Musculoskeletal Clinical
Regulatory Advisers, LLC

MCRA Whitepaper

October 2017

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White Paper
Long Term Use of BiowaveHOME High Frequency Neurostimulation for the Treatment of Chronic Pain in Veterans Following Successful BiowavePRO Neurostimulation Therapy in Veterans Administration Hospitals

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ABSTRACT

The opioid epidemic has created a $78.5 billion dollar issue in today's healthcare industry. The Veteran population is especially susceptible to opioid addiction as they are ten times more likely to develop an addiction and an estimated half of the Veteran population reports chronic pain radiating from at least one anatomical region [1]. Based on a 2014 VA hospital study, it was found that Veterans who were prescribed opioids for pain management spent an average of $13,605 in follow-up healthcare annually and those that were diagnosed as abusers of the drug were found to spend an average of $28,882 annually [13]. With opioids as one of the gold standard methods of pain management, it is not surprising that opioid addiction among Veterans has increased by 55% in recent years, creating a dire need for non-pharmacological, non-invasive, and non-addictive conservative treatment methods. BiowaveHOME, when paired with primary treatment at a VA-care facility with BiowavePRO, provides a new way to manage pain via electrical field generation in deep tissue inside the body. Sixty-six (66) Veterans were treated with BiowavePRO and then were given a BiowaveHOME to continue pain management on an as-needed basis. Ninety percent (90%) of the surveyed subjects reported a significant decrease in pain, increase in range of motion, or an increased ability to participate in activities of daily life after incorporating BiowaveHOME into their pain management regimen. Ninety percent (90%) of these same subjects reported that, compared to the Transcutaneous Electrical Nerve Stimulation (TENS) unit, a device based on electrical stimulation at the surface of skin, the BiowaveHOME was superior. Additionally, 58.7% of patients surveyed who were taking prescription pain medications either stopped using prescription opioids or reduced consumption. Patient satisfaction with the BiowaveHOME was measured by an overall decrease in pain, increase in quality of life, and a decrease in opioid consumption. In conclusion, the BiowaveHOME is a superior alternative to existing medical devices (i.e. a TENS unit) and is an attractive substitute for pain management by medications.

INTRODUCTION

In the United States an estimated 100 million people suffer from chronic pain conditions with opioid prescription pain medications used as the primary treatment [2]. The prevalence of chronic pain among U.S. Veterans is relatively high, with one study citing that half of a selected population of 300 Veterans reported at least one type of chronic pain. This same study reported that 75% of these patients were prescribed at least one analgesic for pain management, and that 44% of those patients prescribed analgesics were prescribed opioids [3]. Other studies report similar statistics, pointing to opioid prescription as a standard for the management of chronic pain. Excess or prolonged use of opioid treatment is a recognized gateway to the addiction crisis faced in the U.S.

In addition to the implications to the patient, the effects of opioid misuse can be felt socioeconomically, with opioid-related death tolls rising to nearly 100 Americans each day [4]. It was reported that approximately 50% of the prime-age male labor force is prescribed a daily regimen of pain medication, resulting in a negative impact on productivity and an increase in related-healthcare costs [5]. Due to the increasing reliance on pain medications, a large portion of the able-bodied workforce are unable to pass drug tests and resort to rehabilitation facilities to combat the addiction, further adding to the labor shortage. This epidemic affects men as well as women, of all races, across all socio-economic levels.

As of 2016, nearly two million Americans met criteria for prescription opioid abuse and

dependence, amassing aggregate costs of over $78.5 billion dollars. One-fourth of the economic burden was funded by the public sector, which includes Veterans' programs [6, 7]. Studies in Veterans Affairs (VA) hospitals of patients with chronic non-cancer pain highlight a link between prescription opioid dose and suicidal behavior [8]. In 2014, it was reported that the VA issued 1.7 million prescriptions for opioids to 443,000 Veterans for in-home pain management. As a result, the estimated number of Veterans with opioid addictions rose 55% between 2010 and 2015 [9, 10]. The high cost associated with opioid prescription, in addition to the fact that the Veteran population is ten times more likely than the average American to abuse opioids, has created a need for effective, non-opioid-based treatment options readily available to those impacted by chronic pain [1].

Although there is considerable documentation on the incidence and severity of both acute and chronic pain using traditional conservative methods in the general population, there is very little data regarding the utilization of non-invasive medical devices. Optimal analgesia encompasses the notion of providing optimal reductions in pain with increasing patient comfort, maximum patient satisfaction, and minimum related side effects for the prescribed treatment. Various treatment algorithms for the management of nonmalignant pain have been proposed which include a stepwise approach at managing pain with emphasis on utilizing the least invasive strategies whenever feasible. Still, pure opioid agonists continue to be the most commonly prescribed regimen for moderate to severe pain in many situations. A significant number of patients experience opioid related side effects, which limit their ability to achieve optimal analgesia and preclude them from various normal activities of daily living ("ADLs"). This is especially relevant to Veterans who are seeking non-opioid solutions to treating pain so that they can perform even simple daily activities to lead a normal life. Thus, there is an unmet need for alternative therapies that lessen the pain experienced by Veterans while minimizing side effects and the dependence of patient on prescription opioids.

PURPOSE

This study sought to examine the effectivity of the BiowaveHOME High Frequency Neurostimulator medical device as a new non-pharmacologic, non-narcotic, non-addictive, non-invasive way to manage pain and potential to reduce opioid use. This longitudinal (18-month long) study compiled data from 66 surveyed veterans in regard to their pain response to incorporating BiowaveHOME into their pain management routine.

MATERIALS/METHODS

The BiowaveHOME device was used to treat pain resulting from various chronic pain conditions in Veterans from three VA Medical Center ("VAMC") Hospitals: James A. Haley VAMC in Tampa, FL; Corporal Michael J. Crescenz VAMC in Philadelphia; and The Durham VAMC in Durham, NC.

Treatment Device

The BiowavePRO and BiowaveHOME neurostimulators are non-pharmacologic, non-narcotic, non-addictive, non-invasive adjunct of pain (Figure 1). The two devices work in an identical manner by delivery back and forth of a summation of two high frequency sinusoidal alternating current signals at 3,858 hz and 3,980 hz to a first electrode and then to a second electrode. The electrodes are placed directly over one or two locations of pain.

Figure 1: BiowaveHOME Neurostimulator

The mechanisms of action that result from the electrical field generated from Biowave devices are similar to chemical anesthetics and are based on Frequency Conduction Block Theory [14]. This is in contrast to Transcutaneous Electrical Nerve Stimulation (TENS) devices which are based on Gate Control Theory which provide a noxious sensation at the surface of skin which may act like a distraction to pain, but which do not block the pain signal.

The electrodes through which the high frequency signals are delivered consist either of:

1. B-set (Figure 2): two 2.0" diameter round electrodes for (i) treating two distinct locations of pain, (ii) the origin of pain and most proximal

location of pain to the origin (for example in the case of a radiculopathy) or (iii) one large area of pain (the electrodes are placed one inch apart from one another).

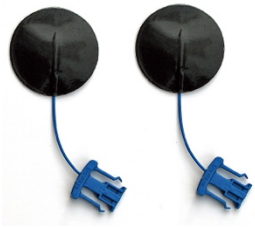

Figure 2: B-Set Electrodes

2. E-set (Figure 3): one 1.375" diameter round electrode placed directly over a single location of pain and one 2" x 4" rectangular dispersive electrode placed over a bony prominence which is a comfortable location to receive stimulation.

Figure 3: E-Set Electrodes

Study Enrollment

In order to participate in the study, subjects had to meet the inclusion/exclusion criteria, outlined below.

Inclusion Criteria

1. Subjects may be male, female or transgender of any race
2. American Society of Anesthesia Physical Classification: ASA 1-3 [11]
3. Ages 16 - 80 yr
4. Subjects must have been using BiowaveHOME for a period of at least 6 months.
5. Subjects must respond to at least one or more treatments from a BiowavePRO neurostimulator at their VAMC. Response includes at least one of the following:
    a. Reduction in VAS pain score of ≥30%,
    b. Increase in range of motion (ROM) of ≥ 10%;
    c. Reduction in pain medication consumption;
    d. Improvement in ADLs.
6. Subjects must be able to understand and operate a BiowaveHOME neurostimulator
7. Subjects must be able to provide a verbal response to a patient questionnaire

Any Veteran who was injured and had a chronic pain condition was eligible to participate. Treatment with Biowave HOME could be performed on an as needed basis or until the condition resolved.

Exclusion Criteria

1. Allergy or intolerance to adhesive materials
2. Clinical evidence of cardiovascular (history of cardiac arrhythmias), pulmonary, renal, psychological, hepatic, neurological (seizures), hematologic, or endocrine abnormalities
3. Rash or wounds in the area where electrodes need to be placed
4. History of pacemaker or implantable AICD

From the initial pool of Veterans eligible for the study, 187 were contacted for responses to the study. Of the 187 potential subjects, sixty-six (66) responded to the 9-question survey.

Treatment Algorithm

Subjects were first treated using a BiowavePRO neurostimulator in a VA Medical Center either in a Pain Clinic, Physical Medicine and Rehabilitation (PM&R) Clinic or in a Spinal Cord Injury (SCI) Clinic.

Subjects were treated three times over a one to three week period. Treatment duration was 30 minutes. Subjects were evaluated following each treatment. At the end of the three treatments, subjects were issued a BiowaveHOME unit through the Department of Prosthetics, if:

1. The subject had ongoing pain management needs; AND
2. The subject's response to the BiowavePRO treatment in the clinic included one of the following:
    a. Reduction in their VAS pain score of ≥30%,
    b. Increase in range of motion (ROM) of ≥ 10%;
    c. Reduction in pain medication consumption;
    d. Improvement in ADLs.

Table 1: Demographics Information

N=66	Male n (%)		Female n (%)	
Study Gender Distribution	61 (92.5)		5(7.5)	
N=66	**Acute n (%)**	**Chronic n (%)**	**Both n (%)**	**Non-Response n (%)**
Type of Pain	5 (8)	51 (77)	8 (12)	2 (3)

Subjects then continued treatment with Biowave-HOME at their home on an as needed basis. BiowaveHOME outputs the identical waveform at the same frequency and intensity as BiowavePRO. Electrode placement was identical at home as compared to treatment in the clinic. Treatment duration at home is also 30 minutes.

Exactly as in the clinic, subjects were instructed to increase the intensity of their BiowaveHOME unit to a strong but comfortable sensation. As the body adapts to the internal electrical field, the sensation from the internal electrical field diminishes, and subjects were instructed to keep increasing the intensity level to maintain a steady state strong sensation throughout the duration of the 30-minute treatment. Subjects were then instructed to continue to treat on an as needed basis.

Subjects who had been issued Biowave devices over a period of 18 months had been contacted and asked a series of 9 questions relative to their experience using the Biowave device:

1. *Do you have acute pain or chronic pain?*
2. *What part of your body are you treating?*
3. *Have you reduced your pain meds or reduced your opioids?*
4. *What other treatments have not worked for you?*
5. *How does Biowave compare to TENS?*
6. *What do you like about Biowave?*
7. *How often do you use Biowave?*
8. *If you're not using it any more, how come? (For example: pain is gone) Are you undergoing any other form of treatment?*
9. *Has Biowave helped improve your quality of life? How*?

Information was captured using a Salesforce database.

RESULTS

Effectiveness

For this study, the responses of 66 veterans meeting all inclusion criteria were analyzed for a reduction in pain, increase in range of motion, reduction in pain medication consumption, and improvement in activities of daily living by way of a 9-question survey.

The results compiled within this section are responses provided by surveyed Veterans after up to 18 months of in-home treatment with Biowave-HOME. The majority of subjects (92.5%) in the study were male (Table 1). Seventy-seven percent (77%) of surveyed subjects reported having chronic pain, 8% reported having acute pain, and 12% reported having both chronic and acute pain before the study (Table 1).

Categorizing the location of pain, 36% of the subjects reported back pain alone while the majority (52%) reported pain presenting in multiple locations (Table 2). The majority of subjects (89%) failed a previous conservative treatment such as TENS, opioid, or physical therapy ("PT") (Table 3).

Table 2: Pain Location

N=66	n (%)
Upper Extremities Only[A]	5 (8)
Lower Extremities Only[B]	1 (2)
Neck	2 (3)
Back	24 (36)
Multiple Regions[C]	34 (52)

[A] Upper extremities include shoulder, arms, and/or hands
[B] Lower extremities include hips, legs, knees, and/or ankles.
[C] Multiple Regions include back, neck, upper extremities, and/or lower extremities

Table 3. Previous Failed Treatments

N=66	n (%)
TENS Treatment Alone	19 (29)
TENS Treatment in Combination with Other Therapies[A]	32 (48)
Other Treatments	8 (12)
No Answer Provided	7 (11)
Total failed using TENS alone or in combination	51 (77)

[A]Other therapies include dry needling, injections, opioids, physical therapy, chiropractic care, acupuncture, nerve block, or IFC.

When surveyed about frequency of utilization, 95.1% of subjects reported regular use at up to 18 months. A high rate of subjects (85.6%) were utilizing the device multiple times a week or more. Of those subjects 50.8% were using it daily (Table 4).

Table 4. Subject Frequency of Use for Biowave

N=66	n (%)
Multiple times a day	20 (30.3)
Once daily	12 (18)
Multiple times per week	22 (33.3)
Once a week	6 (9.1)
As needed	3 (4.5)
Stopped Using	3 (4.5)
Total Using Regularly	90.9%

Out of the subjects who were previously treated with TENS units, 90.7% of surveyed subjects reported that the BiowaveHOME was superior to the TENS unit (Table 5) and over 84.8% of all surveyed subjects say that their pain level had decreased, their range of motion has increased, or their activities of daily life have improved since incorporating the BiowaveHOME into their pain management regimen. Out of the subjects taking pain medication at the beginning of the study, 58.7% have either stopped taking or have significantly reduced the consumption of prescription pain medications since beginning treatments with the BiowaveHOME pain management device (Table 6).

Table 5. Comparison of Biowave to TENS

N=54	n (%)
BiowaveHOME superior to TENS treatment	49 (90.7)

Table 6. Effect on Pain Medicine Consumption

N = 55	n (%)
Consumption was reduced	26 (47.3)
Consumption was eliminated	6 (10.9)
Consumption remained unchanged	23 (41.8)

Eighty-four percent (84.8%) of all subjects surveyed at the end of the study said that their quality of life was improved by introducing BiowaveHOME into their pain management routine (Table 7).

Table 7. Overall Effect on Life

N = 66	n (%)
BiowaveHOME improved quality of life	56 (84.8%)
BiowaveHOME did not improve quality of life	5 (7.6%)
Not sure	5 (7.6%)

Safety

There were no reports of any burns, or any electro-thermal injury or any other adverse events.

DISCUSSION

This study sought to assess the effectiveness of a non-pharmacological alternative for pain management, the BiowaveHOME device. This is the first study to evaluate long term use (6 to 18 months) of the BiowaveHOME device to treat chronic pain in Veterans. This study demonstrates that Biowave is an effective non-pharmacological, non-invasive, non-addictive pain treatment solution. Successful treatment in the physician's office, clinic or hospital with the BiowavePRO high frequency neuro-stimulator (77-85% of those treated receive a 50%-100% reduction in VAS pain scores and an improvement in function for up to 24 hours post treatment [15]) can be continued cost effectively at home on an as needed basis with an outpatient treatment regimen using the BiowaveHOME high frequency neurostimulation medical device.

As of 2016, nearly two million Americans met criteria for prescription opioid abuse and dependence, amassing aggregate costs of over $78.5 billion dollars. One-fourth of the economic burden was funded by the public sector, which includes Veterans' programs [6, 7]. The study was quick to note that these costs do not account for the economic value of loss of productivity and quality of life. The high cost associated with opioid prescription, in

addition to the fact that the Veteran population is ten times more likely than the average American to abuse opioids, has created a need for effective, non-opioid-based treatment options readily available to those impacted by chronic pain. The study demonstrates that Biowave can be a viable alternative or adjunct to chronic pain management and potentially reduce the patients' opioid use.

Another form of conservative therapy that has provided a non-pharmacologic, non-narcotic, non-addictive, non-invasive way to manage pain is the Transcutaneous electrical nerve stimulation, or TENs unit, which is based on the "gate control theory" of pain which focuses on masking pain signals, providing relief for a short period of time. Mixed reviews about if TENs delivers pain relief to common areas of chronic pain has created yet another unmet market need for an effective alternative [12]. The technology behind Biowave is based on the "frequency conduction block theory," which blocks pain signals by preventing the sodium – potassium ion exchange across the membrane of nociceptive pain fibers thereby preventing action potential along the pain fibers. This study found that subjects preferred the Biowave device over TENS device for treatment. While the rationale for preference was not part of this study, it is likely due to the effectiveness of pain reduction as well as treatment comfort that subjects experience with Biowave devices as compared to a TENS treatment.

BiowaveHOME, in addition to providing a non-pharmacological, effective pain management alternative, provides a financially attractive alternative option. While this study did not directly compare the potential cost savings to the VA system, the implications of this are not to be understated. As previously stated, the Veteran population is ten times more likely to develop an opioid addiction than the average American and the pool of Veterans currently battling opioid addiction from using opioids as a side effect of pain management is close to 443,000. The distribution of the BiowaveHOME to chronic pain sufferers could potentially drastically decrease the yearly healthcare budget allocated to dealing with the opioid epidemic and while increasing the quality of life of those affected by addictive methods of pain management. Based on a 2014 VA hospital study, it was found that Veterans prescribed opioids for pain management spent an average of $13,605 in follow-up healthcare annually and those that were diagnosed as abusers of the drug were found to spend an average of $28,882. Outpatient service costs for Veterans prescribed opioids and diagnosed with addiction spent close to $11,192 annually [13]. Comparatively, BiowaveHOME is a low cost alternative, with nearly one-tenth the cost of yearly outpatient services in the first year and nearly one twentieth annual cost for subsequent years.

Based on the results of the study, BiowaveHOME is an effective, well-received non-pharmacologic alternative to the existing pain management options and greatly improves patient quality of life.

CONCLUSIONS

Overall, the BiowaveHOME was found to be well tolerated by the majority of study subjects. The subjects expressed great satisfaction with the treatments, suggesting that this method of pain management is an alternative to existing medical devices (i.e. TENS units) and is an attractive substitute for pain management by medications.

Biowave can help healthcare providers provide their patients with a continuum of care. The first step is to verify treatment success with a BiowavePRO high frequency neurostimulator in a clinic or hospital setting. If the patient responds successfully to treatment in the clinic and has ongoing pain management needs, the provider can then issue a BiowaveHOME high frequency neurostimulator to the patient so the patient can continue to manage their pain at home on an as needed basis and with a reduced level of opioids.

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