GAVIN PUBLISHERS

OPEN ACCESS

Chronic Pain and Management Journal

Dario T, et al. Chron Pain Manag 5: 136.

DOI: 10.29011/2576-957X.100036

Case Report

Differential Target Multiplexed Program Stimulation in Post Burns Peripheral Neuropathic Pain Syndrome: A Case Report

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Citation: Dario T, Emilio DC, Teresa DDM, Giuseppe G, Pietro M, et al. (2021) Differential Target Multiplexed Program Stimulation in Post Burns Peripheral Neuropathic Pain Syndrome: A Case Report. Chron Pain Manag 5: 136. DOI: 10.29011/2576-957X.100036

Received Date: 17 April, 2021; **Accepted Date:** 28 April, 2021; **Published Date:** 03 May, 2021

Abstract

Peripheral neuropathy is a frequent complication after burns. It is often associated with pain, even very intense, not very responsive to pharmacological therapies and paresthesia, allodynia, hyperalgesia. Very often the quality of life is also compromised due to the onset of psychic symptoms. Differential Target Multiplexed (DTM) Spinal Cord Stimulation is a neurostimulation method that in animal models has shown important superiority over high-frequency and low-frequency stimulations. The preclinical results on an animal model were also reflected in the first human studies. We report the clinical case of a patient with important painful symptoms associated with peripheral neuropathy from extensive burns to the lower limbs who showed good response to treatment with DTM.

Keywords: Peripheral neuropathy; Post burns pain syndrome; Differential target multiplexed neurostimulation

Introduction

Peripheral neuropathy is a frequent long-term complication of burns and determines the appearance of various symptoms that compromise the quality of life of patients who experience it [1]. Patients experience pain, often intense, paresthesia or weakness along a specific nerve distribution or experience more extensive peripheral neuropathy. Symptoms can occur early or often several weeks after the initial event. The causes of peripheral neuropathy after burns are still not well identified but appear to be manifold. Some studies have hypothesized that peripheral neuropathy may be due to vascular occlusion of nerve vessels, chronic inflammation, neurotoxin production resulting in apoptosis and nerve destruction from the burn wound as well as direct nerve destruction due to heat trauma [2].

The association between burn and neuropathy varies from 2% to 52% based on the study methodologies and based on the use of different diagnostic modalities (the clinical criterions or the electroneurographic studies). Some factors have been identified as favoring the development of post burn neuropathy. These include age over 20, second and third degree injuries, and extensive burns (greater than 20% of body surface area) [3].

Patients can develop mononeuropathy, multiple mononeuropathies, and polyneuropathies. In the case of mononeuropathies, patients experience weakness, possibly pain, and sensory loss distributed along the innervation territory of a single nerve.

The incidence of this condition is about 19% of cases of post burns peripheral neuropathy. Very often mononeuropathies are related to surgical escarectomies, drug injections, the use of devices rather than direct burn injury.

Electric burns are often associated with the development of mononeuropathy by direct nerve injury. In multiple mononeuropathy, damage occurs to two or more peripheral nerves in separate areas of the body. It has been identified as the most frequent post-burn peripheral neuropathy (with incidence between 56% and 69% of cases).

Multiple mononeuropathy is common in patients who have suffered burns involving more than 20% of the body surface and with third degree burns greater than 15%. Polyneuropathy is less common among burn patients. It occurs more frequently in patients

of advanced age and with long hospital stays in intensive care [4].

Sometimes polypharmacological therapies are not enough to obtain adequate pain relief of patients suffering from post-burn neuropathies. Neuromodulatory techniques, including Spinal Cord Stimulation (SCS), have been used with unsatisfactory results. Even in our personal previous experience, this type of indication has unsatisfactory results with traditional neurostimulation techniques [5-8].

Probably the large changes in neuroplasticity observed in these patients are not adequately susceptible to an satisfactory therapeutic response [9,10]. Glial cells, which represent the main target of neurophysiological alterations in the chronicization mechanisms of neuropathic pain, are not adequately involved in conventional neuromodulation mechanisms [11,12].

In recent years, new waveforms have been developed that can positively interfere with glia cells as well as with traditional spinothalamic pathways. These include Differential Target Multiplexed (DTM) Spinal Cord Stimulation which was first studied in animal models, demonstrating statistically significant superiority compared to both low-frequency and high-frequency stimulation13. Other sudies on genomes of animals with chronic neuropathy suggest that the DTM waveform has a greater impact on neuro-glial interaction than the other frequencies alone [13-16]. These preclinical results have received first encouraging confirmations also in humans [17].

Case Report

We report the clinical case of a 66-year-old woman with a negative medical history of noteworthy diseases. In January 2017 the patient suffered an extensive burn of both lower limbs following the overturning of a domestic brazier, extensively involving the skin up to the sub-umbilical region. The burns were predominantly second degree but with large third degree areas (Figures 1 and 2). The patient was admitted to a specialized center for the treatment of severe burns and underwent a total of 10 surgical interventions in a period of 3 months including escarectomies and skin grafts (autologous and from cadaveric) as well as multiple antibiotic and support therapies throughout the hospital stay. Starting from about the 50th day from the initial event, the patient began to complain of painful symptoms in the lower limbs, in the anterior region, involving the area from the ankle to the pelvis, characterized by high intensity (VAS 9), diffuse paraesthesia, sensation of burning pain, with intense allodynia such as to make it difficult to use the clothing (score equal to 65 with McGill Pain Questionnaire, MPQ). Night's rest was markedly impaired.

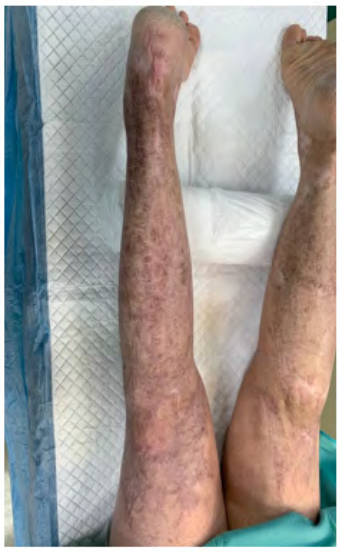

Figure 1: Scarring and skin grafts.

The patient had taken systemic drugs (opiates, NSAIDs, antidepressants, antiepileptics) with negligible response and had developed a reactive depressive syndrome. The electromyographic examination was normal.

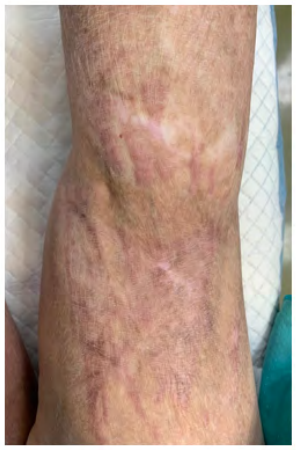

Figure 2: Skin graft detail.

The patient was admitted to the pain therapy center of the Azienda Ospedali dei Colli - Naples (Italy) and subjected to implantation of a spinal neurostimulator (DTM-Intellis™ SCS platform-Medtronic) on March 1, 2021. With percutaneous method, two leads were placed in the spinal canal in the space from the upper limit of soma of T8 and and lower limit of T10 (Figure 3). The leads were fixed

to the lumbar paravertebral fascia and subsequently tunneled in the left supragluteal region and connected to a pulse generator suitably implanted in the subcutis. After 48 hours, the patient was discharged home with an appointment for an outpatient checkup at 7 days.

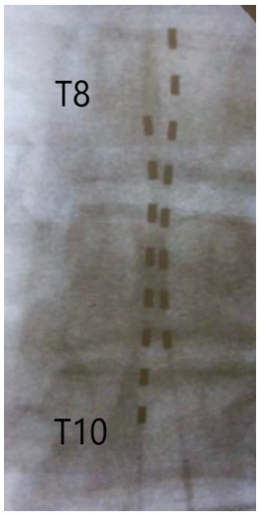

Figure 3: Location of electocateters, vertebrae D8 D9D10.

The stimulation mode chosen was the Differential Target Multiplexed (DTM). Stimulation was applied to the right electrode with 4 programs, one of which at a classical frequency and intensity 3.9 mA, and 3 at high frequency (with intensity from 2 to 2.2 mA).

At the check-up after 7 days, the patient already reported a substantial improvement in painful symptoms (VAS 6) with a marked decrease in paraesthesia and allodynia (MPQ 25). The surgical wound appeared in good condition and the surgical pain was already well controlled after the initial 72 hours of therapy with tramadol and perioperative ketoralac.

At the check-up after a further 30 days, the VAS had settled at 4 and the allodynia had almost completely disappeared (MPQ 15) .The patient reported being able to put on socks and pants. The night's rest had improved markedly.

Conclusion

The incidence of peripheral neuropathy associated with intense pain and paraesthesia in burn patients reported in the literature is high and is mainly described in patients who have experienced significantly higher intensities of acute pain, large body burns and those requiring skin grafts. Pain, predominantly neuropathic, is usually reported 3 months after burns on average and can persist for years. Patients commonly describe the pain as stabbing, burning, often associated with electric shocks and paraesthesia, allodynia, hypoesthesia. The management of burn-related neuropathic pain is extremely difficult and requires a multimodal approach that very often does not allow for good pain relief and a good quality of life. Pain experienced by burn patients is typically treated with opioid, anticonvulsant and / or antidepressant drugs which often compromise patients' quality of life due to side effects as well as not ensuring adequate benefit. The appearance of depressive syndrome is often associated with the presence of chronic pain and the relative impairment of the patient's quality of life.

Spinal cord stimulation (SCS) is a successfully applied therapy indicated for the treatment of chronic pain of the trunk and limbs. Standard SCS, also known as conventional SCS or tonic SCS, typically uses 40 to 60 Hz electrical pulses and has been the primary programming mode since SCS was introduced in the 1960s. Standard SCS is still widely used despite the fact that in recent years SCS modes such as burst, high density and 10 kHz stimulation have been introduced to address more complex and therapy resistant symptoms such as lower back pain. DTM is a programming approach that appears to be promising in preclinical studies; it is based on an approach that uses multiple electrical signals that can be different from each other in aspects such as frequencies, pulsations and amplitudes. In animal models it is the first programming approach that has proven significantly better than low frequency programming (50 Hz) and high frequency programming (1,200 Hz).

Our clinical case has the limit of a short follow up. A longer follow-up and the enrollment of an adequate number of patients will be necessary for a definitive evaluation of DTM in the treatment of burn pain and peripheral neuropathy but the good results shown in our clinical case in which we used DTM for the first time in this pathology, represent a starting point for designing studies on suitable patient samples in order to validate the usefulness of the method.

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