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Vibroacoustic Therapy for Ehlers-Danlos Syndrome: A Case Study

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Abstract

Background: Widespread pain and tenderness are prominent features of Ehlers-Danlos Syndrome Hypermobility Type (EDS-HT). Chronic pain in this condition may be perpetuated by central nervous system sensitization and is refractory to treatment. Vibroacoustic therapy has the potential to modulate pain responses via somatosensory input.

Objective: To examine the effects of a short course of self-administered, home-based vibroacoustic chair therapy as add-on treatment in EDS.

Methods: A patient with painful EDS was supplied with a vibroacoustic chair. The patient used the chair up to seven days per week twice per day for 53 out of a possible 58 sessions over 29 consecutive treatment days (approximately 4 weeks), followed by a two week "washout" period. Responses were assessed using the Brief Pain Inventory, Short Form (BPI-SF) and the Sleep Quality Numerical Rating Scale (SQNRS) administered at study initiation, and at the end of weeks 2, 4 and 6. A patient global impression of change (GIC-P) was obtained at the conclusion of active treatment (week 4). Thirty minute semi-structured interviews were carried out at the end of week 4 and week 6. The change from baseline in the BPI subscales, the Pain Severity Score (PSS) and the Pain Interference Score (PIS), from baseline to end of the active treatment period and patient global impression of change were the primary end points. Changes in the SQNRS over the course of the study and the changes in BPI subscales and from time of treatment termination until the final assessment were the secondary endpoints.

Results: The PSS was 7.75 at baseline and unchanged at termination of treatment. The PIS improved by 2.43 points from baseline (8.86) to termination of active treatment (6.43). Patient Global Impression of Change was "slightly better" following treatment. The patient experienced a mostly positive stimulation of bowel function, relaxation and/or lessening of muscle tension, and an improvement in energy levels. Bothersome tingling sensations were experienced especially close to the time of initiation for a brief period but there were no serious adverse effects. During the washout period, the PSS increased slightly by 0.25 points between the termination of therapy (7.75) and final follow-up (8.0). The PIS changed 1.14 points, from 6.43 at termination of therapy to 7.57 at final assessment. Sleep quality also worsened during the washout period with an increase in the SQNRS scale from 8 to 9 although it did not change from baseline during the active treatment period. There was some overall deterioration in symptom control in the two weeks after treatment termination.

Conclusions: This N of 1 study suggests modest symptom improvement from vibroacoustic therapy in EDS-HT. There was an unexpected effect of bowel stimulation. Larger controlled studies are needed to confirm and extend these findings.

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Introduction

The Ehlers-Danlos Syndromes (EDS) are a heterogeneous group of heritable connective tissue disorders characterized by articular hypermobility, skin extensibility, and tissue fragility. Widespread pain and tenderness are prominent features of the autosomal dominant Ehlers–Danlos syndrome hypermobility type (EDS-HT). Major diagnostic criteria include skin involvement with hyperextensibility and/or smooth, velvety skin as well as generalized joint hypermobility.Joint hypermobility is the dominant clinical manifestation with certain joints, having a propensity to dislocate[1].

It has been postulated that early in the course of the condition mechanical factors account

for the pain but later central nervous system sensitization produces generalized hyperalgesia[2,3]. While pain predominates, depression, fatigue, impaired sleep, and diminished quality of life occur [4].

The pain in this condition is refractory to treatment [5].

Vibroacoustic therapy (VAT) uses sound and mechanical vibrations in the audible range applied directly to the body with therapeutic intent [6]. The mechanisms of action responsible for improvement in these areas may involve stimulation of Pacinian corpuscles, direct mechanical tissue stimulation, induction of the relaxation response and cellular/subcellular effects. Mechanical stimulation in the range of 60-600 Hz activates Pacinian corpuscles, which are involved in somatosensation and may influence pain perception [7-10]. At least some of the benefits may derive from reduced muscle tension [11].

VAT has produced significant gains in the relief of pain of musculoskeletal origin [12,13], including fibromyalgia and back pain [14,15].

Dr. Patrick of the NIH Clinical Center has treated more than 15,000 patients having a wide variety of medical conditions [16]. Skille and other therapists have data from more than 40,000 hours of treatment. No serious adverse reactions have occurred [17].

Given the potential for benefit, the relative safety of VAT and the lack of alternative therapies, we considered that a trial of VAT in a patient diagnosed with EDS-HT was justified.

Materials and Methods

Participant

Diagnosis: The patient was a 19-year-old male student of Ashkenazi Jewish and Polish/Russian background. He carried a diagnosis of Ehlers-Danlos syndrome (EDS) spectrum disorder of the hypermobile type with features of classical type.

Pain onset and symptoms: The patient had the onset of widespread pain prior to his 14th birthday. At that time, he developed flu-like symptoms consisting of a sore throat, abdominal pain, vomiting, fever, cough, night sweats and generalized aching. He was initially treated with a three day course of clarithromycin for suspected pneumonia but a chest x-ray proved normal. The most remarkable feature of a detailed workup was an antistreptolysin O titer of 402. Principal ongoing pain complaints were focused on the lower limbs and only occasionally in the hands. There were intermittent sharp pains superimposed on long-duration pain. The patient rated his baseline pain as eight out of 10. He was unable to walk without a cane and had given up sporting activities.

Medical history: Going back to childhood there were recurrent shoulder and carpal-metacarpal joint dislocations as well as knee buckling. Additionally, he experienced urinary frequency and urgency, depressive symptoms, anxiety, panic attacks and sleep disturbances. Additional medical history included bilateral inguinal hernias at approximately age 10 and a small periumbilical hernia. The inguinal hernias were treated surgically. He was noted to have soft stretchable skin without any skin fragility or easy bruising. There had been no spontaneous skin tearing.

Family history: A brother, seven years older, maternal first cousin and mother's paternal uncle had suffered from similar skin disorders and pain. Another brother, three years older and a sister, three years younger had similar skin but no pain complaints.

Clinical examination: The patient's Beighton score was five out of nine confirming hypermobility. There wereno pseudotumors or piezogenic papules. Brisk deep tendon reflexes at the knees and some brief clonus at the ankles of uncertain significance were noted but no other neurological abnormalities were documented.

Investigations: A skin punch biopsy contained numerous scattered dysmorphic fibrils including many flower-like collagen fibrils with moderate diameter variability. There were no other significant findings by light and electron microscopy and elastin fibers were normal. Genetic testing was extensive but he was known to have a COL5A1 variant, 190 3C >T translocation.

Sleep studies demonstrated arousals at four minute intervals and decreased REM sleep. He had extensive imaging with MRI, including the brain, the knees and proximal muscles. All the studies were negative or normal. MRI studies of the length of the spine showed only a small (incidental) Tarlov cyst at T10-T11 which was radiographically stable for 4 years. An echocardiogram was negative for mitral regurgitation and mitral valve prolapse. The aorta and aortic root appeared normal. A bladder ultrasound, done while he was experiencing a sense of fullness, was associated with only 4 mL of fluid.

Attempted therapies: Sleep hygiene and massage provided some benefit. Physiotherapy improved his shoulder strength. Interventions without substantial benefit included relaxation techniques and medications of varying types. These included tramadol containing medications and opioids, cannabinoids, mirtazapine, dopamine receptor blockers, "Z drugs", baclofen, gabapentinoids and SNRI's.

Inclusion and Exclusion Criteria

Contraindications to the use of VAT were reviewed (Table 1) and determined to be absent before the trial of therapy was initiated [18]. Discussion with our patient confirmed that he had adequate English proficiency for completion of questionnaires, the ability to tolerate the treatment and a willingness to complete the study assessments.

Intervention(VAT)

The study was of six weeks' duration; with four weeks of active treatment followed by two weeks' "washout." It was intended that the patient receive 56 treatment sessions given as two sessions per day over 28 consecutive days. However, the actual usage was 53 sessions over 29 consecutive days. Treatment was self-administered with a vibroacoustic chair (Sound Oasis Model VTS-1000, Sound Oasis Company, Marblehead MA 01945-0526, USA).

The first session of the day included 30 minutes of the Sound Oasis "Energize" program consisting of three music tracks with a component of low frequency gamma entrainment (41 Hz to 73 Hz with 41 Hz dominant; 36 Hz to 61 Hz with 41 Hz dominant; and 36 Hz to 65 Hz with 41 Hz dominant) and with mono and binaural high alpha (10Hz) and beta (15Hz) entrainment. The patient was instructed to play the "Energize" program at an intensity level of 15 and a volume level of 1 or 2. The second session of the day included 30 minutes of the Sound Oasis "Sleep" program consisting of three music tracks with a component of low frequency gamma entrainment (32 Hz; range between 27.5 Hz to 44 Hz; and range between 34 Hz to 52 Hz) and with mono and binaural delta (2Hz) entrainment. The patient was instructed to play the "Sleep" program at an intensity level of 5 and a volume level of 1 or 2.

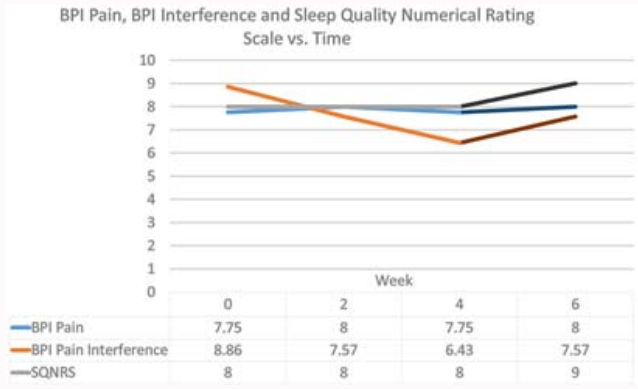

Figure 1: The three measures compatible with a less favorable clinical state two weeks following termination of active treatment.

The patient was given specific instructions (both in person and via a supplied manual) regarding usage of the VAT system. The research coordinator was available to answer any questions. In the event of adverse reactions the patient was advised to discontinue the intervention and report the reaction to one of the study team members.

Measures

The Brief Pain Inventory (Short Form; BPI-SF,Copyright 1991 Charles S. Cleeland, PhD, used with permission) [19] was employed to measure the severity of patient's pain and pain-related functional impairment.The pain severity score (PSS) is calculated by obtaining a mean score from 4 questions that patients report, rating the severity of their pain at its "worst", "least", "average", and "now". These responses are measured on an 11-point scale from 0 (no pain) to 10 (pain as bad as you can imagine). Pain interference is also measured on an 11-point scale and assesses the degree to which pain interferes in 7 categories including: daily activities, general activity, walking, work, mood, enjoyment of life, relations with others and sleep. A mean score is obtained for these 7 items (PIS). Reliability of the PSS and PIS is good as indicated by alpha coefficients of 0.85 and 0.88, respectively [20].

Sleep Quality Numerical Rating Scale (SQNRS). Sleep quality was measured on an 11 point Likert scale with 0 corresponding to best possible sleep and 10 to worst possible sleep was administered [21].

Patient Global Impression of Change (PGIC): A patient global impression of change was collected on a 7 point Likert scale (range 1 =Very much worse, 2= Much worse, 3= slightly worse, 4= No change, 5= slightly better, 6= Much better, 7= Very much better).

Assessments

At the first study visit, written informed consent and consent to the transmission of personal health information via email was obtained. Since the study involved only one participant, Research Ethics Board approval was not required. The trial was conducted in accordance with the principals set out in the Declaration of Helsinki [22]. The BPI-SF and SQNRS were administered at study initiation and at the end of weeks 2, 4 and 6.The PGIC was administered at the end of active treatment (week 4). The patient was given the vibroacoustic therapy system to take home for the duration of active therapy. The patient was contacted by the research coordinator two days following the first visit to ensure he was comfortable using the VAT system.

Forms for data collection were provided to the patient at study initiation.Dates and duration of usage of the study intervention, and the presence or absence of side-effects were recorded by the patient on a calendar. The patient was provided with specific instructions (in person and via instruction manual) regarding how to complete the calendar and was asked to submit the completed calendar via email weekly. The research coordinator contacted the patient weekly to ensure completion and submission of the calendar. The patient was instructed to present himself in person for the completion of assessments, or if this was not possible, to communicate the content of the forms electronically via email. For the first three visits (baseline, weeks 2 and 4), the patient completed the forms in person. The final assessment forms (week 6) were completed at home and sent to the research coordinator via email. There were three telephone treatment check-ins, the first occurred 2 days following the baseline visit, the second occurred one week following the baseline visit and the last occurred at week 6.

Thirty minute semi-structured interviews took place in person at week 4, following active treatment, and over the phone at week 6, following the 2 week washout period. The goal was to explore the patient's experience and perceived effectiveness of the VAT system for managing pain and sleep. The participant was asked about any new treatments started and any changes in medication.

Statistical Analysis

The change from baseline in the PSS and PIS to end of the active treatment period and the PGIC were the primary end points. Secondary endpoints were changes in the SQNRS over the course of the study and changes in the PSS, PIS and from time of treatment termination until the final assessment. Data were managed and results plotted in Microsoft Excel 2010 (Microsoft, Redmond, Washington USA).

Results

Primary findings

The BPI pain severity score measured 7.75 at baseline and was unchanged at termination of treatment. The BPI pain interference score improved by 2.43 points from baseline (8.86) to termination of active treatment (6.43). Following active treatment, the patient assigned a value of 5 on the PGIC scale, corresponding to "slightly better" indicating the patient perceived an improvement in his condition.

Secondary findings

The PSS increased slightly by 0.25 points between the termination of therapy (7.75) and the final follow-up two weeks later (8.0). The PIS increased 1.14 points, from 6.43 at termination of therapy to 7.57 at final assessment, indicating a worsening in pain disability. Sleep quality also worsened during this timeframe reflected in an increase on the SQNRS from 8 to 9. However, the SQNRS (8) remained unchanged from baseline over the course of active treatment.

Therefore, all three measures were compatible with a less favorable clinical state two weeks following termination of active treatment. Figure 1 illustrates these findings.

Freeform Observations

The patient made freeform observations on 9 out of 29 (31%) treatment days and on 11 out of 15 (73%) post-treatment days. These

Table 1: Exclusion Criteria.

Concomitant serious illnesses:
Malignancy
Vertebral Fracture
Active inflammatory conditions e.g. spinal infection, ankylosing spondylitis
Osteoporosis
Scoliosis
Coccydynia
Metabolic bone disease
Bleeding or clotting disorder
Hypotension
Active psychiatric disorders (at discretion of investigators)
Use of antipsychotic medication
Bipolar disorder
Schizophrenia
Severe/psychotic depression or anxiety disorder
Pacemaker implant
Pregnancy

Table 2: Interview Questions at Week 4.

Patient Ratings: 0 – 10 (10 is better)	
Parameter	Numerical rating
Helpfulness for Pain	2
Helpfulness for improving sleep quantity	5
Helpfulness for improving sleep quality	4
Helpfulness for managing daily activities	4

subjective responses will be reported together with responses from the semi-structured interviews at week four and week six.

The patient likened the experience of using the chair to having a massage and felt it would substitute for one.

The patient's use of the chair was extensive.He used it seven days per week and for 53 out of a possible 58 sessions. During the treatment phases there were consistent and/or repeated reports that VAT had significant activating effects on bowel function.Relaxation and/or lessening of muscle tension was reported on four days. The patient remarked that the treatment was relaxing but also helped to mobilize him in the morning.

He described an improvement in energy levels. There appeared to be effects on productivity which in turn elevated his mood. However, he could not be sure that the chair, rather than physiotherapy and additional self-help measures brought about these improvements.

The patient only made one change to his medication regime during the treatment period one day prior to termination. At that time he began taking a medication to counter an overactive bladder. He also began more challenging physiotherapy exercises during the treatment period,focusing on strengthening the shoulder and bladder.

In the post-treatment phase the patient reported increased muscle tightness or pain, headaches, sleep problems and he also reported increasing his bladder mediation dose from 4mg to 8mg/night. The medication dose increase was probably not linked to the termination of active treatment.

With respect to reported side effects, the patient experienced tingling sensations especially close to the time of initiating therapy. The tingling was described as "bothersome."In addition, effects of chills and nausea were reported once each on treatment days. While the patient felt that the use of the chair had mostly positive effects on his bowels, sometimes the stimulating effects led to a short interruption of treatment, which he found mildly bothersome.

Commenting on the shortcomings of the system, the patient noted that the chair did not touch his legs and therefore did not benefit that part of the body. Furthermore, the discrepancies in contours of the chair and of the patient's back diminished the comfort of the treatment. He did find the time commitment to be an additional drawback.

At the termination of active treatment (week 4) the patient was asked to respond to four specific questions and to rate his response from 0, representing not helpful at all to 10, representing extremely helpful.The questions and responses are summarized in table 2.

Following the 2-week washout period, in retrospect he found the VAT to be helpful for increasing his energy levels and providing a restful sleep, which in turn, impacted his mood positively. He reported that the increase in energy and improved mood encouraged him to take an important step and seek out a volunteer opportunity, something he felt unable to do prior to treatment due to his level of pain severity and interference.The patient remained unsure whether the chair or other factors fully accounted for the changes which occurred during the study timeframe. However, post-washout that he now believed the VAT to be mostly responsible for these changes.

Given these positive experience, he indicated that he would choose to use the system in the future and in fact approached us for information as to how he could acquire a chair for personal use. It was his preference to use the chair prior to sleep and on an "as needed" basis rather than twice per day.

Discussion

Use of the vibroacoustic chair was associated with some decline in the pain interference score over the four week treatment interval. However, there was no detectable change in the pain severity score or sleep quality from initiation to termination of active treatment. The patient's global impression of change was positive but only moderately so.

The pain interference score showed some worsening of pain in the washout period. There was also a decline in sleep quality at the final assessment. Although minimal, the BPI pain severity score also showed worsening at the same time point.

Taken together with the patient's narrative reports, these finding are suggestive of very modest treatment effects accruing during the active phase of therapy and declining thereafter. There were no significant adverse effects but bothersome tingling especially in the early treatment sessions which could conceivably limit patient acceptance of the treatment in the event that it proves to be a common rather than isolated experience.

Given that this is an N of 1 unblinded study the significance of the reported findings is difficult to interpret. As this was an add-on therapy, it is not possible to attribute all of the changes seen during the study period to the effects of the chair. In addition to purely placebo effects, the other concurrently applied interventions and random variation may have contributed to the outcomes.

The noticeable lack of effect on the lower limbs, which would not have received direct stimulation in this treatment paradigm, is also of interest. Our expectation was that stimulation of the torso would produce a generalized benefit extending beyond the site of application. The study patient's ongoing pain complaints were concentrated in the lower limbs. It is possible that patients' whose pain lies is largely centered in the torso might show more robust treatment effects.

Regardless of these limitations, the patient's positive responses have to be gauged against the refractory nature of his condition.

VAT requires further study for the treatment of painful Ehlers-Danlos and other chronic pain disorders such as fibromyalgia. The effect of bowel activation was unexpected and suggests that VAT of the torso might be beneficial for conditions are associated with chronic constipation.

Equipment manufactures should consider designing consumer VAT units that provides wide area stimulation including the lower limbs as well as the torso.

Conclusion

VAT offers an innovative, treatment approach that can be self-administered with few side effects in patients with EDS. Further research is necessary to define its role in therapy.

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