Laser therapy in the management of neuropathic pain: preliminary experience on 43 patients

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ABSTRACT
The aim of this case series is to report on the effect of MiS, a new laser therapy device which uses two synchronized emissions with 905 nm and 808 nm wavelengths, pulsed and continuous, respectively, with high peak power, in the management of neuropathic pain. A total of 43 patients (mean age: 53 years, from 23 to 85 years) presenting neuropathic pain associated to different anatomical areas, such as cervical zone, spine, foot/ankle, hand/wrist, shoulder, elbow, hip and knee were treated with laser therapy by MiS. Pain (VAS score) and functionality (therapist evaluation) were evaluated at the end of treatment. The severity of pain decreased over time and was lower at the end of treatment. MiS laser therapy demonstrated to be safe and effective in patients affected by neuropathic pain and represents a valuable tool for the management of these patients.

INTRODUCTION
Pain is described as a complex, subjective experience, involving the transduction of harmful environmental stimuli together with the cognitive and emotional processing by the brain [1,2]. Neuropathic pain is a form of chronic pain resulting from any kind of damage to the central or peripheral nervous system without nociception [3,5]. Neuropathic pain is a painful condition that may comprise different types of pathologies: such as postherpetic neuralgia, painful diabetic polyneuropathy, postsurgery neuropathic pain, multiple sclerosis, spinal cord injury, stroke and cancer. Patients with neuropathic pain often have spontaneous pain, allodynia, and hyperalgesia. The estimation of the incidence and prevalence of neuropathic pain is difficult because of the lack of simple diagnostic criteria for large epidemiological surveys in the general population [6]. A portion of these patients is specifically affected by peripheral neuropathy and seek medical treatment to alleviate the pain and improve the function associated to conditions that are localised at several body levels: spine, being lumbar-sciatic pain a very common problem, cervical area, elbow, wrist and hand, knee, ankle and foot, hip. For instance, sciatica is a form of radicular pain, and is described as a disease of the peripheral nervous system. It is a very common condition and the main cause of absences from work, with great economic impact on society [7]. The trend in terms of life expectations getting longer suggests that more and more people will be experiencing this type of pain in their life. Chronic neuropathic pain is characterised by complexity of neuropathic symptoms, poor outcomes and difficult treatment decisions.

On the biological side, nerve inflammation plays an important role in the development and progression of neuropathic pain. For instance, recent studies have indicated that hypoxia-inducible factor 1a (HIF-1a) is crucial in inflammation [8], while other previous studies have identified the relationship between proinflammatory cytokines, and neuropathic pain development [9-12]. Therapeutic options are in many cases related to conservative treatment, consisting of modifying the pain-precipitating activity, biomechanical correction with physiotherapy or the use of antidepressants, analgesics and/or steroids [13,14]. Specifically, painkillers are the main drugs to treat pain, although these have shown only 30% effectiveness in patients with neuropathic pain [15-17]. Unfortunately, these drugs have undesirable side effects and, currently, there is a worldwide trend in opioid reduction for acute and chronic pain management [18-20]. Physical methods are an interesting alternative to the pharmacological treatment because of the absence of side effects. Recent studies have reported the use of laser therapy in patients with peripheral somatosensory neuropathy and neuropathic pain [21,22]. Specifically, clinical studies on the effects of laser therapy on injured nerves reported an increase in nerve function [21]. Moreover, laser therapy demonstrated to be effective for promoting axonal growth in injured nerves in animal models [23-26]. Positive effects of MLS® therapy in promoting repair processes of peripheral nerves, acting on the recovery of the lesioned function and the muscle mass and inducing faster myelination of the regenerated nerve fibers, have been reported by Gigo-Benato et al. [27]. In vitro studies were carried out to characterize the effect of MLS® pulse and have shown that MLS® treatment induces an increase of NLRP 10, a protein with antiinflammatory action.
NLPR 10 inhibits the activity of caspase 1 and PYCARD protein complex, which promote the maturation of the inflammatory cytokines interleukin-1β (IL-1β) and interleukin 18 (IL-18). Therefore, ultimately, NLPR 10 inhibits the production of pro-inflammatory interleukins IL-1β and IL-18, reducing inflammation [28]. The decrease in inflammation leads to a normalization of vascular function and thus to a decrease of the edema. Obviously, the decrease in inflammation and edema results in a decrease of pain symptoms, that are frequently present in patients.

MiS is a medical device for laser therapy which combines the synchronized pulse of traditional MLS® therapy with the high peak power typical of high intensity laser therapy. These specific characteristics allow MiS to act on pain and its causes, leading to significant and persistent improvement of pain symptomatology and concomitant recovery of functionality.

This case series collects the case reports of two physiotherapy centers that have treated 43 patients for peripheral neuropathy using MiS, a new laser therapy, reporting changes in pain and in function, and safety associated to the use of the device.

**MATERIALS AND METHODS**

This is a case series collecting patients from routine practice in two Italian physiotherapy centers: Fisiolab (Vicenza, Italy) and Rehabilitation Center (Padova, Italy). Forty-three patients of both sexes affected by several conditions related to peripheral neuropathies have been included in the series.

During the treatment, patients and therapists wore safety glasses to prevent eye damage.

Diagnosis and instrumental evaluation (i.e. X-Ray, Ultrasounds, CT, MRI), when available, were recorded. Additionally, patients were evaluated by the specialist performing the treatment before therapy start.

The patients that were included in this series received MiS (ASA Srl, Italy) treatment focused on the peripheral neuropathy as stand-alone treatment or as a part of their treatment programme.

MiS is a class IV NIR laser with two synchronised sources, one consists in 6 pulsed 905 nm laser diodes, the second is a continuous/frequency-modulate 808 nm laser diode. Maximum average power is 6W± 20%, while maximum peak power is 1kW. MiS has 2 interchangeable handpieces (with diameters of 2 and 5 cm).

The total number of sessions and the time of each session were adjusted based on each patient response to the treatment and ranged from 2 to 13 sessions, with a duration ranging from 6 to 20 minutes (according to body location). The used frequency was 30 Hz for all the body areas, while intensity was adapted to the anatomical site as follows: 80% for shoulder and hip, 70% for spine, 60% for elbow, wrist/hand, knee, ankle/foot and 50% for head and cervical area. Dosage was adjusted based on size of the area to be treated, patient and pathology characteristics and condition stage.

Trigger points, when present, were treated in all patients with the following parameters: Frequency: 10 Hz, time: 23 s, intensity: 25%. In the trigger point phase, the hand piece was perpendicular to the treated points.

Pain evaluation was performed before and after each laser session using a Visual Analogue Scale (VAS) scale. It is a scale comprising 10 grades, with 10 representing ‘unbearable pain’ and 0 representing ‘no pain’. It is a pain scale commonly used in the medical field, and it was shown to be a reliable and valid measure of pain [29,30]. Safety has been specifically assessed and the therapists recorded any side effect and/or rebound effect happened during the treatment. Functional evaluation and global assessment were reported by the specialist for each patient.

**RESULTS**

Demographic and clinical characteristics of all patients at baseline were recorded. Patients demographic characteristics are reported in Table I.

For 34 patients, peripheral neuropathy treatment was the focus of the overall therapy cycle, while 9 patients received other MiS treatments beside the peripheral neuropathy protocol (i.e. specific for edema, muscle pain and contracture) in their therapeutic path.

VAS pre and post treatment, along with change in VAS expressed as a percentage of the initial value are reported in Table II, divided by treated anatomic areas. As expected when dealing with neuropathic pain, average pain at baseline was moderate to severe (mean was >7 for all groups). Overall, VAS pre-treatment mean was 7.8 and VAS post-treatment mean was 1.6, corresponding to a decrease in pain of 79.5%. Pain completely disappeared in patients treated for elbow, hip and shoulder problems. Considering all the groups, improvement was at least 60% respect to baseline, meaning that initial pain score was reduced of above 60% at the end of the treatment cycle.

It has to be noted that some patients were not seeking medical treatment for pain, but for symptoms related to nerve irritation, as for example paraesthesia, dysesthesia, hyporeflexia, etc. In these cases, the treatment with MiS...
gave excellent results and the therapists have reported strong improvements in sensitivity and dysesthesia reduction. In general, looking at VAS value trend, it was possible to appreciate pain decrease during time, rather than intra-session. Some patients reported fluctuation in VAS score between the sessions during the treatment cycle. This could be related to a prompt increase of physically demanding activities by the patients after perceiving benefit from the initial laser therapy sessions. In general, laser treatment provided a positive impact on pain and function on the majority of the patients, only for 2 of them no significant improvement after the laser therapy cycle was reported.

**DISCUSSION**

Neuropathic pain can substantially impair quality of life as it often associates with other problems, such as loss of function, anxiety, depression, disturbed sleep and impaired cognition and physical therapies have been suggested as potential alternative for treatment [6]. The results of this case series show that patients treated with MIS for peripheral neuropathy had an improvement in terms of pain symptoms measured with VAS, even when starting from high VAS values, typical of neuropathic pain. The improvement was gradual and was normally seen after some sessions rather than at the end of each laser treatment, suggesting that MIS is able to induce biological responses whose effects depend on the evolution of the underlying biological processes over time, which could be interesting to address in future basic and clinical studies. MIS inherits the wavelengths (808 nm and 905 nm), the characteristic synchronized modulation of continuous and pulsed emissions, and the scientific evidence of the action mechanisms from MLS® laser therapy. Experimental and clinical research demonstrated that MLS® pulse exerts a positive effect in the treatment of many musculoskeletal diseases [31-34]. This effect is related to anti-inflammatory, anti-edema and tissue healing actions [28,35]. Besides relying on MLS® pulse features, MIS is characterised by a very high peak power in the order of kW. The modulation in short pulses allows to control the peak power avoiding damaging thermal effects.

In the literature, Kobiela Ketz et al [36] suggested that the reduction of hypersensitivity mediated by laser treatment in a model of neuropathic pain induced by spinal nerve injury could be exerted by modulating macrophages and microglia components. Preliminary in vivo investigation related to laser therapy use in neuropathic pain relief highlighted therapeutic effects that might be used for clinical application in neuropathic cases [37]. In the specific field of neuropathic pain, preclinical experiments carried out on animal models demonstrated that the treatment with MIS promotes the recovery of the myelin sheat in nerve fibres that have been damaged in the lesion area, as confirmed by histological and immunohistochemical evaluations [38]. These data support the concept that laser therapy by MIS could be a suitable tool in the management of neuropathic pain. No rebound effect has been observed, thus confirming the safety of the device in this cases series, which included individuals with different characteristics, pathologies and stage of conditions. Patients gave a positive feedback on the treatment feeling, especially when the 5 cm handpiece was used on large areas, as its shape allowed a sort of massage over the patient's skin, making the treatment well accepted and contributing to build compliance to session attendance.

**CONCLUSION**

This case series reports on the use of MIS in the management of 43 cases of neuropathic pain localised in different anatomical areas. Based on the results reported, the new MIS laser therapy demonstrated to be safe and effective in patients affected by neuropathic pain. Therefore, laser therapy by MIS may represent a valuable and well-accepted tool for the management of peripheral neuropathies.

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**Table II - VAS pre and post treatment divided by anatomical distribution of the treated areas**

<table>
<thead>
<tr>
<th>Area</th>
<th>Patient #</th>
<th>VAS Pre (mean)</th>
<th>VAS post (mean)</th>
<th>ΔVAS%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>17</td>
<td>8,8</td>
<td>2,2</td>
<td>75%</td>
</tr>
<tr>
<td>Cervical area</td>
<td>3</td>
<td>8,3</td>
<td>3</td>
<td>63,9%</td>
</tr>
<tr>
<td>Elbow</td>
<td>4</td>
<td>9</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Knee</td>
<td>4</td>
<td>8</td>
<td>1,5</td>
<td>81,3%</td>
</tr>
<tr>
<td>Ankle/foot</td>
<td>3</td>
<td>7</td>
<td>2</td>
<td>71,4%</td>
</tr>
<tr>
<td>Hip (mainly pudendal nerve)</td>
<td>9</td>
<td>7</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Shoulder</td>
<td>1</td>
<td>9</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Wrist/Hand</td>
<td>2</td>
<td>7,5</td>
<td>2,5</td>
<td>66,7%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>43</strong></td>
<td><strong>7,8</strong></td>
<td><strong>1,6</strong></td>
<td><strong>79,5%</strong></td>
</tr>
</tbody>
</table>

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REFERENCES


