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Phototherapy (photobiomodulation) for peripheral nerve and muscle injury

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Severe peripheral nerve and muscle injuries are a highly prevalent condition for both civilians and military personnel caused by traffic accidents, work injuries, acts of violence, as well as combat events.

Peripheral nerve injury is a substantial problem that annually affects more than several millions of people all over the world. For most patients who suffer from severe peripheral nerve injuries spontaneous recovery may eventually occur, but it is slow and frequently incomplete. Effective posttraumatic nerve repair and decrease or prevention of corresponding muscle atrophy remain a great challenge to restorative medicine. A certain clinical interest began to appear in the potential therapeutic value of laser phototherapy (new name – laser photobiomodulation) for regeneration enhancement of injured peripheral nerve as well as for restoration or prevention of denervated muscle atrophy. Although a pioneering report regarding 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 end of past century - early 2000s that scientific interest in this therapeutic approach for neural rehabilitation has appeared, leading to publication of several studies that have shown positive effects of phototherapy on peripheral nerve regeneration.[2]

Phototherapy for repair of peripheral nerve injury

Studies investigating the effects of laser phototherapy on injured peripheral nerves in rats have found that it provides:[3] i) immediate protective effects which increase the functional activity of the injured peripheral nerve; ii) maintenance of functional activity of the injured nerve over time; iii) decrease or prevention of scar tissue formation at the site of injury; iv) prevention or decreased degeneration in corresponding motor neurons of the spinal cord; v) increase in rate of axonal growth and myelinization. Moreover, direct laser irradiation to the spinal cord improves recovery of the corresponding injured peripheral nerve.

In acute cases where a peripheral nerve is completely transected, the treatment of choice is direct nerve anastomosis. The therapeutic effect of 780nm laser phototherapy on peripheral nerve regeneration after complete transection and direct anastomosis of rat sciatic nerve was evaluated in double-blind randomized study.[4] The results show that postoperative laser phototherapy significantly enhances the regenerative processes of peripheral nerves after surgery. In cases of complete segmental loss peripheral nerve injury, the treatment of choice is nerve reconstruction using an autogenous nerve graft or a guiding tube for reconstruction of peripheral nerve segmental loss. Although enormous progress has been made in surgical techniques over the past three decades, functional recovery after severe lesion of a peripheral nerve is often incomplete. 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 towards the distal part of the nerve compared to a non-irradiated group.[5] In other double-blind randomized study on rats,[6] median nerves were repaired using end-to-side anastomosis to the intact ulnar nerve and then were treated by laser. Results showed that in laser-treated groups compared to untreated control

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group, 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 pilot clinical double-blind, placebo-controlled randomized study was conducted to evaluate the effectiveness of 780nm low power laser irradiation on patients who had been suffering from incomplete peripheral nerve for 6 months up to several years.[7] The results showed that 780nm laser irradiation can progressively improve peripheral nerve function in patients with incomplete long-term peripheral nerve injury, which leads to significant functional motor recovery (Figure 1).

Phototherapy for repair of muscle

Muscle atrophy as a response to peripheral nerve injury is an acceleration of protein degradation rate followed by progressive muscle atrophy and degeneration. In cases of complete peripheral nerve injury, denervated muscle deteriorates progressively, which leads to loss of muscle fibers and their replacement with fat and fibrous connective tissue. During muscle denervation, the level of creatine kinase (CK) an enzyme that supplies a source of energy to the muscle and muscle weight decrease, and induces significant changes in level of acetylcholine receptors (AChR), which play a special role in neuromuscular transmission. Rochkind *et al.*,[8] using a model of the denervated rat gastrocnemius muscle after complete sciatic nerve injury, revealed a significant protective therapeutic effect of laser photobiomodulation on the denervated muscle during the first 21 days for AChR, and during the first 30 days for CK activity. During the early stages of muscle atrophy, as well as progressive stages of muscle degeneration, laser photobiomodulation treatment may preserve the denervated muscle by maintaining CK activity and the amount of AChR close to their physiological preinjury values.[8,9] It was shown that photobiomodulation leads to significant decrease of muscle atrophy,[10] acceleration of muscle repair process after peripheral nerve crush injury in rats, and has an effect on muscle morphology and gene expression of calcineurin, myogein and acetylcholine receptors.[11]
Crush muscle injuries carry significant morbidity and poor clinical outcome especially when treatment is delayed.
The efficacy of the laser photobiomodulation treatment after crushed muscle injury to the gastrocnemius muscle in a rat model was evaluated.[12] The study results showed a significant recovery of the gastrocnemius muscle during the first 3 days, the most critical clinical period, after the induction of the muscle crushed injury. The findings suggest that the therapeutic approach may help restore the muscle after crush injury. Literature reviewes showed that photobiomodulation promotes recovery of the injured muscle,[13] increases muscle mass, significantly decreases oxidative damage markers, augments collagen synthesis,[14,15] increases mitochondrial activity in muscular fibers, activates fibroblasts and macrophages stimulating angiogenesis,[16] and improves gene expression of biochemical inflammatory markers.

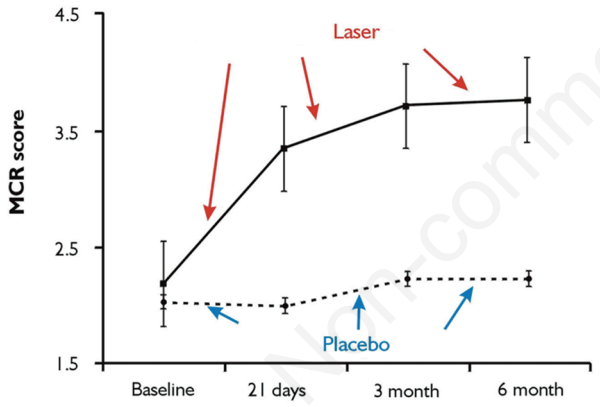

Figure 1. Graph of the motor function follow-up in injured patients who underwent either 780-nm laser phototherapy or placebo treatment. Mean motor function (±SD) of all affected muscles was examined in injured patients using the Medical Research Council (MRC) Grading System. The analysis of the results showed that at baseline the 780-nm laser-treated and placebo groups were in clinically similar conditions (p=0.887). The analysis of motor function during the 6-month follow-up period compared with baseline showed statistically significant improvement (p=0.0001) in the laser-treated group compared with the placebo group (Rochkind *et al.*, Photomedicine and Laser Surgery 25: 436–442, 2007). This clinical trial suggests that in peripheral nerve injured patients 780-nm laser phototherapy progressively improves motor function, thus accelerates patients' return to every day functional activity and working ability.

Conclusions

The experimental and clinical studies results showed an ability of laser phototherapy to promote recovery of injured peripheral nerve, preserve and improve muscle recovery after peripheral nerve injury or muscle crush injury. Laser photobiomodulation was also found to be a safe, non-invasive, low cost, and easy approach to implement and could lead to direct therapeutic application for treatment.
Based on the scientific merit, it possible to suggest that the time for broader clinical trials has come. The obtained results have fundamental significance for the provision of new laser technology for treatment of peripheral nerve and muscle injury.

Conflict of interest: the author declares no potential conflict of interest and confirms accuracy.

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