The research behind low-intensity vibration (LIV) and bone

Context

Osteoporosis effects 44 million people in the United States aged 50 years of more.[1] Over the last 20 years effective anabolic and anti resorptive medications have been available. However, they are associated with reducing compliance, side effects and a desire for alternative solutions over the long term.[2] Bones and muscles respond to dynamic loading and forces. Apply them or take them away and the tissue will respond accordingly.[3] Musculoskeletal deconditioning, that can occur through aging or disability, increases the risk of fractures. Exercise, such as walking and running is known to help maintain a good muscle and bone health. But these strategies may not be possible for frail, disabled or more elderly people. Low-intensity vibration, with accelerations against gravity of less than 1 g (g=acceleration of 9.81m/s^2), is a safe approach to this problem.[4]

Bones respond to both large low frequency and small high-frequency forces and grow more bone as a result.[5] Taking away such forces increases the resorption of bone.[6] Muscle is similarly affected. As we age the faster contracting muscle fibers (10-50Hz) decline proportionately.[7] This can lead to greater musculoskeletal instability and poorer quality. LIV acts as an alternative to these high frequency small sized forces.[8] In scientific studies at a cellular level, LIV has been shown to stimulate bone formation cells (osteoblasts), while reducing production of fat cells by way of a complementary transduction pathway. [9] It also reduces the activity of bone resorption cells (osteoclasts).[10]

LIV and musculoskeletal conditioning

There are a number of human trials that evaluate the use of LIV as we age. In a placebo controlled trial in post-menopausal women LIV was shown in the women with high compliance to reduce loss of bone mineral (BMD) in the femoral neck.[11] In pre-menopausal women using LIV over 12 months, bones (hip and spine) and muscle in the lower back showed increases using

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LIV.[12] A placebo controlled study published in 2020 of postmenopausal women using LIV over twelve months reported tibial stiffness increases 3.86% in active compared with placebo devices and significant marrow fat reductions in active compared with no change in placebo group. Trabecular bone volume fraction and pQCT measured volumetric BMD were significantly better in the active group. This supports that hypothesis that LIV is protective against loss of mechanical strength and minimizes the shift in mesenchymal stem cell fate away from adipocytic toward osteoblastic lineage.[13]

In adults with Thalassemia six months of LIV use showed significant increases in whole body bone mineral content (BMC) and BMD.[14] Adult patients with end-stage renal disease showed an increase in strength and stiffness in distal tibia of 7.8% and 4.7% measured by micro MRI after six months if 70 % compliant with daily use of LIV.[15]

A large study in 710 women over 60 years using LIV for 18 months, showed reductions in falls and fractures in the group using LIV compared to controls.[16] There were significant benefits in muscle strength and balance and in high compliance LIV users 1.4 % hip and 1.12% spine BMD benefit. The study concluded that LIV is effective in reducing falls and associated injuries. This is an important outcome in managing risks associated with the decline in bone and muscle quality with age. In a double-blind, placebo controlled trial of low intensity vibration on bone quality in persons of advanced age,[17] the authors concluded that the variability within groups, as well as relatively small size of the study, hampered their ability to determine the ability of the mechanical signal to protect the skeleton. At 24 months, *a priori* analysis showed that median mid-vertebral trabecular BMD of L1 and L2 in the active group increased 5.3% from baseline, a trend that was 3% greater than that measured in the placebo group. *Post hoc* tests identified a significant interaction of gender and treatment, with women in the active treatment group having 10% (compared to baseline) greater trabecular BMD of the total femur region compared to the combined group of all men (regardless of treatment group) and women in the placebo group.

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Bone loss in Children

LIV provides a safe non-pharmacological intervention for children and young people that are not optimizing bone formation and can be left with a lifetime deficit in bone and associated fracture risks. Children with disabling conditions, including cerebral palsy used LIV for six months and showed 18% benefit in tibial bone quality compared to control.[18] A second study showed increases in cortical bone strength after six months of LIV use.[19] This is important to reducing fracture risk. In a more recent placebo controlled study in boys with Duchenne Muscular Dystrophy, showed significant bone improvements from LIV use compared with placebo control group, where 30% had fractures over the 14 month study.[20] In girls with adolescent idiopathic scoliosis LIV was used for 12 months and significant BMD increases were shown in the femoral neck as well as increase in lumbar spine bone.[21] In children with Crohns Disease, spinal bone was improved compared to placebo.[22] In childhood cancer survivors 10 years from diagnosis whole body BMD and tibial trabecular bone increased significantly over 12 months in a LIV placebo controlled trial.[23]

LIV compared to High Intensity Vibrations

High Intensity Vibration (also called Whole Body Vibration (WBV)) is mainly promoted to increase strength and sports performance. WBV is defined by accelerations above 1g and sometimes go up to 18g. Frequency spectrums of WBV devices normally range between 5 and 70 Hz. Because of these higher intensity levels the recommended usage is 2 to 3 times per week. These accelerations exceed the safety levels described in ISO 2631 human safety standard for whole body vibration. They pose a risk of possible injury.

The working mechanism of WBV is similar to LIV when considering loading. Bone and muscle will respond and adapt to mechanical and functional usage and loading. The major difference is the level of intensity. High intensity loading will stress muscles and bone, which will result in super compensation when appropriate rest is applied. Low-level intensity will stimulate muscle and bone to retain form and function. WBV can be considered training and LIV can be considered therapy. Elderly and frailer people should exercise and be active but also be careful and reduce risk for injuries or falls. High intensity vibrations provoke greater risks than low intensity vibrations in these groups. Cranial acceleration is the greatest risk in WBV and the strength and

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condition of user mitigates that risk.[24] Meta analyses show that LIV is similar to WBV in results without the risks.[25]

On a cellular level there seems to be a difference in the reaction to the high and low intensity vibratory forces. LIV promotes lineage selection towards osteoblast genesis and away from adipogenesis, and even with the challenge of a high-fat diet, keeps fat encroachment into the marrow down. It suppresses visceral and subcutaneous fat. The mechanical pathway is fostered by the LINC nuclear complex, which can deliver LIV signals to the nucleus through acceleration, rather than necessitate cell distortion. IT has been shown that two sessions of LIV per day, separated by a rest period of 3 hours, leverages transient cell adaptations to ratchet up sensitivity of the mechanosensitivity of the cells.[26]Defining stem cell fate to muscle and bone cells and suppressing adipogenesis is the positive effect of LIV mechanical signals within the cell. [27] However, high intensity vibratory signals do not achieve this.[28]

Summary

There are two current clinical studies in adults investigating the effects of LIV.[29] [30] Osteoporosis treatment approvals as a medical device are achieved for LIV in Europe and other geographies. Currently the device is registered as a powered exercise device in the United States. The patented devices user profile can be broadened, such as for children. The technology offers a targeted mechanical bone formation stimulus to augment other management approaches to musculoskeletal health.

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