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Original article

Controlled Pilot Study of High-Impact Low-Frequency Exercise on Bone Loss and Vital-Sign Stabilization in Adolescents With Eating Disorders

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A B S T R A C T

Purpose: Adolescents with anorexia nervosa (AN) face an increased lifetime risk of bone fragility. This randomized controlled study examined the efficacy and safety of a high-impact activity program on markers of bone turnover and stabilization of vital signs (VSS).
Methods: Forty-one hospitalized adolescents with AN were randomly assigned to routine care or routine care plus 20 jumps twice daily. Bone markers were measured at baseline days 1–3 (T1), days 4–6 (T2), and days 7–9 (T3). The primary outcome was change in bone-specific alkaline phosphatase (BSAP) at T3 adjusted for BSAP and % median body mass index at T1. Secondary outcomes were serum N-telopeptide (NTX) and osteocalcin at T3. Safety was determined by comparing weight gain, time to VSS and length of stay for each group.
Results: BSAP, NTX, or osteocalcin did not differ between groups at baseline or at T3. BSAP and NTX at T3 were not associated with group of enrollment or % median body mass index. VSS was significantly reduced in the intervention group compared with the control group (11.6 ± 5.7 days vs. 17 ± 10.5 days, $p = .049$). There was no significant difference in weight gain or length of stay between groups.
Conclusions: Twice-daily jumping activity failed to influence markers of bone turnover in adolescents with AN but was well tolerated, shortened time to vital-sign stabilization and did not slow weight gain.

IMPLICATIONS AND CONTRIBUTION

High-impact low-frequency exercise shortened time to vital sign stabilization in hospitalized adolescents with anorexia nervosa, suggesting that more rapid advancement of physical activity may have a positive effect on vital sign stabilization.

Osteoporosis in childhood and adolescence is an increasingly recognized problem for which there are few treatment options [1,2]. Bone fragility results from reduced bone mass, deterioration of bone microarchitecture, and altered bone turnover. Patients with eating disorders (EDs) are at particular risk, given their poor nutrition; low body weight; suppressed estrogen and testosterone; low insulin-like growth factor 1 levels; elevated cortisol; and deficiencies of calories, protein, calcium, and vitamin D. Both intermediate [3–6] and long-term studies [7,8] have demonstrated reduced bone mass and altered bone microarchitecture in patients with anorexia nervosa (AN) which may not be fully reversible with weight rehabilitation. These findings contribute to the increased lifetime risk of fracture in adults with a past history of AN [9,10]. In children and adolescents, the lifetime prevalence of prior fracture in patients with a history of AN is 60% higher than age-matched controls [11].

Conflicts of Interest: The authors have nothing to disclose.

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Severely malnourished patients with vital-sign instability are often hospitalized for safety and enhanced nutritional support. Many inpatient programs recommend bed rest with little to no physical activity to decrease energy expenditure, promote weight gain, and monitor vital signs. This enforced immobilization may adversely affect the already compromised skeletal health in these patients. Acute bone loss is observed when healthy young men are placed on strict bed rest with a reduction of 1%–2% in whole body bone mass after only a month [12]. Another study observed that adult patients had an increase in biochemical markers of bone resorption within 10 days of bed rest [13]. A study of adolescents and young adults with AN found changes in bone markers in the first 5 days of hospitalization; markers of bone formation declined while resorption markers increased [14].

These findings raise the question of how to safely and effectively counteract the increased bone resorption that accompanies immobilization. Observational and interventional studies [15–22] have found weight-bearing activity to enhance measurements of bone mass, likely through effects on bone geometry. One study of school-age children reported that brief periods of jumping (10 jumps three times per day) for 9 months was sufficient to increase bone mineral content by 2.7% at the intertrochanteric region compared to controls [23]. Another study found that children enrolled in a 7-month school-based program of high-impact jumping exercises 3 times a week had persistently greater bone mass at the hip 8 years later compared to controls [24]. The acute effect of exercise on bone turnover in hospitalized adolescent patients with EDs has not been established.

This randomized controlled pilot study was designed to test the efficacy and safety of a program of daily high-impact activity for a mean of 9 days on markers of bone turnover in teens with AN hospitalized because of medical instability. Bone-specific alkaline phosphatase (BSAP) and osteocalcin (OC), markers of bone formation, and the resorption marker, serum N-telopeptide (NTX), were measured at baseline (days 1–3), days 3–5 and days 7–9 in adolescents with AN hospitalized for medical stabilization. We hypothesized that formation markers would be higher and the resorption markers lower in patients in the high-impact, low-frequency exercise group. To monitor for potential adverse effects of this intervention, we examined the effect of the activity on rates of weight gain, length of stay (LOS), and time to stabilization of vital signs (VSS).

Methods

Inclusion criteria included hospitalization for medical stabilization at Lucile Packard Children's Hospital at Stanford and a diagnosis of AN using Diagnostic and Statistical Manual of Mental Disorders (DSM)-V criteria as confirmed by a child and adolescent psychiatrist. Because the study was started before DSM-V criteria were published, five patients originally met criteria of Eating Disorder Not Otherwise Specified with weight $>$ 85% median BMI (EDNOS) (weight $<$90% median body mass index [BMI]) using DSM-IV criteria. However, all five of these patients met the DSM-V criteria for AN. Exclusion criteria included uncorrected electrolyte abnormalities, cardiac arrhythmias, and use of medications that affect bone metabolism including hormonal contraception, corticosteroids, and bisphosphonates within the prior 3 months. Within 72 hours of admission, interested participants ($\geq$18 years) and parents or guardians for participants $<$18 years signed a Stanford institutional review board–approved informed consent. Minors signed an informed assent prior to enrolling in the study. A movie ticket or a $10 iTunes gift card was offered as an incentive to participate.

Intervention

Following consent, study participants were assigned to one of the two study arms by using a computer-generated list of random numbers. The control arm of the study continued with our standard of care protocol which required gradual advancement from complete bed rest to wheelchair and standard activity as vital signs improved. After a 24-hour monitoring period on bed rest, the intervention group participated in high-impact, low-frequency exercises consisting of 20 vertical jumps to a height of 5 inches off the ground twice daily for 9 days. This exercise protocol was based on a study in healthy school-aged children jumping between classes [23]. The duration of the intervention was chosen to optimize the likelihood subjects would complete the program during the typical LOS (7–14 days) for admissions for this indication. To ensure safety and adherence, the jumps were supervised by a trained member of the research team and completed within 5 minutes. Apart from the jumping activity, the intervention group followed the same protocol as the control group. Vital signs were measured every 4 hours. Resting pulse and blood pressure were measured after 5 minutes of rest and then again after standing for 2 minutes. Patients were considered medically unstable if resting heart rate was $<$ 50 bpm during the day or $<$ 45 bpm at night; blood pressure was lower than 90/45 mm HG; pulse increased $>$ 20 points from lying to standing; or systolic or diastolic blood pressure decreased $>$ 10 mm HG on standing. Patients were discharged home when they achieved a weight at least 75% median BMI and vital signs were stable for 24 hours. The prescribed meal plan and other unit-based activities were not affected by treatment assignment.

Data collection

The participants completed a 10-item questionnaire to collect data on demographics; the amount and rate of weight loss; a history of prior fractures or syncopal episodes; current medications; and a detailed menstrual, 24-hour diet, and exercise history. All participants underwent a physical examination and screening blood tests including sex steroids and vitamin D levels. The initial clinical assessment was performed by an adolescent medicine specialist, a dietician, and a psychologist and/or psychiatrist. Pertinent information by physical exam included height (m), weight (kg), BMI (weight in kg $\div$ height in m^2), percent median BMI (100 $\times$ [patient BMI/median BMI for age]), weight (kg) change since beginning of abnormal eating habits, Tanner staging (staging of breast for females and pubic hair for males). Weight gain was defined as the absolute difference in weight in kilograms from admission to discharge.

Biochemical assessments

Fasting blood was obtained at 6 A.M. from all participants at three times with 3 days in between blood draws during the admission (days 0–3 = time point 1: T1), between days 4–6 (T2), and days 7–9 (T3) for measurement of BSAP, NTX, and OC. Laboratory assessments for serum chemistries including calcium,