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*Guest Editorial**

Phototherapy in Peripheral Nerve Injury for Muscle Preservation and Nerve Regeneration

Posttraumatic nerve repair and prevention of muscle atrophy represent a major challenge for restorative medicine. There is considerable interest in the potential therapeutic value of laser phototherapy for restoration or prevention of denervated muscle atrophy, as well as enhancing regeneration of a severely injured peripheral nerve. Although a pioneering report on the effects of laser phototherapy on the regeneration of traumatically injured peripheral nerves was published in the late 1970s,[1] it is only since the late 1980s that scientific interest was kindled in this therapeutic approach for neural rehabilitation, and there have been a number of published studies that have shown positive effects of phototherapy on peripheral nerve regeneration.[2]

Phototherapy for Muscle Preservation in Peripheral Nerve Injury

When muscles are denervated, in cases of complete peripheral nerve injury, they deteriorate progressively. Surgical repair is the preferred modality of treatment for complete or severe peripheral nerve injury. In most cases, the results can be successful if the surgery is performed in the first 6 months after injury. However, in long-term cases, surgical management is less successful. The reason for early surgical intervention has to do with the fact that between 1 and 3 years post-injury, denervated muscle undergoes necrotic degeneration, which leads to loss of muscle fibers that are replaced with fat and fibrous connective tissue.

In a recent study,[3] using a model of the denervated rat gastrocnemius muscle after complete sciatic nerve injury, the influence of laser phototherapy on the creatine kinase (CK) content (which is an important enzyme for supplying a source of energy to the muscle) and the level of acetylcholine receptors (AChR) (which play a special role in neuromuscular transmission) in denervated muscle were investigated in order to estimate biochemical transformation on cellular and tissue levels. Muscle response to peripheral nerve injury is acceleration of the protein degradation rate followed by muscular atrophy and degeneration. For decrease or temporary prevention of this process, especially in cases of complete peripheral nerve injury, where affected nerve is reconstructed by nerve grafts, tube or primary anastomosis, laser phototherapy can be an effective tool in preserving denervated muscle until nerve sprouting into the muscle occurs. The temporary prevention of denervation-induced biochemical changes may be prompted by increasing synthesis of CK, thus preserving a reservoir of high-energy phosphate available for quick resynthesis of ATP. This is supported Bolognani and Volpi,[4] who showed that laser irradiation increased ATP production in the mitochondria. In the early stage of muscle degeneration, laser treatment may temporarily preserve the denervated muscle close to its pre-injury physiological status and partially maintain the amount of AChR during progressive stages of muscle degeneration in the denervated muscle. This experimental study suggests that denervated muscles can be partially preserved by temporary prevention of denervation-induced biochemical changes. The function of denervated muscles can be restored, not completely but to a very substantial degree, by laser treatment, initiated at the earliest possible stage post-injury, and this could have direct therapeutic applications.

Phototherapy for Repair of Peripheral Nerve Injury

For most patients who suffer from peripheral nerve injuries, spontaneous recovery is often unsatisfactory. The usual results after severe peripheral nerve injury are degeneration of the axons and retrograde degeneration of the corresponding neurons of the spinal cord, followed by a very slow regeneration. Recovery may eventually occur, but it is slow and frequently incomplete. Although enormous progress has been made in surgical techniques over the past three decades, functional recovery after a severe lesion of a peripheral nerve is often incomplete. Studies investigating the effects of low-power laser irradiation on incomplete injured peripheral nerves of rats have found that it provides[5]: (1) immediate protective effects that increase the functional activity of the injured peripheral nerve; (2) maintenance of functional activity of the injured nerve over time; (3) decrease or prevention of scar tissue formation at the site of injury; (4) prevention or decreased degeneration in corresponding motor neurons of the spinal cord; and (5) increase in rate of

***Editor's Note:** We are pleased to present the second in a series of six Guest Editorials written by luminaries in their respective disciplines to be published in Volume 27 of *Photomedicine and Laser Surgery*.

axonal growth and myelinization. Moreover, direct laser irradiation of the spinal cord improves recovery of the corresponding injured peripheral nerve. These results, as those of Anders et al.,[6] suggest that laser phototherapy accelerates and improves the regeneration of the incomplete injured peripheral nerve.

In acute cases where a peripheral nerve is completely transected, the treatment of choice is direct anastomosis. Means of enhancing regeneration are essential, since degeneration is always inevitable in severely damaged peripheral nerves. The therapeutic effect of 780 nm laser phototherapy on peripheral nerve regeneration after complete transection and direct anastomosis of rat sciatic nerve was evaluated in double-blind randomized study.7 The study showed that postoperative laser phototherapy significantly enhanced the regenerative processes of peripheral nerves after surgery.

In cases where the peripheral nerve is injured and complete segmental loss exists (for example ballistic injury), the treatment of choice is nerve reconstruction using an autogenous nerve graft. The use of a regenerating guiding tube for the reconstruction of segmental loss of a peripheral nerve has some advantages over the regular nerve grafting procedure. The double-blind randomized study evaluating the efficacy of 780-nm laser phototherapy on the acceleration of axonal growth and regeneration after experimental peripheral nerve reconstruction by guiding tube shows the intensive growth of myelinated axons through the composite neurotube to the distal part of the nerve compared to the non-irradiated group.[8] In other double-blind randomized study in the rat median nerve model, Gigo-Benato et al.[9] investigated the effects of low-power laser irradiation after the employment of an innovative technique in nerve surgery, namely, end-to-side anastomosis which can be used in case of a particularly severe nerve lesion characterized by complete loss of the proximal nerve stump. In such cases, when grafting is impossible, it has been shown that regeneration along the severed nerve can be obtained by inducing collateral axonal sprouting from a neighboring intact nerve. Median nerves were repaired by end-to-side anastomosis on the ulnar intact nerve and then laser irradiated. Results showed that in laser-treated groups compared to untreated controls, phototherapy induced a significantly faster recovery of the motor function and of target muscle mass, and a significantly faster myelinization of the regenerated nerve axons.

Based on the outcome of animal studies, a clinical double-blind, placebo-controlled randomized study was performed to measure the effectiveness of 780-nm low-power laser irradiation on patients who had been suffering from incomplete peripheral nerve for from 6 months up to several years.[10] This trial suggests that in 780-nm laser phototherapy progressively improves peripheral nerve function in peripheral nerve-injured patients. This outcome encourages continuation of this study in a multicenter trial.

Conclusions

The experimental study on denervated muscles suggests that laser treatment can restore its function to a substantial degree when initiated at the earliest possible post-injury stage. These findings could have direct therapeutic applications on preserving the function of denervated muscle after peripheral nerve injury.

The extensive review articles, which were published in *Muscle and Nerve*[2] and *Neurosurgical Focus*[5] revealed that most of experimental studies showed phototherapy to promote the recovery of the severely injured peripheral nerve. These reviews make it possible to suggest that a time for broader clinical trials has arrived. The significance of the experimental and clinical studies is the provision of new laser technology for treatment of severe nerve injury.

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Dr. Shimon Rochkind
Specialist in Neurosurgery & Microsurgery
Director, Division of Peripheral Nerve Reconstruction
Tel Aviv Sourasky Medical Center
Tel Aviv University
6 Weizmann Street
Tel Aviv, 69423
Israel

E-mail: rochkind@zahav.net.il