Effect of Acute and Chronic Whole-Body Vibration Exercise on Serum Insulin-Like Growth Factor–1 Levels in Women with Fibromyalgia

Eduard Alentorn-Geli, M.D., M.S., Ph.D.,1,2 Gerard Moras, Ph.D.,1 Jaume Padilla, Ph.D.,3 Joaquim Fernández-Sola, M.D., Ph.D.,2,4 Robert M. Bennett, M.D.,5 Cristina Lázaro-Haro, B.Sc.,6 and Sebastià Pons, Ph.D.7

Abstract

Objective: The purpose of this study was to investigate the effect of acute and chronic whole-body vibration exercise on serum insulin-like growth factor-1 (IGF-1) levels in women with fibromyalgia.

Methods: A randomized controlled two-factor mixed experimental design was used. Twenty-four women with fibromyalgia (age ± standard error of the mean, 54.95 ± 2.03) were randomized into the vibration group or the control group. The vibration group underwent a protocol of static and dynamic tasks with whole-body vibration exercise twice a week for a total of six weeks, whereas the control group performed the same protocol without vibratory stimulus. Both groups continued their usual pharmacological treatment. Serum IGF-1 levels were determined using enzyme-linked immunosorbent assay (ELISA). To test the effects of long-term whole-body vibration exercise, serum IGF-1 measurements were taken at baseline and at weeks 1, 3, and 6 of the intervention. To test the short-term effects, at week 1, serum IGF-1 measurements were taken before and immediately following a session of whole-body vibration exercise.

Results: Treatment adherence was 93% in the vibration group and 92% in the control group. None of the subjects dropped out of the study. There was an absence of change in IGF-1 at week 1 and week 6 of whole-body vibration exercise.

Conclusion: Results show no change in serum IGF-1 levels in women with fibromyalgia undergoing whole-body vibration exercise. Although high-intensity exercise and whole-body vibration exercise have been shown to increase serum IGF-1 in healthy individuals, the effectiveness of whole-body vibration exercise as a strategy to produce improvements in serum IGF-1 levels in women with fibromyalgia could not be demonstrated.

Introduction

Fibromyalgia (FM) syndrome is a chronic rheumatic condition of unknown etiology characterized by widespread noninflammatory musculoskeletal pain with tenderness on palpation in a minimum of 11 of the 18 tender points for at least 3 months.1 Numerous symptoms may also be associated with this syndrome, including fatigue, anxiety, depression, nonrestorative sleep, muscular stiffness, and irritable bowel syndrome. The management of FM is based on a symptomatic multidisciplinary treatment through pharmacologic and nonpharmacologic strategies. Among all nonpharmacologic treatments, exercise has the strongest evidence of efficacy.2

1Laboratory of Biomechanics, INEF Exercise and Sport Sciences School, University of Barcelona, Spain.
2Department of Medicine, Hospital Clinic Medical School, University of Barcelona, Spain.
3Department of Kinesiology, Indiana University, Bloomington, IN.
4CIBEROBN Fisiopatología de la Obesidad y la Nutrición, Instituto de Salud Carlos III, Barcelona, Spain.
5Department of Medicine, Oregon Health Sciences University, Portland, OR.
6Department of Research and Postgraduate Studies, INEF Exercise and Sport Sciences School, University of Barcelona, Spain.
7Department of Neurobiology, Institute for Biomedical Research of Barcelona, IIBB-CSIC-IDIBAPS, Barcelona, Spain.
Whole-body vibration (WBV) is a mode of exercise that has been used to improve muscle strength, bone density, and balance in healthy adults\textsuperscript{3} and aging populations.\textsuperscript{4,5} In this therapy, the subject stands on a platform that generates sinusoidal vertical vibrations, while performing different exercises with a frequency and amplitude ranging from 20 to 50 Hz and 2.0 to 10.5 mm, respectively. Previously, we demonstrated significant improvements in pain and fatigue following a WBV intervention in patients with FM.\textsuperscript{6} Also, WBV has been shown to induce increases in serotonin, 5-hydroxyindoleacetic acid, and growth hormone (GH).\textsuperscript{7–10} The effects on GH have been attributed to a muscle afferent–pituitary axis.\textsuperscript{3,11–12} GH is a 191-amino-acid polypeptide hormone synthesized and secreted in a pulsatile manner by the anterior pituitary gland. Serum insulin-like growth factor-1 (IGF-1) is secreted mainly by the liver in response to GH release.\textsuperscript{13} Although some authors have failed to demonstrate changes in serum hormone levels in non-FM patients following WBV,\textsuperscript{6,14} Cardinale et al. recently demonstrated a significant increase in serum IGF-1 following a single exposure to WBV in elderly patients.\textsuperscript{15}

An impairment of the hypothalamic–pituitary–GH–IGF-1 axis has been postulated as one among several mechanisms implicated in the pathophysiology of FM.\textsuperscript{16–18} This impairment is manifested by a reduction in serum IGF-1 levels,\textsuperscript{17–21} which in turn has been related to sleep disturbances, poor muscle performance, fatigue, and muscle pain.\textsuperscript{17} Indeed, GH therapy has shown improvements in symptoms and daily functioning in women with FM,\textsuperscript{22} but the high cost of this therapy prevents extended use. Therefore, investigating the effectiveness of a low cost physiologic strategy—WBV—to increase IGF-1 levels in women with FM seems appropriate. The application of acute and chronic WBV in women with FM has been neglected.

The purpose of this study was to investigate the effect of acute and chronic WBV on serum IGF-1 levels in women with FM. It was hypothesized that women with FM would exhibit an increase in IGF-1.

**Patients and Methods**

**Subjects**

Participants were recruited by referral from family physicians and through public announcements distributed in local FM associations in Barcelona, Spain. Ninety-two (92) women expressed interest in the study, and those who met the American College of Rheumatology criteria for FM for at least three years were considered for the study.\textsuperscript{7} Of 92 women, 24 were recruited for this study (Table 1). None of the participants had a medical history of liver disease that could alter IGF-1 levels (Table 2). Women were excluded if they had any orthopedic limitation; a cardiovascular, pulmonary, or metabolic disease that would preclude exercise; or were participating in any other study (Fig. 1). Written informed consent was obtained from each subject prior to participation in the study according to procedures approved by the Committee on Biomedical Ethics of the Jordi Gol Gurina Foundation (Spain).

**Study design**

To investigate the effect of WBV, a two-factor (group × time) mixed experimental design was employed in this study.

<table>
<thead>
<tr>
<th>Table 1. Demographic Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Vibration group</strong></td>
</tr>
<tr>
<td><strong>Control group</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Height, cm</td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
</tr>
<tr>
<td>Duration of diagnosis, years</td>
</tr>
<tr>
<td>Baseline FIQ scores</td>
</tr>
</tbody>
</table>

Shown as mean ± standard error of the mean. BMI, body–mass index; FIQ, Fibromyalgia Impact Questionnaire.

Women were randomized into two treatment groups: vibration (VG) and control (CG). To test the effect of long-term (chronic) WBV, serum IGF-1 measurements were taken at baseline and at weeks 1, 3, and 6 of intervention. To test the effect of short-term (acute) WBV, at week 1, serum IGF-1 measurements were taken before and immediately following a session of WBV. Prior to the start of the study, an individualized interview with each patient obtained the following information: 1) complete medical history, 2) current medications, 3) physical activity habits, and 4) preferred types of exercises. Six subjects reported participating in 30 minutes of cardiovascular exercise at least three times per week, meeting the American College of Sports Medicine exercise recommendations.\textsuperscript{23} Active subjects were distributed equally between the two groups. Medication and physical activity regimens were monitored throughout the study. Participants were instructed to report any changes in both aspects. Additionally, an individualized weekly medical interview was conducted in order to monitor FM-related symptoms.

**Treatment groups**

The VG underwent a protocol with WBV twice a week for a total of six weeks, whereas the CG performed the same protocol without vibratory stimulus. For the CG, the vibratory

<table>
<thead>
<tr>
<th>Table 2. Comorbidities and Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vibration group</strong></td>
</tr>
<tr>
<td><strong>Control group</strong></td>
</tr>
<tr>
<td><strong>(n = 12)</strong></td>
</tr>
<tr>
<td><strong>(n = 12)</strong></td>
</tr>
<tr>
<td>Comorbidity</td>
</tr>
<tr>
<td>Gonarthrosis</td>
</tr>
<tr>
<td>Spondyloarthrosis</td>
</tr>
<tr>
<td>Disc degeneration</td>
</tr>
<tr>
<td>Coxarthrosis</td>
</tr>
<tr>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Cardiopathy</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Circulatory disease</td>
</tr>
<tr>
<td>Carpal tunnel</td>
</tr>
<tr>
<td>Irritable bowel</td>
</tr>
<tr>
<td>Medication</td>
</tr>
<tr>
<td>Antidepressants</td>
</tr>
<tr>
<td>Anxiolytics</td>
</tr>
<tr>
<td>NSAIDs</td>
</tr>
<tr>
<td>Analgesics</td>
</tr>
<tr>
<td>Muscle relaxants</td>
</tr>
</tbody>
</table>

NSAIDs, non-steroidal anti-inflammatory drugs.
The protocol consisted of performing static and dynamic tasks while standing on a WBV platform (PowerPlate, Badhoevedorp, The Netherlands). The tasks were: a) static squat at 100° of knee flexion; b) dynamic squat between 90° and 130° of knee flexion; c) maintained ankle plantar flexion with legs in extension; d) flexo-extension of the right leg between 100° and 130° of knee flexion; e) flexo-extension of the left leg between 100° and 130° of knee flexion; f) squat at 100° of knee flexion, shifting the body weight from one leg to the other. For all tasks, subjects held onto the supporting bar. The six exercises (30 seconds each) were repeated six times with a recovery time of 3 minutes in between. To facilitate an optimal training progression, workload was reduced during the first two sessions, with subjects only performing three (exercises a, b, and c; each repeated three times) of the six exercises.

Whole-body vibration

The WBV intensity was kept constant at 30 Hz frequency and 2 mm amplitude (low amplitude); whereas for the CG, the apparatus did not produce vibrations. The intensity of vibration was chosen based on the literature.\(^3,6,25\) Thirty Hz has been shown to induce the maximal muscular electrical activity. Lower frequencies (20 Hz) were not used because they evoke muscular relaxation, whereas higher frequencies (50 Hz) and amplitudes were not employed because they can generate severe soreness in untrained individuals.\(^3,25\) The duration of WBV was 4.5 minutes per session for the first two sessions, and 18 minutes for the remaining ten sessions. Thus, the total duration after completion of 6 weeks (12 sessions) was 189 minutes.

Blood collection and hormonal analysis

Blood samples were obtained non-fasting from the antecubital vein. To minimize diurnal hormonal variations, all samples were collected by the same experienced nurses at the same time of day (between 9:00 AM and 11:00 AM). The blood samples were allowed to clot, centrifuged at 3000 rpm for 10 minutes, and the serum was stored at \(-70\)°C. Serum IGF-1 concentration was determined by enzyme-linked immunosorbent assay (ELISA) (R&D Systems, Minneapolis, MN). Prior to assay, each sample was acid-alcohol extracted to minimize IGF-1 binding protein interference.\(^26\) The intra-assay coefficient of variance was 8.32%.

Statistical analysis

Descriptive statistics were used to summarize the demographic characteristics of the subjects and independent t-test was used to compare the demographic variables between the VG and CG. To test the effect of WBV on IGF-1 at week 1 and at week 6, a 2×2 (group×time) mixed design repeated measures ANOVA was performed, respectively. All data are presented as mean ± standard error of the mean.
Results

There were no differences \((p > 0.05)\) between the groups for any demographic variables. Both the VG and CG adhered to the treatments 93% and 92%, respectively. None of the subjects dropped out of the study. All participants reported maintaining their prescribed medications throughout the study.

This program did not exacerbate FM-related symptoms nor did it result in musculoskeletal injuries. However, one patient exhibited a mild anxiety attack on the first session of WBV. This patient responded normally for the remaining of the sessions. Fig. 2 illustrates the absence of change in IGF-1 following acute \((F(1,22) = 0.40; p = 0.532)\) and chronic \((F(1,3) = 0.51; p = 0.674)\) WBV.

Discussion

Patients with FM exhibit low levels of serum IGF-1,\(^{17-21}\) which has been related to symptoms of FM.\(^{17}\) In fact, daily injections of GH improve symptoms of FM.\(^{22}\) In the present investigation, we assessed the effectiveness of a nonpharmacologic strategy to increase IGF-1 levels in patients with FM. Contrary to our hypothesis, acute and chronic WBV did not elicit a change in serum IGF-1.

The characteristics of participants in this intervention were similar to those of other studies in terms of comorbidities, medications, and demographics. Although we expected significant results, the absence of change in IGF-1 following WBV in our study can be supported by other investigators.\(^{8,14,27}\) Cardinale and colleagues assessed acute responses of testosterone and IGF-1 levels following a session of WBV in healthy young individuals.\(^{8}\) The protocol consisted of 20 minutes (2 sets of 10 minutes each with a recovery time of 5 minutes between sets) of WBV with a frequency of 30 Hz and peak-to-peak amplitudes of 1.5 mm and 3 mm. Each set consisted of 10 repetitions of static half squat for 1 minute with a recovery time of 1 minute. No changes in testosterone and IGF-1 were found at 10 minutes of WBV, immediately after the WBV, or 24 hours after the session. Di Loreto et al. similarly assessed the responses of testosterone and IGF-1 levels following a session of WBV in healthy men.\(^{14}\) The protocol consisted of 10 minutes of WBV with a frequency of 30 Hz and peak-to-peak amplitude of 4 mm. No changes in testosterone and IGF-1 were found up to 1 hour following the session of WBV. The consistency of findings between our study and that of Cardinale\(^{8}\) and Di Loreto\(^{14}\) could be attributed to similarities in duration, frequency, and amplitude in WBV among these studies. In contrast, in a recent study, Cardinale et al. demonstrated a significant increase in serum IGF-1 levels after an acute exposure of 5 minutes to WBV in elderly patients without FM.\(^{15}\) The protocol consisted of 5 repetitions of static half squat of 1 minute each, with a 1 minute recovery time, at a frequency of 30 Hz and a peak-to-peak amplitude of 4 mm. Participants undergoing WBV showed a significant increase in serum IGF-1 immediately after finishing the WBV session compared to the control group. Improvements were maintained up to 2 hours after the vibration stimulus. The discrepancy in results between our study and that of Cardinale et al.\(^{15}\) could be attributed to different subject populations (we use FM patients) or differences in exercise/recovery time ratio (frequency and amplitude of vibration were similar).\(^{15}\)

There are no studies evaluating the effect of long-term WBV on IGF-1 in FM or in any other population. Jones et al. investigated the effect of 6 months of exercise on serum IGF-1 in patients with FM.\(^{27}\) The intervention consisted of 60 minutes, 3 times per week, and included aerobic exercise, strength, flexibility, balance training, and relaxation. No change in IGF-1 was found following the 6-month exercise intervention. Therefore, patients with FM do not exhibit any change in serum IGF-1 levels following exposure to WBV for 6 weeks or exposure to traditional exercise for 6 months.\(^{27}\)

The lack of effect of WBV on serum IGF-1 levels in patients with FM could be explained by an increased somatostatin tone (an inhibiting factor for GH release) or an insufficient WBV stimulus.\(^{27-29}\) The intensity-dependent speculation is supported by evidence that moderate-intensity exercise does not change IGF-1 levels,\(^{30,31}\) whereas strenuous exercise does.\(^{32}\) During all forms of exercise, acute endocrine activation is triggered by collaterals of the central motor command to the hypothalamic neurosecretory and autonomic centers.\(^{8}\) The intensity required for these hormone-induced responses to occur seems to be high.\(^{32}\) Patients with FM may be unable to exercise at a high enough intensity to stimulate IGF-1 secretion without exacerbating FM-related symptoms.\(^{27}\) Thus, the use of WBV/exercise as a strategy to induce improvements in serum IGF-1 levels may be unrealistic. However, recent findings\(^{15}\) justify the need for future research to determine if a higher intensity WBV protocol can be safely applied to patients with FM to increase their serum IGF-1 levels.

There are some limitations to this study. First, to investigate the acute effect of WBV on serum IGF-1, the use of a fully
repeated measures design (subjects serving as their own controls) may appear more appropriate than the mixed repeated measures design; however, we are confident that a change in the design would not have altered the findings of the study. Second, no other biomarkers (GH-releasing hormone, GH, or somatostatin) were measured, thus impeding potential explanations for the lack of IGF-1 response. Future research should explore the presence of an interaction between somatostatin and IGF-1 following WBV/exercise. Third, given that no specific muscle IGF-1 isoforms (mechano growth factor, or IGF-IEb) were measured,33 we cannot exclude the potential effect of WBV on other IGF-1 markers. We chose to assess serum IGF-1 to be consistent with the literature.8,14,15,17–21,27,30–32

Conclusions

In conclusion, our results suggest no changes in serum IGF-1 following 1 week or 6 weeks of WBV in women with FM. These findings are in agreement with most of the literature regarding healthy subjects. Although high-intensity exercise and WBV have been shown to increase serum IGF-1 in healthy individuals, the effectiveness of WBV as a strategy to produce improvements in serum IGF-1 levels in women with FM remains questionable at this time. Future research should focus on characterizing the WBV/IGF-1 dose response in patients with FM; elucidating the mechanism for this apparent blunted response in FM patients; and providing recommendations on effective and safe WBV protocols for patients with FM.

Acknowledgments

The authors thank Antonio Manuel Ballesta Gimeno, M.D., Ph.D., as well as Carlos García Martínez, M.S.; Sergio Rodríguez, M.S.; Moisés Vila Blanch, M.S.; David Ubach De Fuentes, B.Sc.; and Mercè Sola Gonfaus, M.D., for their efficient and professional assistance. We also thank Lísimaco Vallejo Cuéllar, Ph.D., for his support during the data collection, and all the participants for their time, effort, and willingness to participate in the study. The authors also thank CIBEROBN, an initiative of the Instituto de Salud Carlos III, Spain.

Disclosure Statement

No conflict of interest is declared.

References


Address reprint requests to:
Eduard Alentorn-Geli, M.D., M.S., Ph.D.
c/o Dr. Gerard Moras
INEFC-Barcelona
Av. Estadi s/n (anella olímpica)
08038 Barcelona
Spain
E-mail: ealentorngelifm@yahoo.es