

Original Article

Effect of whole body vibration training on quadriceps strength, bone mineral density, and functional capacity in children with hemophilia: a randomized clinical trial

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Abstract

Objectives: The objective was to evaluate the effects of whole body vibration training on quadriceps strength, bone mineral density, and functional capacity in children with hemophilia. **Methods:** Thirty children with hemophilia with age ranging from 9 to 13 years were selected and randomly assigned to either the study group that received whole body vibration training (30-40 Hz, 2-4 mm of peak-to-peak vertical plate displacement for 15 minutes/day, 3 days/week/ 12 weeks) plus the conventional physical therapy program or the control group that performed a conventional physical therapy program only. Outcomes included quadriceps strength, bone mineral density, and the functional capacity. **Results:** Children in the study group showed a significant improvement in all outcomes compared with the control group. The quadriceps peak torque after treatment was 70.26 and 56.46 Nm for the study and control group, respectively ($p < 0.001$). The lumbar spine bone mineral density after treatment was 0.85 and 0.72 g/cm² for the study and control group, respectively ($p < 0.001$). The functional capacity after treatment was 325 and 290 m for the study and control group, respectively ($p = 0.006$). **Conclusions:** Whole body vibration training is an effective modality in increasing quadriceps strength, bone mineral density, and functional capacity in children with hemophilia.

Keywords: Hemophilia, Whole Body Vibration, Muscle Strength, Bone Mineral Density, Functional Capacity

Introduction

Hemophilia is an inherited coagulation disorder caused by a genetic defect of X-chromosome. It has a general prevalence of 1 in 10,000 male births. The severity of the bleeding in hemophilia depends on the level of coagulation factor activity¹. Symptoms of hemophilia include hemarthrosis, soft tissue hematomas, bruises, intraperitoneal bleeding, intracranial hemorrhage, and postoperative bleeding².

Most of bleeding episodes in hemarthrosis occur in the knee, ankle, and elbow joints; with the knee being the most affected joint (45%)³. Repeated joint bleeds result in erosion of articular cartilage and loss of joint space, leading to loss

of joint range and strength with functional impairment and structural deformity⁴.

Tlacuilo-Parra and colleagues demonstrated a significant decrease in lumbar bone mineral density (BMD) in children with hemophilia (38%), compared with sex and age-matched healthy children (16%), this reduction in BMD was independent of differences in age and body size. Among the children with hemophilia, 77% were considered to be inactive versus 51% in controls. These results support that prolonged immobilization and reduction in weight bearing activities, as a consequence of joint bleeds in knees and ankles, play an important role in the pathogenesis of low BMD in these patients⁵. Low bone mass is defined as areal BMD Z-scores that are less than or equal to -2.0 standard deviation⁶.

Because hemophilia has dramatic effects on social, economic, physical, and emotional life of children with hemophilia and their families⁷ and its complications are serious and abundant in a severe type of the disease, appropriate treatment is necessary to provide children with a chance of living a nearly normal life with high health-related quality of life⁸.

Physical therapy interventions have an essential and

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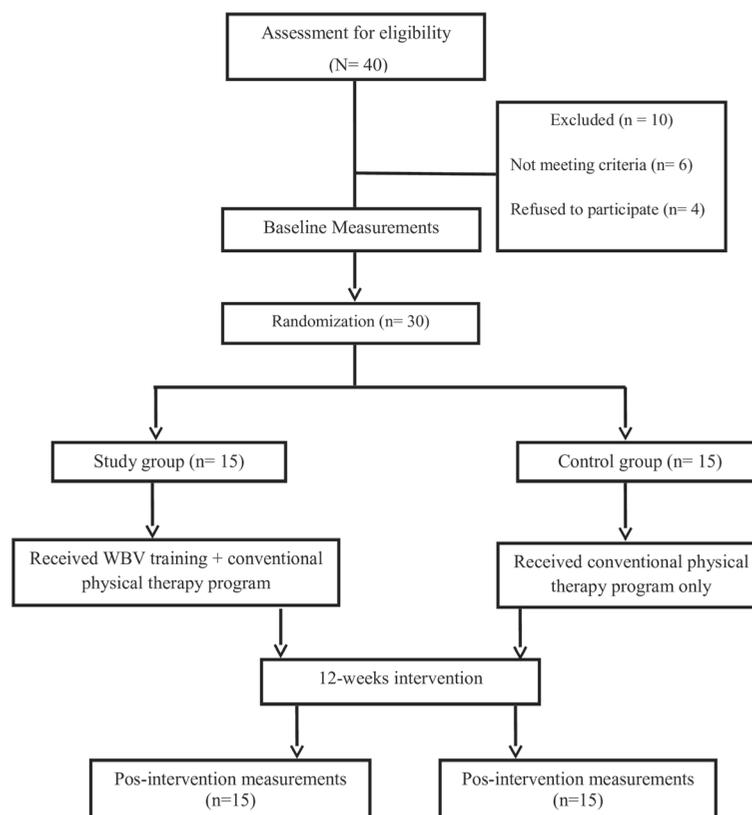


Figure 1. Flow chart showing the experimental design of the study.

an effective role in the rehabilitation of these children⁹. Recently, whole body vibration (WBV) has emerged as a useful exercise method for improving overall health. WBV is a training method which exposes the whole body of an individual to low frequency, low amplitude mechanical stimuli via a vibrating platform. The vibration stimulates the muscle spindles, sending nerve impulses to initiate muscle contractions according to the tonic vibration reflex¹⁰.

Whole body vibration may increase BMD¹¹, muscle strength, and power in humans¹²; there is also strong evidence supporting the use of WBV to preserve bone and muscle function during activity restriction, such as bed rest in adults. Mechanistically, WBV may increase bone mass directly through the force imparted by the metal plate onto the skeleton or through the pull of the tendon attachment site on the bone¹³.

Although there is support for the use of WBV and exercise in non hemophiliacs to improve bone mass and density, the effects of WBV and exercise on these parameters in children with hemophilia have not been reported. Therefore the purpose of this study was to evaluate the effects of WBV training on muscular strength, bone density, and functional capacity in children with hemophilia.

Materials and methods

Participants

Thirty boys with hemophilia type A were enrolled in this study. Their ages ranged from 9 to 13 years. They were selected from Al-Noor Hospital, Makkah, Saudi Arabia and randomly assigned into two equal groups (study and control groups). They suffered from bilateral hemarthrosis which ranges from mild to moderate according to the classification of hemophilia¹⁴. They were able to walk independently. No vertebral compressions were present in those children. All children were medically and clinically stable and received the same medical treatment in the form of prophylactic factor VIII replacement therapy. Children with progressive radiographic changes or congenital or acquired skeletal deformities in both lower limbs were excluded. This study was approved by the ethical committee of the Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia. A written consent form was obtained from the parents of all children prior to participation.

Randomization

Forty children were recruited for this study; 6 children were excluded because they failed to meet the inclusion criteria, 4

children refused to participate in the study. Randomization was performed using sealed envelopes. The investigator prepared the sealed envelopes, which contained a piece of paper indicating whether each participant was in the study group (WBV training and conventional physical therapy program) or the control group (the same conventional physical therapy program only). The experimental design of this study was shown in Figure 1.

Procedures

All procedures for evaluation were explained to all children and their parents. All children were measured with a Cardinal® Detecto Scale (Weigh Beam Eye-Level, Model 2392, Webb City, USA) without shoes and minimal clothing to the nearest 0.1 cm and weighted to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (in kilograms) divided by squared height (in meters). Puberty was classified according to Tanner's staging system¹⁵. All children were evaluated for quadriceps strength, BMD, and functional capacity before and after 12 weeks of treatment.

Outcomes

Isokinetic testing

Quadriceps muscle strength was evaluated using a Biodex System-4 dynamometer (Biodex Medical System, Shirley, NY). Children' thighs were securely strapped to the Biodex seat, and knees were positioned such that the axis of rotation of the dynamometer head was even with the joint line of the dominant knee used for testing. The knee joint of the dominant leg was positioned at 90° flexion and, anterior/posterior ankle pads on the dynamometer attached. The pads were attached superior of the malleoli with the posterior pad in contact with the distal soleus-gastrocnemius complex. The pads were secured so as to ensure that the children had no movement within the pads. After a warm-up session consisting of 3 (no load) repetitions, children were instructed to generate maximum voluntary concentric torque via a verbal command to push as hard and fast as they can, then relax. The test procedure included three trials at the maximum concentric contraction of the quadriceps muscle, with a rest period of 30 secs between trials. The isokinetic test was performed at an angular velocity of 150°/s. Because it is the most comfortable speed and yields the highest peak torque values compared to 90 or 180°/s. The mean peak torque (Nm) achieved during the three trials was recorded¹⁶.

DEXA scan

Bone mineral density (g/cm²) was measured using energy X-ray absorptiometry (DEXA), with a pediatric version of the QDR-Explorer software (Hologic Inc, Bedford, MA, USA). DEXA consists of a central device with a padded platform and a mechanical scanner that is adjusted to emit low dose X-ray on the area required to be measured and X-ray generator. The equipment is combined with a computer device with specific software to determine BMD. DEXA equipment was calibrated

daily with a lumbar spine phantom and step densities phantom following the Hologic guidelines. The assessments in pre- and post-treatment were performed by the same technician who had been fully trained in the operation of the scanner, the positioning of subjects, and the analysis of results¹⁷. Two examinations were conducted at the lumbar spine (L₁-L₄) and proximal region of the femur (hip and femoral neck) from antero-posterior view. Calibration and all measurements were completed using Hologic pediatric software (Software version 12.4, Bedford, MA 01730).

Six minute walk test

Functional capacity was evaluated using the six minute walk test (6MWT). The 6MWT was performed according to the standardization proposed by the American Thoracic Society¹⁸. A single 6MWT was performed along a flat and straight corridor of 20 m on a hard surface. Prior to testing, each child walked along the length of the track with the therapist and was shown the beginning and end of the course. Standard verbal encouragement was used during the test. Children were informed that the purpose of the test was to find out how far children walk in 6 minutes. They were told to walk like they were trying to get somewhere they really wanted to go, but hopping, skipping, running, and jumping were not allowed. To ensure safety and to measure the exact distance walked in 6 min, the therapist followed closely with a stopwatch¹⁹.

Interventions

Conventional physical therapy program

Both treatment groups received the conventional physical therapy program, which included hot packs, muscle stretching, strengthening exercises, proprioceptive training, balance and gait training, for 12 consecutive weeks (one hour/day, three days/week).

WBV training protocol

The study group underwent additional WBV training using a vibration plate. The vibration plate (Power Plate Next Generation Vibration Platform; Power Plate North America, Chicago, IL, USA) simultaneously oscillates in the vertical, anterior-posterior, and mediolateral planes, although the predominant plate displacement is vertical²⁰. The vibration frequency, amplitude, and duration were selected based on previous studies reporting no injuries, but demonstrating improvements in strength and BMD²¹. Therefore, the frequency, amplitude, and duration utilized in this study were as follows: frequency: 30-40 Hz, 2-4 mm of peak-to-peak vertical plate displacement, and exercise durations ranging from 12 to 15 min. Children in the study group performed two vibration exercises three times per week for 12 consecutive weeks. The first vibration exercise, a warm-up and familiarization set, consisted of sitting in a chair with both legs on the platform and performing one repetition, which lasted 3 min. Then children performed

Table 1. Demographic and clinical characteristics of the children at baseline.

Character	Study group	Control group	T-Value	P-Value
	Mean±SD	Mean±SD		
Age (years)	12.22±2.33	11.90±2.74	0.38	0.71*
Height (cm)	145.9±10.76	146.03±11.38	0.03	0.97*
Weight (kg)	44.03±10.2	44.47±9.87	0.12	0.91*
BMI (kg/m ²)	20.16±2.24	20.55±1.65	0.53	0.59*
Tanner stages of puberty				
Stage I	12 (80%)	11 (73%)	Chi-square sig. 0.775*	
Stage 2	3 (20%)	4 (27%)		

*Level of significance at P<0.05. * Nonsignificant. SD: standard.*

three sets of 3-min semi-squats on the vibration platform. Vibration exercise time was increased by 15 seconds each week, with 3 min of rest being given between repetitions. The children were barefooted and wore similar cotton socks for each vibration session. While administering the vibration protocol, a therapist carefully monitored the children for pain, discomfort, numbness, redness, itching, or muscle soreness, and they discontinued the session if any of these symptoms were present¹⁶.

Statistical analysis

The results were expressed as mean (standard deviation). Our data were normally distributed which tested by Shapiro-Wilk test, so the mean values of all measured parameters, comparison of assessments before and immediately after the treatment in each group (study or control) was performed using paired t-test, whereas the comparison of assessments between both groups before and immediately after treatment was carried out using an unpaired t-test. The Statistical Package for the Social Sciences (SPSS) computer program version 16.00 was used for data analysis. P value of less than 0.05 was considered to be statistically significant.

Results

Thirty boys with hemophilia type A participated in this study. Children were randomized to the control and study groups. The demographic and clinical characteristics of the participating children in both groups are represented in Table 1. No significant differences were found between both groups regarding the demographic characteristics.

Before treatment, there were no statistically significant differences in the mean values of quadriceps peak torque (Nm) in both groups ($p=0.41$). In contrast, there was a statistically significant difference between the mean values of quadriceps peak torque at baseline and after treatment ($p<0.001$) (Table 2).

No significant difference was noted in the mean values of BMD (g/cm^2) at baseline between the study and control groups

($p=0.57$). In contrast, there was a statistically significant difference between the mean values of BMD obtained during the baseline and after treatment ($p<0.001$) (Table 3).

At baseline, no significant difference was noted in the mean values of 6 MWT (m) at baseline between the study and control groups ($p=0.94$). In contrast, there was a statistically significant difference between the mean values of 6 MWT obtained during the baseline and after treatment ($p=0.006$) (Table 4).

Discussion

The results of this study indicated that a program of combined WBV training and conventional physical therapy produced better improvement in quadriceps muscle strength, BMD, and functional capacity in children with hemophilia compared with a 12-week program of conventional physical therapy alone. Improvement was noted in both groups in all measured variables after 12 weeks of treatment. However, higher improvement was achieved in the study group.

Recently, WBV has received much attention for its proven ability to improve BMD, flexibility, balance and mobility²², aerobic capacity and notably, muscle function²³. WBV has been theorized to act on muscle function in part via the stimulation of muscle spindles, leading to the excitation of alpha motor neurons, which contract the motor units and in turn produce tonic contraction of the muscle²⁴.

This implicates that primary endings of the muscle spindle are stimulated by the vibrations, which excites the motor neurons causing contraction of motor units, resulting in tonic contraction of the muscle known as tonic vibration reflex (TVR). It is thought that the results of this study demonstrate the improvement in muscular functions by increasing the co-contraction ability of the synergist muscles²⁵.

The possible mechanisms of strength increase in this study may be attributed to the mechanical vibrations evoke reflex muscle contractions which are according to Cardinale and Bosco²⁶, mediated not only by monosynaptic but also by polysynaptic pathways. In a recent study by Pollock et al²⁷, recorded recruitment thresholds from 38 motor units (MU)

Table 2. Pre and post-treatment mean values of quadriceps peak torque (Nm) for the study and control groups.

Character		Study group	Control group	T-Value	P-Value
		Mean \pm SD	Mean \pm SD		
Quadriceps Peak Torque (Nm)	Pre	49.47 \pm 1.99	50.06 \pm 1.94	-0.83	0.41*
	Post	70.26 \pm 2.60	56.46 \pm 1.35	18.2	<0.001**
Effect size		Cohen's d= 6.66			
T-Value		-52.95	-11.81		
P-Value		< 0.001**	< 0.001**		

Level of significance at $P < 0.05$. * Nonsignificant. ** Significant.

Table 3. Pre and post-treatment mean values of BMD (g/cm^2) and Z-scores for the study and control groups.

Character		Study group	Control group	T-Value	P-Value
		Mean \pm SD	Mean \pm SD		
L1-L4 BMD (g/cm^2)	Pre	0.69 \pm 0.07	0.67 \pm 0.08	0.56	0.57*
	Post	0.85 \pm 0.04	0.72 \pm 0.05	6.69	<0.001**
Effect size		Cohen's d=2.87			
L1-L4 Z-score	Pre	-1.65 \pm 0.44	-1.55 \pm 0.39	-0.65	0.52*
	Post	-0.87 \pm 0.33	-1.28 \pm 0.37	3.2	0.003**
Effect size		Cohen's d=1.17			
Proximal Femur BMD (g/cm^2)	Pre	0.53 \pm 0.08	0.56 \pm 0.06	-1.14	0.26*
	Post	0.75 \pm 0.05	0.62 \pm 0.04	7.23	<0.001**
Effect size		Cohen's d=2.87			
Proximal Femur Z-score	Pre	-0.83 \pm 0.26	-0.77 \pm 0.33	-0.61	0.55*
	Post	-0.41 \pm 0.26	-0.57 \pm 0.29	1.6	0.12*
Effect size		Cohen's d=0.58			

BMD: Bone Mineral Density. Level of significance at $P < 0.05$. * Nonsignificant. ** Significant.

Table 4. Pre and post-treatment mean values of 6MWT for the study and control groups.

Character		Study group	Control group	T-Value	P-Value
		Mean \pm SD	Mean \pm SD		
Functional Capacity (6MWT) (m)	Pre	275.93 \pm 31.37	276.87 \pm 42.13	-0.07	0.94*
	Post	325.13 \pm 19.73	290.27 \pm 41.1	2.96	0.006**
Effect size		Cohen's d=1.08			
T-Value		-9.98	-6.98		
P-Value		< 0.001**	< 0.001**		

6MWT: Six Minute Walk Test. Level of significance at $P < 0.05$. * Nonsignificant. ** Significant.

before and after WBV. This information indicates that WBV has a preferential effect on higher MU, which is responsible for strength and power output.

The effect of WBV on the neuromuscular properties of skeletal muscles and spinal mechanisms is demonstrated by a decreased electromechanical delay, an increased rate

of force development, and a presynaptic inhibition of skeletal muscles²⁸. WBV also effectively induces a small degree of post-activation potentiation²⁹.

Skeletal muscle strength improvements after WBV were associated with reflex muscle activity and not body-weight exercises³⁰. The current study also demonstrated

improvements in quadriceps strength after WBV; these gains were significantly larger than those observed in a group performing the same exercises without vibration.

The improvement in BMD after WBV training is caused when children stand on an oscillating plate, and the motor transmits vertical acceleration to muscle and bone. Bone will increase where the load is placed, which leads to the remodeling of bone; it was also found that the morphology of a bone will be changed by the external forces acting on it^{31,32}. WBV can produce osteogenic effects by changing the flow of bone fluid through direct bone stimulation and mechanotransduction, or it can generate indirect bone stimulation through skeletal muscle activation by means of tone stretch reflex³³.

The regional protection in bone observed here was not surprising given the previously reported kinetics of WBV. Abercromby and colleagues studied the transmission of WBV through the skeleton using two vibration platforms: a predominantly vertical vibration device identical to the one used in this study and a rotational vibration device. Using an accelerometer attached to a bite bar, they showed that a significant amount of vibration was transmitted from the plate to the head; greater transmission was evident through the skeleton using the predominantly vertical vibration device than the rotational device. Synchronous plate was chosen because vibration transmission through the body is known to be more pronounced in vertical than in rotational vibration devices^{20,34}.

Previous research supports the results of this study and refers the improvement in BMD to the anabolic effects of WBV on bone in a variety of populations, including postmenopausal women, the elderly, and patients with restricted mobility¹⁰. The results of this study agree with Bosveld and Field-Fote³⁵, they suggest that even a single session of WBV is associated with a meaningful short-term increase in quadriceps force-generating capacity in persons with motor-incomplete spinal cord injury. The multi-session use of WBV as part of a strengthening program deserves exploration.

Edionwe et al¹⁶, confirm the findings of this study. They concluded that, use of exercise in conjunction with WBV is well tolerated, improves strength, and may have had a small protective effect on bone loss in the leg and trunk in children recovering from burns. Also the results of this study come in agreement with Matute-Llorente et al¹⁷; they suggest that WBV training might be useful to improve BMD in children and adolescents with Down syndrome. In our study, there was a great difference in the effect of WBV because children with Down syndrome were older and had more Tanner stages (IV and V).

The WBV protocol used in this study was chosen following previous studies^{16,17}, which indicated that WBV treatment might be more efficient when it is used in a structured way two or three times per week for 10 min each time. So it would be possible to hypothesize that a protocol with higher intensities, time, and amplitude could have achieved greater improvements in those children. Regarding the safety aspect of vibration training, our vibration protocol did not result in any vibration-related adverse effects, which is concordant with previous vibration studies^{20,36}. Also, there was no

evidence that the level of compliance with study protocol affected study outcomes.

The significant improvement in muscle strength, BMD, and functional capacity observed in the control group is likely caused by the fact that the regular exercise program (30 min at least three times per week) was designed to increase muscle strength, joint mobility, flexibility, balance and functionality, thus improving daily life activities³⁷⁻⁴⁰. This explanation mirrors the conclusion of Eid and colleagues⁴¹; they demonstrated that, resistance and aerobic exercise training are effective in increasing BMD and improving both muscle strength and functional ability in children with hemophilia.

This study is not exempt of limitations; firstly, the lack of data about vitamin D data, as vitamin D affects muscle function and can be a confounder to response to therapy. Secondly, the absence of a sex and age-matched normal control group hinder us to demonstrate the anthropometric measurements in Z-scores as children with hemophilia can suffer from growth delay. And finally, lack of follow-up data, which reduces the clinical application of our results on the short-term effects of WBV. Further studies taking into account these factors will help us to define whether an intervention of WBV alone is effective in this determined population.

Therefore, we can conclude that the WBV training is an effective physical therapy modality for children with hemophilia. It produces an increase in quadriceps strength, BMD, and functional capacity in those children.

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