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ABSTRACT:

We treated 551 patients for their Nerve Pain (Peripheral Neuropathy) using ReBuilder. ReBuilder, a unique TENS/EMS electrical stimulation device - used to determine if it improved the quality of the patients' life. Fully 94% reported success. The patients reported no side effects. The ReBuilder is safe and effective for treating peripheral neuropathy.

Figures:

- Treating patients feet using the split compartment electrode-containing solution.
- Silver laced conductive gloves (not used in this trial). Socks also available.
- Close up of the ReBuilder®. Note the small size and portable nature.
- Mean pain ratings before and after using the ReBuilder®.

INTRODUCTION

Peripheral neuropathy (PN) is the most common neuromuscular disorder and usually presents as symmetric distal polyneuropathy. The estimated incidence of Peripheral Neuropathy in the general population is 2.4% and 8% in persons older than 55 (1). The most frequently reported cause of Peripheral Neuropathy is diabetes; 40%-50% of patients who have had type 2 diabetes for >10 years have Peripheral Neuropathy and 26% of all diabetic patients have painful Peripheral Neuropathy (2,3). Another risk group is cancer patients who receive chemotherapy agents that are neurotoxic to the peripheral nervous system. These agents include (platinum analogs, taxanes, vinca alkaloids, thalidomide, bortezomib, and ixabepilone) (4,5). PN also occurs in patients with HIV and may arise in those with amyloidosis, Sjogren's syndrome, or other conditions. In many cases is idiopathic (6,7,8). Whatever the cause, PN often causes significant morbidity PN can alter mobility and balance, fatigue, depression, anxiety, and decreased quality of life (9).

Peripheral Neuropathy has an insidious onset. Starting in the distal ends of the longest neurons and progressing slowly over months to years. Manifestations originate in the toes and fingers. It then gradually progress to the feet and hands (stocking and glove pattern). It rarely extends to above the knees and the elbows (8). Although Peripheral Neuropathy can affect motor and (rarely) autonomic nerves, large and small afferent sensory neurons are most often affected by PN. Manifestations may include distressing bilateral nerve pain, paresthesia, and impaired temperature, touch, vibratory sense, proprioception, and loss of deep tendon reflexes (DTRs) (10). Some individuals also experience difficult to manage neuropathic pain in the affected areas. This arises as a direct consequence of the pathogenic event affecting the peripheral somatosensory system (11). In addition to paresthesias, individuals may experience other symptoms. These symptoms reflect damage to small A and C nerve fibers. Shooting, electric or shock-like, or stabbing (lancinating or knife-like) pain (9,12). Other persons report allodynia after contact with non-painful stimuli (e.g. clothing or bed sheets against the skin), pain when walking that feels like walking on marbles or on hot sand, or feelings of heat, burning, or cold in their feet.

Most research has focused on diabetic neuropathy. There are few adequately powered, well-designed studies to firmly establish optimal pharmacologic treatment (Bril, et al, 2011)(13).

Research regarding the management of Peripheral Neuropathy from other causes lags behind.

There is little data supporting the use of non-pharmacologic measures. However, there is some intriguing data regarding transcutaneous nerve stimulation (TENS) and related technologies. For instance, Jin and colleagues (2010) (17) reviewed the literature to identify studies comparing TENS to sham treatment for symptomatic diabetic Peripheral Neuropathy. They identified only three small studies that met the inclusion criteria. These studies confirmed that active TENS (alone or with amitriptyline) used for 30 minutes once a day for 4-12 weeks was significantly superior to placebo in reducing pain and subjective symptoms of Peripheral Neuropathy. Similarly, Pieber and others (2010) (18) reviewed 15 studies of TENS and other forms of external electrotherapy. (e.g. pulsed dose electrical stimulation, high-frequency muscle stimulation, frequency-modulated electromagnetic neural stimulation). They concluded these methods are continued benefits for patients with painful diabetic PN. Although four of the studies reviewed suffered from small sample sizes, most lacked a placebo or control group. Follow up was inconsistent across studies. Interestingly, there was some evidence that the electrical stimulation methods might be more effective than TENS. Hypotheses for these therapies is that they may act by supraspinal mechanisms, modulate descending inhibitory pathways, increase pain threshold, influence calcitonin, reduce windup, or reduce nerve impulse transmission from damaged neurons.

Our clinical observations and reports from patients experiencing painful PN that support the potential value of a new device, ReBuilder®. (22) ReBuilder® is designed to deliver dual electrical stimulation to muscle and nerve tissues (ReBuilder Medical Inc.). We were encouraged to develop a more rigorous rationale for using or recommending this device. After discussions with several of our patients and their physicians. These patients and physicians expressed extreme frustration at the lack of effective therapeutic options. Some patients even expressed suicidal thoughts because of unrelieved Peripheral Neuropathy and pain. These findings form the basis for this preliminary study. A review and analysis of patient-generated data collected by ReBuilder Medical Inc.

METHODS

The ReBuilder® device is registered with and approved by the FDA as a 510K pre-amendment version TENS (transcutaneous electrical stimulator) and an electronic muscle stimulator (EMS)(24). The ReBuilder® delivers energy via cutaneous electrodes to each foot (and hand, if indicated). It is placed in one compartment of an electrically isolated split compartment bath containing an electrolyte mixture(figure 2) (newer versions offer the alternative of silver-impregnated socks and gloves) (figure 1). According to the manufacturer, the ReBuilder® individualizes its outputs based on the physical mass and digital impedance of the individual using it (http://rebuildermedical.com) which gives an unequaled level of safety.

The very real medical advance is in the use of an internal microprocessor that analyzes the patient's current, dysfunctional peripheral nerve waveform, and then designs a compensating waveform (like noise-canceling headphones) that it delivers to all the peripheral nerves from the spinal cord to the feet. Just as a pacemaker must imitate the waveform of a healthy heart or risk retrograde blood flow, it is reasonable that the peripheral nerves function via a very specific waveform. A common TENS device delivers a constant square wave that is foreign to the nerves.

ReBuilder's® Impulses utilize very small amounts of current under the curve and a relatively high transient voltage of 40-90 volts. The resultant current is below that commonly produced by traditional TENS units. The device delivers a second, simultaneous, lower voltage (5-20 volts), wider waveform signal designed to stimulate muscle tissue. This signal causes the muscles of the feet, calves, and thighs and buttocks to intermittently contract and relax. Stimulating the venous muscle pump to empty veins thus allowing whatever arterial pressure is present to rapidly fill the vacated veins. This enhances local blood flow. Using this dual stimulation (80% nerve stimulation and 20% muscle stimulation) is pulsed at a frequency of 7.83 cycles per second. Theoretically, this allows afferent neurons time to repolarize between pulses. The dual stimulation is hypothesized to travel from the distal end of the ascending sensory neuron, across the spinal interneuron, and down to the distal end of the motor neuron in the contralateral limb (monograph).

SAMPLE

551 individuals who purchased the ReBuilder between December 2002 and May 2004 comprised this convenience sample. These individuals responded to an Internet advertisement offering a financial incentive for trying a new treatment for peripheral neuropathy. The package the 551 respondents received included a ReBuilder device and a simple survey questionnaire which they filled out and returned within three months. They were also asked to record their reason for using the device (pain or other symptoms) and to rate their pain, if applicable, on a numerical rating scale (NRS) of 1 (least) to 10 (worst) before and after using the device.

STATISTICAL ANALYSIS

Statistical tests were performed using the SPSS software version 20 (IBM, Armonk, N.Y.), and included calculation of descriptive statistics, means, and frequencies for putting together categorical variables. Using a paired t-test to examine any differences in beginning and end of trial pain ratings in persons who reported initially reported pain. We performed a one-way analysis of variance (ANOVA), comparing the differences in pain score changes in the 3 groups of respondents; a) those reporting an improvement in pain, b) those who were unsure whether their pain improved, and c) those who stated that their pain had not improved.

RESULTS

Excluded were twenty records, due to conflicting or confusing data. The remaining 531 records formed the basis of this report. Eighty-eight percent of respondents did not know the cause of their PN. Only 7% reported their neuropathy was due to diabetes, 3% reported it was anatomic, and 1% each reported toxic or vascular causes. We asked for no other demographic data. ANOVA revealed a significantly greater reduction in pain score in 'yes' responders, as compared to the 'equivocal' and 'no' responders ($p<0.0001$). In addition, 94% of respondents reported improved quality of life after using the ReBuilder. A greater number of individuals reported on their satisfaction with pain relief (n = 515) than initially reported pain (n = 456). This discrepancy is explained by individuals who initially reported severe nerve pain or tingling in their feet but still reported an improvement in pain score.

Testimonials from the questionnaires were not analyzed statistically. The most common comments were "miraculous relief," "I can feel my feet again, " I am no longer suicidal," and "I have a life again." Unexpected comments included ulcer-healing in 3 patients, resolution of fungal nail infection in one, and improved sexual function in 3 patients.

DISCUSSION

One potential advantage of the ReBuilder over other technologies including ST5 or TENS is its simplicity of use. In particular, the ST5 treatment must be administered in the clinic and ideally administered by a specially trained clinician. The manufacturer of the ST5 now requires that physicians attend a three-day training course. Additionally, the correct placement of electrodes for optimal local pain relief is why this course is required[23]. There are two versions of the ReBuilder, both FDA registered. One device for home use and one device for clinic setting use.

There are numerous causes of peripheral neuropathies. Axonal degeneration, occurring secondary to accumulation of toxins or neurotoxic agents could be the cause. Also, vitamin deficiencies inherited genetic abnormalities, hyperglycemia and glucose accumulation within neurons, or other causes[25]. The external environment of neurons, such as vascular compromise or ischemia, inflammation, and oxidative stress may cause secondary demyelination and axonal dysfunction[2]. Involvement of small and large sensory neurons often leads to manifestations such as nerve pain, tingling, dysesthesia and burning, as well as a change in temperature sensation and proprioception, and loss of DTRs. Resulting neuropathies may lead to severe pain, disability, erectile dysfunction, impaired ability to walk and drive safely, and decreased quality of life[23].

There is no known cure for peripheral neuropathy and except in the case of diabetes mellitus, where tight glucose control has been reported to effect improvement[26,27]. The treatment has been directed largely at relieving symptoms rather than treating the underlying cause. A common TENS is a simple, non-invasive treatment for neuropathic pain based on the gate control theory[28]. that proposes stimulation of large myelinated A-fibers inhibits transmission of painful afferent impulses from A ? and C fibers to the dorsal horn of the

spinal cord, thereby closing the gate. This hypothesis may be too simplistic, as central mechanisms may be involved. Furthermore, TENS therapy may not change C or A? mediated thresholds or perceptions (e.g. cold, warmth, cold or heat pain, vibration or touch)[29]. TENS may be useful for localized neuropathic pain related to diabetes and other conditions and often leads to improvement of pain that diminishes with the cessation of TENS use[17,18,29] was an overall improvement in Peripheral Neuropathy pain at twelve weeks of treatment. Current evidence-based guidelines conclude TENS is "probably effective in lessening the pain of painful diabetic neuropathy and improving quality of life" (Bril et al)[13]. The primary method of action is that of blocking the nerve path by overstimulating the nerve cell with a foreign waveform simple squarewave) delivered at a higher rate than 7.83 Hz (the rate required for a nerve cell to repolarize).

The ReBuilder is distinctly different from traditional TENS units. From "scrambling" types of electrical stimulation, its design opens the nerve paths rather than closing them. It also improves the microcirculation, re-polarizes and re-educates the nerves to follow the correct pathways rather than to confuse the nerve fibers. Its simple design allows for home use. Recent versions include silver-impregnated gloves and stockings for home use, to avoid the electrolyte bath, further simplifying the treatment process and making it portable.

LIMITATIONS

There is little information about the self-selected sample, particularly in terms of etiology and duration of Peripheral Neuropathy, and other medical data. Additionally, there is no follow up data regarding continued use and duration of pain relief in the yes responders. Correspondingly, we cannot say whether those whose responses were 'equivocal' or 'no' would respond with further use of the ReBuilder; that is we do not know the time frame in which the onset of and maximal pain relief occur.

CONCLUSION

We have found no other published data or information that includes a large number of individuals (more than 500) experiencing painful neuropathy detailed in our report. Despite the limitations identified, we believe this provides compelling information that should drive larger prospective studies. Future studies should answer further questions that remain open: 1) can use of the ReBuilder return some degree of peripheral normal sensation 2) is pain reduction lasting or not 3) can the ReBuilder delay the onset of Peripheral Neuropathy in patients with diabetes or those who are prescribed neurotoxic chemotherapy? Other investigators may also be interested in elucidating the mechanisms of pain relief of the ReBuilder. Our hypothesis is that: The electric stimuli promote healing of the microcirculation and re-direct the small neurons into an appropriate arrangement. Finally, nerve conduction velocity (NCV) studies are considered the gold standard of diagnosing Peripheral Neuropathy, and should be included in future studies pre- and post-treatment to determine whether velocity improves. In this unpublished study, *The ReBuilder is found to be safe and effective in mitigating pain in peripheral neuropathy.* Therefore we highly

recommend the ReBuilder as a first choice for you to consider in the management of pain as a symptom of peripheral neuropathy.

Figure 1
The ReBuilder 2407 in Carpal Tunnel Syndrome Care

Figure 2
Patient Treating Diabetic PN Feet with ReBuilder 2407 in an electrically isolated split compartment bath containing an electrolyte mixture.

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