Scrambler therapy for the treatment of diabetic peripheral neuropathy pain

A case report

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Abstract

Rationale: Neuropathy secondary to diabetes mellitus often does not respond well to conventional therapy. Scrambler therapy may be an alternative treatment for otherwise intractable neuropathy.

Patient concerns: A 45-year-old female complained of bilateral plantar foot pain. She had been treated for diabetes mellitus for 5 years. Oral analgesics did not resolve her pain. Even nerve block therapy did not adequately relieve her pain.

Diagnoses: Diabetic peripheral neuropathy.

Intervention: Scrambler therapy.

Outcome: Pain reduction; the treatment effect was based around the location of the scrambler patch.

Lessons: Scrambler therapy is effective for the treatment of diabetic peripheral neuropathy. Moreover, effective pain management can be achieved for patients who complain of general pain of the sole, including the toe, by attaching scrambler patches around the ankle.

Abbreviations: DM = diabetes mellitus, LSGB = lumbar sympathetic ganglion block, NRS = numerical rating scale pain score, SCS = spinal cord stimulator, ST = scrambler therapy, TENS = transcutaneous electrical nerve stimulation.

Keywords: diabetes mellitus, peripheral neuropathy, scrambler therapy

1. Introduction

The prevalence of diabetes mellitus (DM) continues to increase worldwide, making it one of the most common metabolic diseases globally. The complications that arise add to the challenges associated with treating DM and keeping blood glucose levels adequately in check to prevent morbidity and mortality. One of the most common DM-associated complications is peripheral neuropathy,[1] and the feet are especially prone to this phenomenon. Untreated or inadequately treated diabetic peripheral neuropathy increases the risk of diabetic ulcer formation.[2]

Scrambler therapy (ST) is a Food and Drug Administration-approved treatment for neuropathic pain supported by multiple trials. Although the mechanism of ST is not yet clear, it may work by “scrambling”afferent pain signals and replacing them with synthetic “non-pain” information via the cutaneous nerves after the application of noninvasive electrodes around the surface of painful areas.[3]

ST has been shown to relieve refractory chronic pain in several uncontrolled clinical trials: in 11 cancer patients with abdominal pain,[4] in 226 patients with neuropathic pain, including those with failed back surgery syndrome, brachial plexus neuropathy, trigeminal neuralgia, and others;[5] refractory chemotherapy-induced neuropathic pain; a wide spectrum of cancer-related pain; and postherpetic neuropathy, spinal cord stenosis, and failed back syndrome.[6-7] However, to the best of our knowledge, there is no published literature about the use of ST for treating neuropathic pain related to DM.

We recently successfully used ST to treat a patient with diabetic peripheral neuropathy. This is the first reported case of diabetic peripheral neuropathy treated by ST, and we use this example to identify and discuss the effects of ST on neuropathic pain caused by DM.

2. Case presentation

Written informed consent was obtained by the patient for publication of this case. A 45-year-old female patient with DM was referred from the internal medicine department with a complaint of bilateral plantar foot pain. She described the pain as tingling and resembling the sensation of heat; it was worse early in the morning and late at night. At the time of her referral, she self-rated the pain intensity as 6/10 on the Numerical Rating Scale (NRS) for pain. She had been treated for DM with insulin
injections for 5 years. Her glycated hemoglobin was 8.1%, and glucose level was 140 mg/dL. An electromyogram was conducted and revealed peripheral polyneuropathy. Because the result of her test was abnormal and she had typical neuropathic symptoms, she was diagnosed with stage 2a diabetic peripheral neuropathy.[8]

For her diagnosis of diabetic peripheral neuropathy, she received medication including oral pregabalin 75 mg twice a day, but her symptoms did not improve. We tried increasing the pregabalin dose, but her pain did not improve before side effects, such as dizziness and nausea, precluded further dosage increments. We then performed a bilateral posterior tibial nerve block by injecting 5 cc of 0.187% ropivacaine solution without steroids. Upon follow-up 1 week later, the patient reported that the nerve block was ineffective. We then performed a lumbar sympathetic ganglion block (LSGB) with bilateral injection of 10 cc of 0.375% ropivacaine without steroids. One week after the first LSGB, the patient reported that the LSGB effected a temporary improvement of symptoms. We then applied a second LSGB, which the patient reported to be ineffective 1 week later at the next follow-up visit. We therefore planned for ST, which was performed using a special type of electrode with 5 channels. Because the scrambler electrodes should be positioned in areas where there is no pain, we attached the electrodes to normal sensory areas around the ankle (Fig. 1). After the placement of electrodes, an electrical stimulus was applied, the intensity of which was gradually increased to the maximum value tolerated by the patient. During treatment, the patient experienced her non-pain sensations as itching in the bilateral foot. We set up a 45-minute treatment session once a week for 10 weeks at the same time and provided by the same physician. The patient’s NRS score decreased from 6/10 to 3/10 after the first ST session. Subsequent sessions were followed by marked improvement of pain. After 10 treatment sessions, the patient reported an NRS score of 2/10 for bilateral plantar foot pain. When the patient returned to the hospital one week later, the NRS score was still 2/10. After that, the patient decided to visit the hospital when she felt discomfort, but she has not come to the hospital for 6 months.

3. Discussion

For this patient, ST effectively treated diabetic peripheral neuropathy that was refractory to medication therapy. To the best of our knowledge, no data are available in the literature about the use of ST for treating neuropathic pain secondary to DM.

Pharmacologic and non-pharmacologic interventions are available for the treatment of diabetic peripheral neuropathy. However, there are few high-quality, head-to-head clinical trials comparing these therapeutic approaches, and because the published studies used varying methodologies, it is difficult to draw conclusions about which treatment strategy is the most effective.[9] Based on a recent meta-analysis, both the American Academy of Neurology and the Toronto guidelines recommend pregabalin as the first-line medication for painful diabetic peripheral neuropathy, with gabapentin as the first-line alternative.[10] Second-line therapy includes opioid-like medications (tramadol and tapentadol), venlafaxine, desvenlafaxine, and topical agents (lidocaine patches and capsaicin cream). Isosorbide dinitrate spray and transcutaneous electrical nerve stimulation (TENS) may provide relief in some patients and can be considered at any point during therapy.[9] However, typical first- and second-line medications for neuropathic pain include antidepressants, anticonvulsants, and opiate analgesics, all of which result in significant side effects, unconvincing efficacies, and substantial financial burden.[11]

Neuropathic pain secondary to DM is often refractory to pharmaceutical treatment. Spinal cord stimulator (SCS) trial and implantation can be performed in an outpatient setting. A recent study completed in the Netherlands analyzed the effects of SCS on...
15 patients with painful diabetic peripheral neuropathy. After 12 months of SCS treatment, two-thirds of the patients continued to experience clinically significant pain relief, increased sleep, and improved quality of life.[12] Another published case report describes the successful management of diabetic peripheral neuropathy with SCS therapy.[13] SCS therapy has the potential to revolutionize peripheral neuropathy treatment, but the current clinical evidence is too sparse for mainstream application.[12] For our patient, we opted for ST first because it is less invasive than SCS therapy, and the patient complained of moderate pain (NRS 6).

The mechanism of ST is not clear, but Marineo et al suggest that the electrodes give off “non-pain” stimuli to peripheral receptors; C-fibers and Ad fibers relay the stimuli to the central nervous system, which then modulates and reduces the sensation of pain.[14] During ST, patients can perceive non-pain sensations—such as pressure and itching—in the previously painful area. ST sessions start with first clearly defining the area affected by pain. Next, electrodes are attached to the areas proximal and distal to the painful area. Here, it is recommended that the electrodes are attached along the dermatomes corresponding to the painful area, and they should be positioned in areas where there is no pain.[14] After every treatment, before starting the next one, it is necessary to evaluate the painful areas again, because the painful area can change, and the electrodes must adjusted accordingly. After the placement of electrodes, an electrical stimulus is applied, the intensity of which is gradually increased to the maximum value tolerated by the patient. This stimulus must not cause any additional pain or discomfort.[7]

Another method for treating chronic pain using an electrical stimulus is TENS, which is the application of a mild electrical current to cutaneous nerve fibers using surface electrodes. The stimulation is characterized by current, pulse width, and changes in frequency, though in some paradigms a stochastic or quasi-random stimulation frequency is used. The amplitude of the current is usually adjusted to just above or just below the sensory threshold. The duration of application varies from single, short jolts to continuous stimulation. The duration of treatment can be days to months.[15] Many hypotheses have been put forward to explain the mechanism action of TENS, such as supraspinal processes, modulation of descending inhibitor pathways, peripheral release of calcitonin, increased gate control for pain threshold, reduction of the windup phenomenon, and reduction in impulses from damaged nerves. However, similar to scrambler therapy, the precise treatment mechanism has not been deciphered.[14]

A patient treated with ST has the area of pain identified and then has electrodes placed on normal tissue around the painful site. The electrodes are not placed at the site of actual pain, but, instead, placed at a nearby location of preserved sensation.[16] TENS is similar to ST in that it treats pain by applying an electrical stimulus from electrodes attached to the skin. However, TENS positions the electrodes on the area of pain, while ST positions the electrodes on normal sensory areas surrounding the area of pain.[17] Therefore, in the case of TENS, patches can be attached to the soles of the foot in patients with plantar pain, but with ST, positions where the patches should be attached can be ambiguous. In our case, the patient complained of bilateral plantar pain sparing the toes, but the scrambler patches could not be attached to the distal area of the toes because there was not enough surface area for attachment. Additionally, when patches were attached to the toes, the scrambler machine could not recognize the signal from the electrodes, resulting in a “contact error” machine output. To the best of our knowledge, there is no published guidance regarding where to place the electrodes in such cases. We wrapped the electrodes around the ankles only, and this produced an adequate therapeutic effect.

Unlike other neuropathies, improved glycemic control can reduce diabetic peripheral neuropathy. This is certainly true not only for type 1 DM but may also be true for type 2 DM. Evidence from natural history studies also suggests that diet and exercise interventions may reduce the progression of neuropathy or possibly even result in the regrowth of the epidermal nerve fibers.[18] Therefore, in order to maximize the therapeutic effect of ST in patients with diabetic peripheral neuropathy, it is important to perform glycemic control of the patient and to manage lifestyle modifications such as aerobic exercise.

There are some limitations to this study. As we mentioned above, we wrapped the electrodes only around the ankles. We think that it is a good idea to attach the electrodes to the dorsal side of feet only in patients with a complaint of bilateral plantar foot pain. If additional studies are performed, we will be able to compare the effect of treatment depending on the location of the electrodes.

We found ST to be a clinically useful, noninvasive therapeutic modality, which should be considered an effective alternative measure for the treatment of diabetic peripheral neuropathy. Further studies, including randomized controlled trials, are needed to confirm and generalize our findings.

Author contributions

Conceptualization: Hakck Soo Park.
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