Journal of Back and Musculoskeletal Rehabilitation 18 (2005) 79–83
IOS Press

Pulsed magnetic field therapy in refractory carpal tunnel syndrome: Electrodiagnostic parameters – pilot study

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Abstract. *Context:* Neuropathic pain arises from ectopic firing of nociceptors. Since pulsed electromagnetic fields (PEMF) generate extremely low frequency (ELF) quasi-rectangular currents which influence biological activity, it was hypothesized that directing this energy into the carpal tunnel region could influence neuronal firing patterns and lower VAS scores of neuropathic pain.
Objective: To determine if nine consecutive one-hour treatments (excluding weekends) of a pulsed signal therapy can reduce neuropathic pain scores in refractory hands with carpal tunnel syndrome.
Design/setting/patients: 35 consecutive hands were enrolled in this non-placebo pilot study between July and November 2002. All subjects had to be constantly symptomatic and a failure to therapy. Primary endpoints were comparison of visual analog scores (VAS 0–10) at end of 9 days of treatment and end of 30 days follow-up compared to baseline pain scores. Additionally, at end of study, patients responded to a questionnaire (PGIC) describing their response to treatment. Secondary endpoints were comparison of sensory and motor distal latencies of median nerve after treatment with baseline. Additionally, clinical examination changes were tabulated with baseline. Five hands were surgical failures.
Intervention/device: Non-invasive pulsed signal therapy generated a patented unidirectional quasi-rectangular waveform with strength less than 20 gauss and frequency less than 30 Hz into the carpal tunnel region for nine consecutive one-hour treatments (excluding weekends). The specific amount of energy directed at the target site was unknown.
Results: Statistical reduction (ANOVA) of pain scores at end of treatment (23%) and also end of follow-up (37%) were noted in the 33 hands that completed the study. The PGIC questionnaire revealed 67% improvement. Clinical and electrodiagnostic examination data did not change from baseline to end of study. There were no adverse events or safety issues.
Conclusion: Our pilot data suggests that directing PEMF to the carpal tunnel region can provide modest, short-term relief for a majority of individuals. The precise mechanism is unclear in the absence of electrophysiological changes. This provocative data requires confirmation with randomized, placebo-controlled, double-blind trials and additional electrophysiological markers.

Keywords: Carpal tunnel syndrome, pulsed magnetic field stimulation, neuropathic pain

1. Introduction

Entrapment of the median nerve at the level of the carpal tunnel is the most common cause of sensory and motor disturbances in the hands. The incidence of carpal tunnel syndrome (CTS) has been increasing over the past two decades and estimated to affect over 10 million Americans. Standard non-surgical therapy exists, i.e. splinting, analgesics, steroid injections, and are considered the cornerstone for management of mild cases [31]. Other therapies such as acupuncture, yoga, massage and Vitamin B6 have been utilized with varying results. However, as the condition ad-

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ISSN 1053-8127/05/$17.00

vances in severity, there is persistent acroparesthesiae with neuropathic pain producing disability and functional impairment. Most conventional medical treatment approaches are unsatisfactory producing refractory complaints and ultimately surgical decompression is required. Despite surgical advances and techniques, complications exist in 1–30% of cases [4]. In view of the limitations and shortcomings of current conventional approaches in CTS, exploration of new and safe strategies appear warranted.

Novel electromagnetic approaches exist (laser [35], static magnets [36]) that are safe and, when directed to the carpal tunnel, appear to slow and alter the neuronal dysfunction. The precise molecular mechanism producing a re-modulation of neuronal firing with reduction of neuropathic pain and increased nerve conduction is not known. Since substantial evidence exists that pulsed electromagnetic fields, (PEMF), safely induce small electrical eddy currents within the body that can depolarize, repolarize and hyperpolarize neurons [1,10, 13,20,33], it was hypothesized that this energy directed to the most symptomatic wrist could potentially reduce neuropathic pain scores.

2. Methods

2.1. Study design

This pilot study was designed to determine whether cumulative pulsed signal therapy could be an effective treatment for symptomatic neuropathic pain. The primary outcome measure was visual analog scores (VAS 0–10) tabulated daily through the treatment period and also up to 30 days. This would be compared to one week of baseline pretreatment scores. Additionally, at the end of the 30 day period, patients would respond to a standardized Patients Global Impression of Change (PGIC) [7] questionnaire with seven options describing their responses to treatment. Secondary endpoints were electrodiagnostic distal latencies, i.e. compound muscle action potentials (CMAP) and sensory nerve action potentials (SNAP) antidromic. American Academy of Electrodiagnostic Medicine and American Academy of Neurology criteria [18] for abnormality was CMAP distal latency (DL $>$ 4.0 m/sec) and SNAP (DL $>$ 3.7 m/sec) [6]. A 7–8 cm conduction distance was used at ambient room temperatures. Since latencies may vary due to test-retest variability, significant change was noted to be two standard deviations. Additional secondary endpoints included examination findings compared to baseline.

This is an open, non-placebo study with protocol approved by the Phelps Hospital Investigational Review Board (IRB). After a complete description of the study to the patients, written informed consent was obtained prior to enrollment. No new analgesics were allowed, however, patients could remain on their current regimens.

2.2. Subjects

Thirty-five (35) consecutive hands were enrolled in this study between July and November 2002 who met the following inclusionary criteria: A) Neuropathic symptoms of numbness, tingling, or burning pain in the territory of the median nerve on a daily basis. Neurologic examination at least positive changes of sensory/motor or presence of Tinel or Phalen sign were required compatible with diagnosis of carpal tunnel syndrome. B) Failure to standard therapies of splinting, vitamin B_6, steroid wrist injections, pharmacotherapy, analgesics, etc. C) No history of other diseases producing similar symptoms. D) Ability to keep visual analog scores (VAS) of neuropathic pain for the symptoms of numbness, tingling and burning for the duration of the study. Three enrolled subjects had bilateral CTS.

2.3. Device

Pulsed signal therapy (PST$^{\mathrm{tm}}$) is a patented variant of pulsed electromagnetic field (PEMF) which has specific signal characteristics attempting to mimic the body's signal loss and energy imbalance. The PSTtm generates extremely low-frequency (ELF), quasi-rectangular waveforms that are uni-directional and have changing amplitudes using covered electric coils and a DC generator. The wrist is comfortably placed inside a closed circuit coil for one hour on nine consecutive days in the physician's office, excluding weekends (Saturday/Sunday). The device generates a pure magnetic field output signal that employs direct current with unidirectional biological frequencies below 30 Hz. The waveform is quasi-rectangular with measured field strengths generally below 2 mT or 20 gauss. The system is controlled through a pulsed unidirectional magnetic DC field with multiple output frequencies implemented via a free-wheeling diode to optimize the induction characteristics. Various frequency/amplitude combinations are switched over automatically and are transmitted under continuous con-

trol during the treatment period. Induction of treatment takes place during the first 10 minutes followed by a combination of pulsed signals that deliver the therapy over the remaining 50 minutes. A one-hour duty cycle timecard is inserted which starts the induction and treatment process. This is noiseless and non-thermal.

2.4. Masking

The investigator (MIW) was not blinded. All patients were informed that this was an open-label trial of active magnetic stimulation. There were no placebo controls.

2.5. Statistical analyses

Oneway repeated measures analysis of variance (ANOVA) were used to assess changes in pain scores over the course of the study at baseline, end of treatment, and at end of follow-up. Reductions in pain scores from baseline to end of treatment and from baseline to end of follow-up were tested with a *priori* contrasts. An intent-to-treat ANOVA was conducted in which the last recorded pain score during treatment was substituted for missing final treatment and follow-up scores for the patients who did not complete treatment. For all tests, *p-value* of 0.05 or less was considered to indicate statistical significance. The Statistical Package of the Social Sciences (ver.10.0) was used to analyze the data (SPSS, Inc., 233 South Wacker Drive, Chicago, Ill, 60606.)

2.6. Funding

There was no funding for this study. Two PST portable devices with duty cycle time cards were provided on loan by Bio Magnetic Therapy System, Inc., (Boca Raton, Florida) and Dr. Richard Markoll, inventor and patent holder. The authors had complete independence regarding study design, data analysis and manuscript preparation.

3. Results

Of the 35 hands enrolled in the study, 33 (94%) completed 9 hourly sessions of treatment. Of the 35 hands, 5 had mild pain scores at baseline (VAS scores < 5), 5 had moderate pain (VAS scores of 5 or 6), and 25 had severe pain (VAS scores 7 or more). For the 35 hands, patient ages ranged from 13 to 85 ($M = 57.37 \pm 15.45$) and duration of symptoms ranged from 0.33 to 25 years ($M = 3.86 \pm 4.70$).

A oneway repeated measures analysis of variance (baseline, end of treatment, end of follow-up) demonstrated a statistically significant reduction in pain scores for the 33 patients who completed treatment, $F(1, 32) = 19.14,\ p < 0.001$, eta$^2 = 0.37$) Results of a *priori* contrasts revealed significant reductions in pain scores from baseline to end of treatment and from baseline to end of follow-up. Pain scores decreased 23% from baseline (7.10 $\pm$ 2.40) to end of treatment (5.50 $\pm$ 3.19), $p < 0.001$. Pain scores decreased 37% from baseline to end of follow-up (4.50 $\pm$ 2.95), $p < 0.001$.

An intent-to-treat analysis (baseline, end of treatment, end of follow-up) based on all 35 hands demonstrated a statistically significant reduction in pain scores, $F(1, 34) = 18.74,\ p < 0.001$, eta$^2 = 0.36$. Pain decreased 35% from baseline to end of follow-up (4.73 $\pm$ 2.96), $p < 0.001$.

Data from PGIC questionnaire and end of study revealed improvement from baseline for 22 hands (67%) and no change from baseline in 10 hands (30%). 1 hand (3%) was reported to be minimally worse.

Secondary outcomes of electrodiagnostic parameters (CMAP/SNAP) did not reveal any significant changes greater than two standard deviations on test-retest. The clinical examination also did not change significantly in the majority of patients.

There were no adverse events or safety issues.

4. Discussion

Electrically-induced osteogenesis, via PEMF, was approved by FDA in 1979 despite the fact that the biological mechanism of action was unclear [32]. The low biological frequencies and energy field strength (range of 0.5–1.5 mT and 10–20 Hz) at which this device operates is in the physiological range. Bassett [2], Wilson [37,38], Ito [17], Macias [22] and others [14,26, 30,32] have demonstrated that PEMF can enhance soft tissue healing, nerve regeneration, as well as return of conduction after complete nerve transection, etc. Specific signal characteristics with different repetitive rates and pulse characteristics of amplitude, duration, degree of symmetry, asymmetry, etc. could modulate pain and thereby induce a specific quantitative response in cells that are magnetically susceptible. It is not yet clear if the clinical benefit is from the electrical or magnetic energy nor clear how long exposure must last (duration)

so as to induce significant and prolonged biological changes [11,12,19,21].

Galvani in 1794, described a "current of injury" representing an electrical charge generated at the site of injury and damage in living organisms [8,9]. It is this presumed damage to the small unmyelinated C-fibers and small myelinated A-delta fibers that leads to ectopic firing, accumulation of voltage-gated sodium channels and production of acroparesthesiae and neuropathic pain [5,16,25,27,34]. Benthall has proposed that cellular repolarization takes place in damaged cells exposed to low energy high frequency PEMF [3]. The specific magnetic flux density at the target area is not known. Thus, irrespective of the precise mechanisms, (direct or indirect), interruption and suppression of the afferent signal traffic of the C-fibers or A-delta firing pattern occurs thereby producing an anti-nociceptive effect.

Loss of modulation is a significant factor in the development of acroparesthesiae [29]. Constant nerve depolarization and accumulation of sodium channels has been identified [34] especially in C-fibers, yet the precise molecular mechanism in terms of energy loss has not been tabulated. Voltage-gated sodium channels have a low threshold for activation and rapid inactivation and therefore aspects of repolarization and hyperpolarization exist.

An anti-nociceptive effect was noted after 9 days of one-hour treatment. The precise mechanism of the short-term benefit is open to speculation. Anecdotal reports from Europe, especially Germany, indicated that a nine-day protocol of one-hour treatment achieved benefit. We skeptically looked at this and attempted to reproduce those results. We did not test specifically the role of placebo which could potentially be responsible for the above benefits.

This pilot data has various strengths. Since PEMF has proven biological benefits, it is logical to attempt to apply this to refractory clinical disorders such as carpal tunnel syndrome. We empirically attempted to duplicate the results of Weintraub [36] using static magnetic field exposure tonically for a one month period of time. In addition, anecdotal reports from Europe suggested that nine exposures could reduce neuropathic pain [23, 28]. The surprising benefit in 67% of refractory cases (PGIC) without significant changes in electrodiagnostic testing, suggests that a short-term neuromodulation of the neuronal firing pattern occurred. This study was not designed to look at placebo responses and obviously these positive responses could represent placebo response. We also relied on self-reported VAS which has been validated in numerous pain studies [15].

The obvious design weakness of this pilot data is absence of placebo controls. We did not anticipate spontaneous improvement to occur in these patients with refractory and postsurgical failure. Pain scores 5 or higher interfere substantially with the quality of life and is defined as substantial pain [29]. Again, we could not rule out a placebo response. A larger cohort may also have been more informative. Distal latency (CMAP/SNAP) did not change over a 30-day period with nine days of magnetic field exposure. Perhaps a longer duration of treatment trial, i.e. 30 days, would have led to changes in large A-fiber conduction. We did not measure C-fiber functions and perhaps future trials could utilize quantitative sensory testing QST. We also do not know if participation in this study led to change patterns of hand use or better adherence to other aspects of therapy. Principal investigator advised all patients to utilize their hands with activities of daily living as usual.

In conclusion, our improved knowledge of time-varying and static magnetic fields and our favorable results with PST, suggests that modulation of neuropathic pain is feasible using non-pharmacological strategies. These are safe and cost-effective. Thus, while PEMF is already accepted as a proven treatment for delayed fracture and wound healing, the above pilot data suggests a positive clinical application. Future randomized, placebo-control trials are needed with a 2–3 month time window of treatment and observation to establish definitively if PEMF will be added to treatment armamentarium.

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