Tolerability and feasibility of whole body vibration and its effects on muscle function and bone health in patients with dystrophinopathy

Anna Petryk[1], Lynda E. Polgreen[2], Jamie Marsh[3], Dawn Lowe[4], James Hodges[5], Peter Karachunski[3]

[1]Division of Pediatric Endocrinology, University of Minnesota, Minneapolis, MN, USA, [2]Division of Pediatric Endocrinology and Metabolism, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, USA, [3]Department of Neurology, University of Minnesota, Minneapolis, MN, USA, [4]Department of Physical Medicine & Rehabilitation, University of Minnesota, Minneapolis,MN, USA, [5]Division of Biostatistics, University of Minnesota, Minneapolis, MN, USA

Background

Dystrophinopathies, including Duchenne (DMD) and Becker (BMD) muscular dystrophy, are X-linked muscle wasting disorders caused by mutations in the dystrophin gene. Dystrophin deficiency compromises functional integrity of the muscle fibers leading to progressive weakness, accompanied by a gradual bone loss.

Objective and hypothesis

This study's goal was to evaluate the effect of whole body low magnitude vibration (WBLMV) on timed motor performance and bone health. The hypothesis was that WBLMV would stabilize muscle function and prevent bone loss in patients with dystrophinopathies.

Methods

This pilot study included 3 DMD (5.9; 7.5; 12.5 years old) and 2 BMD (16.4 and 21.7 years old) boys, all ambulatory (able to walk ≥75 meters unassisted). Each patient was given a Marodyne Low Intensity Vibration plate with an oscillating frequency of 30-90 Hz for daily use at home for 10 consecutive minutes/day for 6 months. Baseline measurements were taken twice within two weeks before treatment began, then at 6 months and 12 months, and included 6 min walk distance, 10 meter walk, “stair climb” test, “supine to stand” test and peripheral quantitative computed tomography (pQCT) of the tibia (3% and 38% sites) to evaluate trabecular and cortical bone. Statistical analyses used mixed linear models to account for correlation of measurement times within subject.

Results

Initially six patients were enrolled in the study, but one patient (Patient 6) with prior history of headaches and attention deficit hyperactivity disorder experienced worsening of headaches during the first 2 weeks of intervention. He found the exercise routine an excessive burden and dropped out of the study after 2 weeks. The remaining 5 patients completed the study and did not report any difficulty with using the platform, muscle pain, cramps, or any other adverse events.

Patient characteristics at baseline

Patients	1	2	3	4	5	6
Age (years)	5.9	7.5	12.4	16.4	21.7	9.8
Race	White	White	White	White	White	White
Ethnicity	Hispanic	Not Hispanic	Not Hispanic	Not Hispanic	Not Hispanic	Not Hispanic
Tanner stage	1	2	2	5	5	1
Height Z-score	-2.2	-2.0	-3.6	-0.7	0.3	-0.1
BMI (kg/m^2)	14.8	18.2	21.0	23.7	29.2	14.7
BMI Z-score	-0.5	1.2	1.0	0.9	1.7	-1.2
Diagnosis	DMD	DMD	DMD	BMD	BMD	DMD
Gene mutation	dup exon 49 OOF	del 55 OOF	exon 32 c.C4414T; p.Q1472X OOF	del exon 3-7 IF	del exon 3-7 IF	dup exon 2 OOF
Interventions in addition to WBLIV	DFZ, NTS, stretching	DFZ, NTS, stretching	DFZ, NTS, Ataluren stretching	stretching	stretching	PRED, NTS, stretching

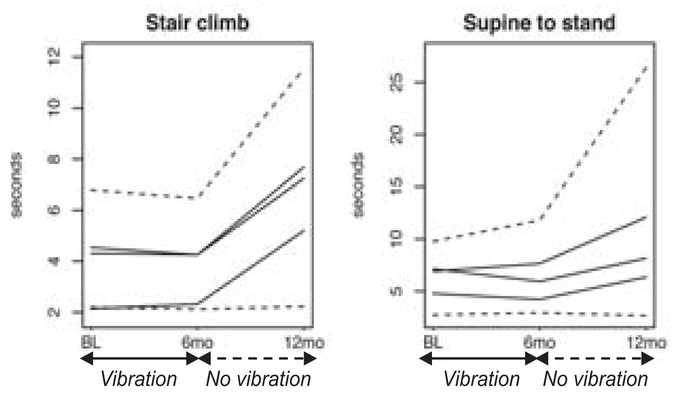
BMD, Becker muscular dystrophy; DFZ, deflazacort; DMD, Duchenne muscular dystrophy; del, deletion; dup, duplication; IF, in-frame; OOF, out-of-frame; WBLIV, whole body low intensity vibration; NTS, night time splint; PRED, prednisone

Timed motor function tests before and after 6 months of vibration training as well as 6 months following discontinuation of vibration

	Timepoints			Estimated change ± SE and % change					
	0	6 mo	12 mo	0-6 mo	%	6-12 mo	%	0-12 mo	%
6 min walk [m]	412	395	396	-16.8±12.0	-4.1	0.8±13.9	0.2	-16.0±12.0	-3.9
10 m walk [s]	5.6	6.0	7.0	0.4±0.5	6.4	1.0±0.6	16.2	1.3±0.5	23.6[a]
Stair climb [s]	4.0	3.9	6.8	-0.1±0.4	-2.9	2.9±0.5[c]	74.8[c]	2.8±0.4[c]	69.9[c]
Supine to stand [s]	6.3	6.5	11.1	0.2±1.6	3.9	4.6±1.9[a]	70.9[a]	4.9±1.6[b]	77.6[b]

Data are shown as adjusted means, estimated change ± SE, and percent change; [a]p<0.05, [b]p<0.01, [c]p<0.001.

Motor function remained stable during the 6 months of intervention with WBLMV, followed by deterioration during the subsequent 6 months without WBLMV in a “stair climb” test (73% slower at 12 mo vs. 6 months, p<0.0001) and “supine to stand” test (74% slower at 12 mo vs. 6 months, p=0.027).



Dashed lines indicate patients with Becker muscular dystrophy and solid lines indicate patients with Duchenne muscular dystrophy.

pQCT bone measures for the tibia before and after 6 months of vibration training as well as 6 months following discontinuation of vibration

	Timepoints			Estimated change ± SE and % change					
	0	6 mo	12 mo	0-6 mo	%	6-12 mo	%	0-12 mo	%
Trabecular vBMD	201.2	207.0	199.0	6.2±5.4	3.1	-8.5±6.2	-4.1	-2.2±8.1	-1.1
Trabecular CSA	544.0	680.0	627.0	136.1±66.7	25.0	-52.8±75.8	-7.8	83.3±99.9	15.3
Cortical vBMD	1111.6	1129.0	1134.0	17.0±25.1	1.5	5.7±28.3	0.5	22.7±35.4	2.0
Cortical CSA	178.8	175.0	171.0	-3.6±7.2	-2.0	-4.0±8.1	-2.3	-7.6±10.2	-4.2
Cortical BMC	202.2	198.5	195.8	-3.7±7.4	-1.8	-2.7±8.4	-1.4	-6.4±10.5	-3.2
Cortical thickness	3.99	4.01	3.97	0.03±0.1	0.8	-0.04±0.11	-1.0	-0.02±0.14	-0.5
BSI	60.8	60.0	58.0	-1.0±1.5	-1.6	-1.6±1.7	-2.7	-2.6±2.2	-4.3
Zp	1042.7	998.0	928.0	-44.8±46.9	-4.3	-70.1±53.0	-7.0	-115.0±66.3	-11.0
SSI	928.1	886.0	834.0	-41.6±37.0	-4.5	-52.2±41.9	-5.9	-93.8±52.3	-10.1

Data are shown as adjusted means for the tibia length, estimated change ± SE, and percent change. BMC, bone mineral content (mg/mm); BSI, bone strength index is expressed in mg^2/mm^4; cortical thickness is expressed in mm; CSA, cross-sectional area (mm^2); vBMD, volumetric bone mineral density (mg/cm^3); Zp, polar section modulus and SSI, strength strain index are expressed in mm^3.

There was a trend toward an increase in trabecular cross-sectional area during the intervention phase (680 vs. 544 mm2 at 6 mo vs. baseline, respectively, p=0.069). Other indices of bone geometry did not change significantly.

Conclusion

WBLMV was generally well tolerated and appeared to have a stabilizing effect on lower extremity muscle function and bone measures in patients with dystrophinopathies.

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