

Editorial

Whole Lotta Shakin' Goin' On

Olof Johnell¹ and John Eisman²

INTRODUCTION

SHAKE, RATTLE, AND roll have now entered the osteoporosis quietness with two papers on the clinical effect of whole body vibration in the March issue of *JBMR*. Besides, we can already see these products at scientific meetings. To what extent does the present knowledge address the potential for such approaches in the prevention of fractures?

GOOD VIBRATIONS

Clinical studies have been based on animal experiments that have shown a positive effect on bone strength and mass of various forms of loading. The basis of these experiments is the concept that trabecular bone adapts to its mechanical environment—Wolff's law. Support for these experiments has also come from epidemiological findings that greater physical activity—mechanical stimulation is associated with greater bone mass, and in some studies, fewer fractures.

The question of the ideal form of stimulation has been addressed in animal studies. High-frequency (30 Hz), low-magnitude (200 μ strain) signals stimulated large increases in cortical bone in turkeys.^(1–3) However, higher amplitude and lower frequency was not anabolic in that model. In a longer-term study in sheep over 1 year, daily 20-minute sessions of high-frequency mechanical stimulation of sheep produced a 35% increase in BMD. This kind of vibration may also affect the sarcopenia that occurs at the same time as bone loss with aging. Other animal studies have shown similar results. Low-magnitude mechanical loading became osteogenic when rest is inserted between each load cycle.⁽⁴⁾ Effects of loading frequency on mechanically induced bone formation and periosteal osteogenesis suggested a complex interaction between extracellular fluid forces and cellular mechanics in mechanotransduction, best predicted by a mathematical model that assumed that (1) bone cells are activated by fluid shear stresses and (2) stiffness of the bone cells and the extracellular matrix near the cells increases at higher loading frequencies because of viscoelasticity.⁽⁵⁾ These animal experiments have formed the scientific basis for studies in humans.

The authors have no conflict of interest.

SHAKIN' ALL OVER

In humans, extremely low-level, high-frequency mechanical accelerations have been shown to be readily transmitted into the lower appendicular and axial skeleton of the standing individual.⁽⁶⁾ In a recent study, 21 male and 35 female volunteers (age, 19–38 years) were randomly assigned to a vibration or control group. Individuals stood on a vibration platform that was either stationary or oscillated in an ascending order from 25 to 45 Hz, corresponding to maximum vertical accelerations from 2g to 8g, for 4 minutes/day, 3–5 times/week, over an 8-month period.⁽⁷⁾ Although there was no effect on bone mass, serum markers, or other performance and balance tests, there was an increase in vertical jump height in the vibration group.

In this issue, Verschuere et al.⁽⁸⁾ report on a 6-month study of whole body vibration in older women with respect to hip density, muscle strength, and postural control. The 70 volunteer women, 60–70 years of age, who were healthy and had a BMD T score > -2, were randomized to a control group with no organized training; resistance training knee extensor by dynamic leg press and leg extension exercises or whole body vibration, where the subjects performed the same exercises for 20 minutes/day on a vibration platform that had a vibration frequency of 35–40 Hz and peak acceleration of 2.3–5.1g. The vibration training improved the isometric and dynamic muscle strength by 15% and 16%, respectively, and increased BMD by 0.93%. No hip BMD change was observed in the resistance training or the age-matched controls. Serum markers of bone turnover did not change in any groups. The authors concluded that whole body vibration training might be a feasible and effective way to modify well-recognized risk factors for falls and fractures in elderly women.

Also in this issue, Rubin et al.⁽⁹⁾ report another trial for 1 year in 70 healthy women who were 3–8 years postmenopausal (mean age, 57 years). Those randomized to the vibration platform were exposed to a peak vertebral acceleration of 0.2g at a frequency of 30 Hz. Compliance was not good as in many other exercise (and pharmacologic) interventions, and the intention-to-treat analysis did not show an effect. In an analysis limited to those in the highest quartile

¹Department of Orthopaedics, Malmö University Hospital, Lund University, Malmö, Sweden; ²Garvan Institute of Medical Research, University of New South Wales, St Vincent's Hospital, Sydney, Australia.

of compliance (86% compliant), vibration subjects gained 0.04% in femoral neck BMD, whereas placebo subjects lost 2.13% over 1 year in the femoral neck. The corresponding figures for the lumbar spine were +0.1% and -1.6%. Interestingly, the lower body weight (<65 kg) women experienced the greatest benefit: a 3.4% increase in the highest compliance group and a 2.7% increase in the mean compliance group. The authors concluded that these preliminary results indicate a potential for a noninvasive mechanical mediated intervention for osteoporosis that is perhaps more effective in lighter women, who are at greatest need of intervention.

How shall interpret these trials? First, there are differences in age. The study by Torvinen et al.⁽⁷⁾ had younger and perhaps more healthy participants. The greater benefit in lighter individuals in the Rubin study could explain some of these differences. Although there were differences in study duration, these overlapped and do not seem to explain any of the differences reported. The Torvinen study used a short exposure period (4 minutes) for each treatment and somewhat greater loads, although at similar frequency.⁽⁷⁾ None of the studies showed any differences in bone turnover markers, but there were observable differences in muscle strength (e.g., jump height). These possibilities require examination in further studies with respect to study sample age and weight, as well as vibration exposure and amplitude.

Any side effects?

Vibration of the human body has been proposed from epidemiological studies to cause back pain. However, no such major side effects were reported from these studies, and whole body vibration exercise has been proposed for treatment of chronic low back pain.⁽¹⁰⁾ Another possible safety aspect is that the displacement could be large enough for the patient to fall, but this was not reported in these studies.

What could be the biological mechanisms of this whole body vibration?

The vibration is sufficiently low to be unappreciable by the participants, so it seems unlikely to be a direct effect of the mechanical strain. It could be an indirect effect through amplifying of signals by intramedullary pressure⁽¹¹⁾ or through fluid flow^(12,13) in the bone tissue. For the neuromuscular or muscular effects, stimulation of the skeletal muscular pump has also been proposed to affect circulatory flows and flow through the bone tissue.⁽¹⁴⁾ However, these potential mechanisms still need to be fully studied.

How do these effects compare with published studies on pharmacologic interventions?

Leaving aside any potential muscle or balance effects, the net benefit versus placebo ranged from 1.55% to 2.2% and up to 3.4% in those of lower weight and best compliance. These effects over 1 year are difficult to compare with pharmacologic studies over 2–3 years, but in a bisphosphonate study with a 1-year endpoint,⁽¹⁵⁾ the difference from placebo was 2.4%. This comparison might suggest some-

what similar benefit, provided that good compliance can be achieved. However, it is recognized that change in BMD cannot be easily translated to fracture reduction. Thus, the burning question is what fracture reduction could be achieved with whole body vibration.

Future

A tantalizing possibility is that there could be an interaction between whole body vibration and pharmacologic treatment. Could whole body vibration enhance the effect of an anabolic agent or an antiresorptive? In one study in rat tail, there was a synergistic effect of parathyroid hormone (PTH) and mechanical stimulation on trabecular bone formation.⁽¹⁶⁾ It remains to be seen whether similar interactions could be seen in humans, where no major effect on bone turnover from whole body vibration has been observed. A further development in the future might be shock wave treatment, which in animals, has been shown to be positive with increased bone mass in fractured limbs.⁽¹⁷⁾

WHAT'S SHAKIN'?

What are the requirements to bring this equipment to the market place? Vibration platforms are regarded as "devices" and not a pharmaceutical intervention; therefore, they are subject to different regulatory criteria for safety and efficacy. Therefore, for considerations of clinical application, it is important to determine what kinds of data are needed to support vibration as a valid and rational treatment option. Should BMD change be sufficient or should we require fracture reduction data? Is analysis by compliance reasonable in light of our judgments about other randomized placebo controlled trials, where intention to treat (ITT) is and should remain the gold standard? Although vibration platforms seem to be relatively safe, it will be important to establish their antifracture and BMD efficacy as well as their safety in larger and more adequately powered randomized double-blinded controlled trials.

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Address reprint requests to:
Olof Johnell, MD
Department of Orthopaedics
Malmö University Hospital
Malmö SE-205 02, Sweden
E-mail: Olof.johnell@orto.mas.lu.se

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