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The Brain-Derived Neurotrophic Factor, Nerve Growth Factor, Neurotrophin-3, and Induced Nitric Oxide Synthase Expressions After Low-Level Laser Therapy in an Axonotmesis Experimental Model

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Abstract

Background data: A robust body of evidence has shown that low-level laser therapy (LLLT) improves peripheral nerve regeneration. However, the biochemical background triggered in this process is not yet fully understood. ***Objective:*** The purpose of this study was to evaluate the mRNA expression of neurotrophic factors (brain-derived neurotrophic factor [BDNF], nerve growth factor [NGF], and neurotrophin-3, [NT-3]) and also an inflammatory marker (induced nitric oxide synthase [iNOS]) in an axonotmesis experimental model after low-level laser therapy. ***Methods:*** Thirty-six adult male Wistar rats (250–350 g) were subjected to right sciatic nerve crush injury, and 24 h later, the animals in the three different experimental groups ($n = 18$) were irradiated on a daily basis with helium-neon laser (collimated HeNe laser, continuous emission, wavelength: 632.8 nm, power density: 0.5 mW/cm^2, irradiation time: 20 sec, energy density: 10 J/cm^2) during 7, 14, and 21 consecutive days, respectively. The control group ($n = 18$) underwent the same procedures, but with the equipment turned off. At the end of the experiments, animals were killed with an overdose of anesthesia to remove samples from the sciatic nerve lesion epicenter to determine the mRNA expression of BDNF, NGF, NT-3 and iNOS enzyme. ***Results:*** Comparisons between groups showed that HeNe laser increased the mRNA expression of both BDNF and NGF factors after 14 days of LLLT, with peak expression at the 21st day. Increase in NT-3 mRNA expression was not observed. In addition, HeNe laser produced iNOS expression reduction, which played an important role in the inflammatory process. ***Conclusions:*** The reported data could have a relevant practical value because LLLT is a noninvasive procedure, and have revealed significant increase in neurotrophic factor expressions and inflammatory process reduction, opening the possibility of using LLLT as an important aid to nerve regeneration process.

Introduction

Peripheral nerves are frequent targets of traumatic injuries ranging from minor injuries to nerve transection, lacerations, or avulsions.[1] Peripheral nerve injuries can be classified as neuropraxia: a lesion with mild motor and sensory loss without structural change; axonotmesis: in which there is loss of continuity and subsequent axonal Wallerian degeneration of the distal segment without losing Schwann cells, and the recovery will depend upon the nerve disorganization degree and also the organ distance target; and neurotmesis: nerve section with complete axon disorganization caused by tissue fibrosis, proximal and distal degeneration, and consequent axonal growth disruption.[2]

After axonotmesis, the inflammatory process is triggered; the proximal stump axons degenerate and distal fibers from the lesion undergo Wallerian degeneration between 48 and 96 h after nerve transection. Particularly, but not exclusively, after axonotmesis, pro-inflammatory cytokine mobilization and increased activity of induced nitric oxide synthase (iNOS), which results in inflammatory cell recruitments to the affected site, occurs, leading to increased production and releasing of several pro-inflammatory mediators, which ultimately reduces significantly the nerve recovery process. In addition, there are also myelin debris degradation and other structural proteins that finally inhibit axonal growth.[3,4]

Simultaneously, substances known as neurotrophic factors (e.g., nerve growth factor [NGF], brain-derived neurotrophic

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