by dual-energy X-ray absorptiometry (DXA; Hologic QDR-1000/W). One investigator performed all measurements and analyses. The coefficients of variation of repeated DXA measures at each site were calculated.

Blood and urine were collected at baseline and 3, 6, 9, and 12 months for markers of bone resorption and formation (osteocalcin and N-telopeptides). Weight, height, and health and exercise histories were obtained at baseline and 12 months.

Mean percent change in BMD (±SE) was calculated for all bone sites and considered with respect to coefficients of variation obtained for repeat scans at each site. Repeated-measures *t* tests were performed on the data (excluding the Fosamax patient) to make preliminary comparisons between (1) subject baseline BMD and NHANES II normative values and (2) subject BMD at baseline and 12 months. Repeated-measures analysis of variance (ANOVA) were performed to identify differences between baseline and 6- and 12-month BMD.

Results

Six Caucasian women with low bone mass at the hip (average dominant hip *z* score = –1.7, *t* score = –1.9; average nondominant hip *z* score = –1.7, *t* score = –2.0) were recruited. One withdrew after 3 weeks of participation in the trial, complaining of vertigo during and after the vibration sessions. Only data from the remaining five subjects were analyzed. Average subject age was 37.8 ± 2.9 years (mean ± SE), height was 164.3 ± 4.4 cm, and weight was 64.2 ± 2.3 kg. Weight remained stable in all subjects throughout the study. No subject smoked or consumed consequential amounts of alcohol. One subject frequently performed nonweight-bearing exercise (swimming), while the others participated in only small amounts of low-intensity exercise.

Despite the small sample size, Kolmogorov–Smirnov and Shapiro–Wilk tests indicated that data normality can be assumed. Subjects exhibited significantly lower BMD at the whole body (WB) ($P < 0.05$), dominant (leg the subject would kick a ball with) proximal femur (PF) ($P < 0.0006$), nondominant PF ($P < 0.002$), and lumbar spine (LS) ($P < 0.05$), but not distal radius, from age-matched normals (NHANES II) at baseline. The subject on Fosamax exhibited particularly low bone mass with baseline *z* scores of WB, –2.65; dominant PF, –2.12; nondominant PF, –2.29; LS, –4.76; and DR, –2.05.

Figure 1 illustrates mean percent change in BMD at all measured sites from baseline to 12 months (excluding the Fosamax subject). Although power was clearly low for statistical analysis, following a year of intervention, *t*-test analysis detected a significant percent change in nondominant proximal femur BMD (2.03% ± 0.33%, $P <$

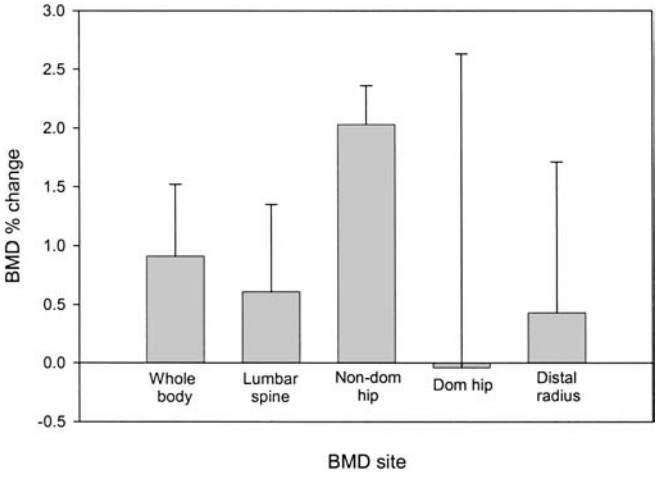

Fig. 1. Mean percent change in bone mineral density (*BMD*) following 12 months of 2×10 min/day of low-strain, high-frequency mechanical stimulation in premenopausal women with low bone mass. *Non-dom*, nondominant

0.02). Nonsignificant mean percent increases were observed at all other measured sites (WB = 0.91%, LS = 0.61%, DR = 0.43%), with the exception of the dominant proximal femur (–0.04%). Repeated-measures ANOVA to evaluate actual BMD change between baseline and 6 and 12 months confirmed the finding of non-dominant proximal femur improvement ($P = 0.008$), with no significant changes detected at any other site. Bone resorption and formation markers at baseline and 3, 6, 9, and 12 months showed no consistent trend across the year or across subjects. The subject taking Fosamax demonstrated BMD changes of 0.35% at the whole body, 6.1% at the lumbar spine, 0% at the dominant hip, 0.29% at the nondominant hip, and 4.6% at the distal radius. Scans taken before enrolling in the current study indicate 10 months of Fosamax treatment alone produced a change of 8.8% at the lumbar spine and –1.9% at the nondominant hip. These observations suggest that Fosamax treatment may have largely accounted for the change at the spine during the current study, but that the addition of a vibration stimulus may have provided protection against loss at the hip that occurred with Fosamax alone.

Discussion

Despite intense research over the past 20 years, the scientific community has been unable to establish any markedly and universally effective nonpharmaceutical treatment for osteoporosis and fracture prevention in adults. Negative side effects associated with drug interventions may render them unsuitable for some. Although it is known that mechanical loading is a positive stimulus for bone, with the exception of the paediatric population most exercise interventions typically produce only modest effects in all but those with very insubstantial skeletons. Furthermore, for many, long-term exercise compliance is highly challenging, and removal of the exercise stimulus typically precipitates loss of any bone benefits originally derived.

Recently, a positive effect of vibration loading on bone has been reported in postmenopausal women [4,5]. Our pilot trial was designed to determine if the same response could be affected in premenopausal women with low bone mass. While subject numbers were clearly insufficient to draw strong conclusions, our preliminary data provide cause for optimism. Indeed, a significant difference was detected between BMD at baseline and after 12 months of passive vibration stimulation at the nondominant proximal femur. The lack of effect at the dominant proximal femur may reflect the phenomenon of diminishing returns; that is, bones with greater initial mass respond less to mechanical stimulation than bones of lower mass [7].

Subject compliance across 12 months for all subjects ranged from 33% to 87.5% (mean, 60% ± 24%). Compliance in the first 6 months averaged approximately 70% but dropped to 50% in the second 6 months. These figures suggest that the issue of compliance may be a limiting feature of vibration intervention for normal ambulatory individuals. Of note, one subject was blind, which prohibited exercising outside the home without assistance. That subject recorded compliance of 84% in the first 6 months and 91% in the second, suggesting that for those with few active mechanical strain options, vibration compliance may be very good. Frail or nonambulatory individuals with many risk factors for falling may similarly find the safe, passive, non-pharmaceutical nature of the intervention appealing.

Clearly a larger trial must be completed to make conclusions representative to the greater premenopausal population regarding the bone strength changes that may be associated with vibration loading. Such a trial would also determine the prevalence of the side effect that precluded the participation of one individual in the current study. As the prevention of osteoporosis-related fracture cannot be accomplished by improving bone mass alone, it would be appropriate in future studies to also assess changes in bone geometry and fall risk factors, such as leg muscle strength and balance.

Acknowledgments Optimass Mechanical Strain Systems were provided by Exogen, Inc., Piscataway, NJ, USA

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