Focused low-intensity medical shockwaves for the treatment of peripheral neuropathic pain: a case report.

Kenneth Craig, Bruce Twaddle

Abstract

Introduction: Neuropathic pain is a condition that emanates from multiple etiologies where the specific cellular and molecular mechanism of this syndrome has not been fully elucidated, and remains a clinical challenge to manage. Neuropathic pain is associated with disability, quality of life impairment, and emotional stress. Current treatments for patients suffering from neuropathic pain involve mainly the use of pharmacogenics targeted at pain modulation.

Case Background: A 43 year old female with a 15 year history of Type II diabetes was referred to our clinic complaining of chronic bilateral heel pain. The patient did not respond to physical therapy, customized foot orthoses, anti-inflammatory drugs and analgesics. Gabapentin was effective in providing relief but was ill tolerated by the patient. Ambulation and weightbearing was severely restricted and extremely painful, which simultaneously cause emotional distress.

Intervention: Three sessions of focused low-intensity medical shockwaves (Li-MST) of 1400 impulses were applied at one week intervals at energy flux density levels ranging from 0.11 – 0.17 mj/mm². Concurrent therapy included the utilization of an over the counter shockstop insole at week 3 to replace existing orthoses. All analgesics and anti-inflammatory medication were ceased prior to treatment commencement and remained discontinued throughout the follow-up period.

Results: Reduction in pain symptoms was significant from pre-treatment VAS scores of 9.5/10, to a score of 1 - 2 at weeks 3, 12, and 24. Pre-treatment DN4 scored as 5/10, was score as 0/10 post intervention. Emotional disposition and outlook were markedly more positive with visible improvements in energy levels and motivation.

Conclusion: Li-MST provides a novel non-invasive, and non-pharmacogenic intervention for the treatment of peripheral neuropathic pain. More research is warranted to further determine the role of Li-MST in this area.

Keywords: neuropathic pain; trauma, shockwave therapy, diabetes.
**Introduction**

Neuropathic pain is dissimilar to nociceptive pain where the later is propagated by the physiological stimulation of nociceptive potential or tissue injury, the former arises as a consequence of neuronal lesion or pathologic syndromes of the somatosensory system.\(^7\), \(^{12,13}\), \(^{27,32,34}\) Nerve damage may occur at any point, of the periphery, or at the cortical neurons in the brain, and can occur synergistically. The specific mechanism of neuropathic pain is yet to be fully elucidated, and presents a clinical challenge as it is often more severe and less responsive to conventional phamacotherapeutics, and can coexist with nociceptive pain.\(^{10,33}\) Commonly seen contributory factors of neuronal lesions and somatosensory syndromes that give rise to neuropathic pain include: metabolic disease, autoimmune disease, vascular disease, trauma, infection, and cancer.\(^7,27\) Notable symptoms associated with the neuropathic episode include: attacks of pain without apparent provocation, hyperalgesia, allodynia, paresthesia, dyesthesias, and sensory deficits, with the latter being a negative sign for neuropathic pain.\(^2,7,27\) Multidimensional degrees of sensory and behavioral aspects of the neuronal assembly, signaling, and activation are expressed by the pain perception, movement patterns, and emotional disposition of patients suffering from neuropathic pain syndrome (e.g., hyperalgesia, allodynia, fear avoidance, sleep disruption, and depression). Hyperalgesia is classified as an exaggerated sensory reaction to a normally painful stimulus due to high threshold (HT) fiber activity (Figure 1), while allodynia is classified as an exaggerated sensory reaction to a non-painful stimulus, due to low threshold (LT) fiber activity (Figure 2).\(^2,7,10,12,27,33,34\)

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**Figure 1.** Adapted from the 2008 IASP task force definition. All forms of pain amplification including the lowering of pain threshold are classified under the umbrella term hyperalgesia. This includes cases where the distinction of low or high sensory threshold fiber involvement is unknown. \(T_0\) refers to normal pain threshold, and \(T_S\) (red region) refers to pain threshold after sensitization.
Figure 2 Adapted from the 2008 IASP task force definition for allodynia, where pain is clearly induced by low threshold fibers. $T_{0/s}$ refers to the normal threshold for touch sensation which is identical to (or near) the stimulation threshold for allodynia.

This case-study reports on the exploratory use of low-intensity medical shockwave therapy (Li-MST) for the treatment of chronic neuropathic pain in a patient who was also a Type II diabetic.

**Case Report**

A 43 year old South African female, made redundant due to the inability to remain in employment resulting from pain related dysfunction was referred to our clinic. Region of complaint was diffused around the foot and ankle region. Patient had a 15 year history of Type II diabetes with a reported plasma glucose concentration level of 7.2 mmol/L, controlled with metformin Hcl. twice daily, and long acting insulin glargine, once daily. The patient was simultaneously being treated for hypertension, hypercholesterolemia, and peptic ulcers. Medical history associated with this complaint included: rest, ice, physiotherapy, customised foot orthoses, cortisone injections, non-steroidal anti-inflammatory drugs (NSAID’s), and gabapentin. Gabapentin was successful in providing pain relief, however was ill tolerated by the patient and was discontinued. The result of prolonged inactivity has simultaneously caused an increase in adiposity, and emotional stress due to the pain experience and the loss of employment.
Assessment

The chief complaint was a 14 month history of bilateral heel pain after landing awkwardly from jumping over earthworks on her driveway. Pain was noticed after several weeks, with the right heel being the more severely affected. The patient reported being unable to spend more than 10 – 15 minutes on her feet, and even sedentary ambulation was unbearable. Pain symptoms were exacerbated when ambulating and in static stance, with worst symptoms experienced after activity. Symptoms were described as sharp pain upon ambulation and weight-bearing, with persistent dull burning, and the occasional electric-shock like sensation shooting up the ankle and leg bilaterally. Persistent dull burning and electric shock like sensations were present, but to a lesser degree prior to the inciting trauma. Region of discomfort was diffused and experienced inferior to the tarsal tunnel, distal aspect of the medial calcaneal tubercle, and medial proximal region of the medial longitudinal arch (PMLA). Neuropathic Pain Diagnostic Questionnaire (DN4) was scored as a 5/10, being diagnostic of neuropathic pain. The patient’s foot type was neutral with mild end range joint motion restrictions occurring bilaterally at the 1st metatarsal phalangeal joint (MTPJ), with increased weight-bearing over the left foot during static stance, with the right heel barely able to make ground contact. Visual examination of both feet was unremarkable except for the slight swelling and redness present at the plantar heel, more pronounced in the right foot. Gait was restricted and slow due to discomfort, with obvious signs of fear to weight-bear and ambulate, and the obvious favoring of the right foot. Basic neurovascular assessments were unremarkable bilaterally (Table 1). Achilles tendon reflex of the right ankle was unascertainable due a hyperalgesic response upon palpation pressure and percussion from the tendon hammer over this region (Table 1). There was no visible redness, nodularity or thickening of the tendo-achilles giving rise to suspicions of secondary hyperalgesia due to aberrant sensitization of this region.7, 19 Palpation pressure over at the region inferior to the tarsal tunnel, heel, medial arch, and the tendo-achilles regions all evoked hyperalgesic responses bilaterally, with the right foot being the more severely affected. There were no visible signs of muscle wasting. After consideration of the possible differentials, the working diagnosis was: trauma induced neuropathic pain syndrome.
Table 1. Pre-treatment basic bilateral neurovascular assessment findings: (+++) indicative of normal response. Patient’s peripheral senses were intact, with the only *abnormality seen as a hyperalgesic response to stimulus from a tendon hammer at the right tendo-achilles.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Present</th>
<th>Absent</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharp / Blunt (Neurotip™)</td>
<td>++</td>
<td></td>
<td>Distinguished and detected. Hyperalgesic reaction at heel region bilaterally.</td>
</tr>
<tr>
<td>10g monofilament</td>
<td>++</td>
<td></td>
<td>Detected over all 10 regions</td>
</tr>
<tr>
<td>128Hz Tuning fork</td>
<td>++</td>
<td></td>
<td>Detected over hallux &amp; ankles</td>
</tr>
<tr>
<td>Thermal Perception</td>
<td>++</td>
<td></td>
<td>Distinguished hot from cold</td>
</tr>
<tr>
<td>Capillary Infill Time</td>
<td>++</td>
<td></td>
<td>&lt;5 seconds: within normal limits</td>
</tr>
<tr>
<td>Pedal Pulses</td>
<td>++</td>
<td></td>
<td>DP &amp; PT pulses detectable</td>
</tr>
<tr>
<td>Deep Tendon Reflexes</td>
<td>L</td>
<td>R*</td>
<td>Patellar reflex present. The Right Achilles reflex was unascertainable due a hyperalgesic response</td>
</tr>
<tr>
<td>Light Touch Perception</td>
<td>++</td>
<td></td>
<td>Detected</td>
</tr>
<tr>
<td>Skin Temperature and Color</td>
<td>++</td>
<td></td>
<td>Homogenously warm bilaterally devoid of aberrant appearances.</td>
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**Intervention and Method**

Assessments conducted prior to each Li-MST session determined, peripheral sensory and vibration perception, as well as the location, quality and presentation of pain symptoms. All NSAID’s and analgesics were ceased prior to treatment commencement and remained discontinued throughout the entire follow-up period, and The Pain Outcomes Profile (POP) questionnaire was utilized to monitor function, emotional status, and social capacity impacted by the pain experience at baseline and throughout the follow-up period. Three sessions of Li-MST was administered bilaterally at one week intervals propagated by a focused electro-hydraulic generator (MediSpec Ltd. Germantown). The first Li-MST session comprised of 1,400 impulses administered on each foot with a focal zone of 35mm x 90mm over the plantar aspect of the heel. Energy density flux level (EDFL) of 0.11mj / mm² was utilized during the first session. This focal region effectively provided a therapeutic dose over the medial tubercle of the calcaneus and the PMLA. Target regions and number of impulses were identical during the second and third treatments respectively. EDFL was increased to 0.14mj/mm² for the second treatment, and to 0.17mj / mm² for the third treatment. The first Li-MST was conducted on November 26, 2010, and third and final treatment was conducted on December 10, 2010. Concurrent intervention included the removal of the fabricated foot orthoses, as it was too rigid, and a ShockStop™ insole (Foot Science International, Christchurch, New Zealand) was fitted.
into footwear at week 3 to provide additional shock attenuation during weight-bearing and ambulation.

**Result**

A significant difference in pain reduction was observed at the 12 and 24 week follow-up periods. The post activity VAS scores dropped from the pre-treatment values of 9.5 and 7 respectively to a 3 at 12 weeks and to a 0.5 at 24 and 32 weeks (Figure 3). Rest pain scores reduced from pre-treatment values of 8.5 and 7 respectively to a 1.5 at 12 weeks and 0.5 at 24 weeks. Dysesthesia experienced as a constant burning and episodes of electric shock sensations was absent bilaterally at three and six months (Figure 3). Patient reported activity increase, and the ability to weight-bear and ambulate for longer periods without pain. Patient's peripheral vibration and sensory perceptions remained intact (Table 2). Both patellar and Achilles tendon stretch reflexes were present at 12 and 24 weeks (Table 2). DN4 questionnaire screened at 12 and 24 weeks scored a zero respectively.

Fear of palpation during physical assessments and movements were markedly reduced at week 3, and was no longer apparent at 12, 24 and 32 weeks. POP questionnaire showed improvement in emotional and physical status throughout the follow-up period (Figure 4 & 5).

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**Table 2.** Post treatment basic neurovascular assessment findings: (++) indicative of normal response to assessment. Patient’s peripheral senses remained intact, and the Achilles tendon reflexes were now ascertainable bilaterally.
Figure 3. Subjective pain perception after activity using VAS comparing pre-treatment and post Li-MST scores. Subjective changes were recorded prior to each Li-MST session. Pain medications were discontinued, and customized orthoses were removed prior to Li-MST commencement and remained as such throughout the follow-up period. 1st Li-MST was commenced after pre-treatment assessment, 2nd and 3rd Li-MST was conducted on weeks 2 and 3. ShockStop™ insoles were introduced in week 3. Note: pain symptoms and function was improved prior to introduction of ShockStop insoles.

Figure 4. Emotional status from pre-treatment to post intervention at 32 weeks, utilizing the POP questionnaire showed improvements in anxiety and depression levels from baseline. Self esteem recorded marked improvement from week 3 onward. Between weeks 24 and 32, the patient was in employment, which may have further enhanced the overall psychological status.
Figure 5. Physical activity levels, energy, endurance and concentration status from pre-treatment to post intervention at 32 weeks utilizing the POP questionnaire recorded marked improvements in physical activity and energy levels from week 3, and continued to improve up to week 32. Similar improvements were recorded in endurance and concentration levels.

Discussion

Medical shockwaves are acoustic pressure waves propagated in this instance by an underwater discharge that rises and travels at supersonic speeds at low amplitudes within the water membrane lasting for approximately 300 nanoseconds.\textsuperscript{20, 21, 23} When shockwaves transfer from the water medium into human tissue a cavitation effect or micro bubble phenomenon occurs, characterized by negative and positive compressive oscillatory cycles, resulting in secondary moments of localized high shear stress in tissue, microstreaming and implosion (Figure 6).\textsuperscript{20, 21, 23} A dose dependant stimulus from its sonic energy is seen to actuate a complex spectrum of favorable cellular and molecular effects promoting recovery of compromised tissue.\textsuperscript{1, 9, 15, 20, 22 - 26, 29, 31, 35 – 41} Medical shockwaves are seen to trigger a localized cellular and bio-molecular response that improves regional blood circulation, regulate endothelial nitric oxide syntheses (eNOS), collagen syntheses, progenitor cell expression, with down regulation and mediation of cytokines and neurotransmitter such as tumor necrosis factor alpha (TNF-\(\alpha\)), glutamate, substance P (SP) and calcitonin gene related peptide (CRGP) among other cellular and bio-molecular effects.\textsuperscript{1, 9, 15, 20, 22 - 26, 29, 31, 35 - 41}
Neuropathic pain is a condition that emanates from multiple etiologies where the specific cellular and molecular mechanism for this syndrome has yet to be fully elucidated, and remains a clinical challenge to manage. Neuropathic pain is often associated with an exaggerated pain response such as hyperalgesia and or, allodynia.\(^7, 27\) Hyperalgesia and allodynia when temporary, may be considered as a protective response, where the hypershift downward in pain threshold levels is activated due to a nocifensive response to protect the vulnerable site from further damage, causing hypersensitivity to very light contact, or normally sedentary activities.\(^7, 27\) The duration of neuropathic pain conditions may be used to determine if the condition is temporary or chronic. When neuropathic pain is continuously experienced for a period of over 12 months, it is considered as a chronic condition. Therefore the heightened and exaggerated pain expressed by the patient in this case-study was considered to be a chronic neuropathic pain syndrome, and not a nocifensive response given the duration and presentations of the complaint.

Secondary hyperalgesia was present at the distal mid-stem portion of the tendo-achilles region when palpation pressure and percussion from the tendon hammer was applied over this region. Secondary hyperalgesia is seen to occur due to the aberrant hyper-excitability of neurons after trauma, where in chronic states induce a series of biochemical events that lead up to an altered central processing via mechanosensitive receptor inputs, producing a

**Figure 6.** The water – tissue penetration cavitation phenomenon triggered by medical shockwaves generated by controlled underwater explosions (electrohydraulic propagation): rapid rise time over a short duration (Cavitation phenomenon adapted from Journal of “Mineralstoffwechsel” 2004; 11(4), 7-18.
heightened sensitivity or pain response from the surrounding uninjured tissue.\textsuperscript{3, 7, 14, 19} Projections of neuropathic pain are seen to occur within the territory of the damaged nerve or pathway, and the spatial organization in the primary somatosensory cortex.\textsuperscript{3, 14} The primary lesion in this case-study was considered to be at the medial tubercle of the calcaneus, and the medial aspect of the PMLA. The innervations of these regions arise from the bifurcation of the tibial nerve, and share a common neuronal pathway.\textsuperscript{4, 3, 14} It is plausible to suggest that the aberrant neural hyper-excitability occurring at the primary lesion triggered the secondary hyperalgesic reaction experienced at the tendo-achilles, as they share a common signaling pathway, and a close spatial proximity in the primary somatosensory cortex.\textsuperscript{3, 14} In this instance, the resolution of the aberrance at the primary lesion triggered a desensitization at the secondary point. However, given the complexities involved in neuropathic pain phenomenon, it is pertinent to note that the desensitization of the primary lesion may not always automatically desensitize the secondary point of hyperalgesia.

Some form of diabetes related neuropathy was present as the patient recalled having symptoms of dysesthesia occurring at the extremities, prior to the inciting trauma. It is not uncommon for diabetic patients to develop some form of peripheral neuropathy that affect small and thin peripheral nerve fibers\textsuperscript{11, 19, 32} due to hyperglycemia induced metabolic aberrances that cause neuronal degeneration, dysfunction and aberrant signal activity.\textsuperscript{17, 28, 32, 38} A necessary caution when dealing with peripheral neuropathic pain in diabetic patients is to be cognizant that in the early stages, heightened pain sensations may later become absent or significantly reduced due to the onset of neural insensitivity due to nerve morphology associated with the metabolic disorder.\textsuperscript{17, 32} It is therefore pertinent to ensure that the absence of pain symptoms in diabetic patients after a lapse of time or treatment is not an onset of neuropathic insensitivity due to disease progression. The resolution of the neuropathic pain symptoms in this case-study however, was considered a positive treatment outcome, and unrelated to the onset of peripheral insensitivity, as the patient’s vibration and sensory perceptions all remained intact throughout the follow-up period.

Emotional states are an important factor to consider in patients with chronic disorders including that of pain. In this case study, the combination of the metabolic disorder,
persistent pain, disability, and job loss experienced by the patient had severe biopsychosocial implications. Such conditions in combination can have negative impact on an individual’s cognitive functioning and introduce: cognitive decline, neurochemical and neuroendocrine imbalances. The POP questionnaire helped us monitor the emotional disposition of the patient throughout the treatment and follow-up periods. It was evident that as the pain symptoms resolved, and activity levels increased, the patient’s emotional and cognitive status improved. The emotional status may have been further enhanced with re-employment.

The overall outcome of this case-study was positive however, some of its shortcomings may be seen in the purely subjective nature of baseline and post intervention outcomes scores. The use of quantitative investigations such as nerve conduction velocity, and sensory perception studies would have helped provide for more quantitative nerve sensory and conduction observations. The use of shock-stop insoles limits the ability to fully determine the actual impact of Li-MST on the overall treatment outcome. Furthermore results from a case study are insufficient grounds to determine the efficacy of any modality as it is restricted to a single instance. Nevertheless the positive treatment outcome, the small number of treatments, the discontinuance of NSAID’s and analgesics, the rapid onset of treatment benefit, and the treatment survival curve, provides the premise for further investigations to be undertaken to determine the role of Li-MST in the treatment of neuropathic pain syndromes. The use of Li-MST has not been previously explored in an attempt to treat neuropathic pain in a Type II diabetic. The rationale for its use in this instance was considered as we have previously utilized Li-ESWT to successfully restored peripheral sensitivity in an insensate diabetic foot. (cite pending publication).

**Conclusion**

The nature of neuropathic pain which is often indocile to conventional treatments warrants the exploration of treatment methods that may provide for a safe and effective solution to treat this often impervious phenomenon. The rationale for the attempt to utilize Li-MST in this instance was based on the mechanism of its action on human tissue that is seen to rehabilitate the cellular and bio-molecular disruptions such as microvascular and neuronal impairments caused by trauma, and the metabolic aberrances induced by hyperglycemia. Li-MST may provide an effective non-invasive, non-pharmacogenic, and economical
intervention for the treatment of certain types of neuropathic pain conditions, and encourages the development of a hypothesis to be tested for its potential use in these instances. Further investigation is necessary to determine the impact of Li-ESWT on neuronal signaling and pain modulation in chronic states.

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Reference


