Transcranial Infrared Laser Therapy Improves Clinical Rating Scores After Embolic Strokes in Rabbits

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Background and Purpose—Because photon energy delivered using a low-energy infrared laser may be useful to treat stroke, we determined whether transcranial laser therapy would improve behavioral deficits in a rabbit small clot embolic stroke model (RSCEM).

Methods—In this study, the behavioral and physiological effects of laser treatment were measured. The RSCEM was used to assess whether low-energy laser treatment (7.5 or 25 mW/cm^2) altered clinical rating scores (behavior) when given to rabbits beginning 1 to 24 hours postembolization. Behavioral analysis was conducted from 24 hours to 21 days after embolization, allowing for the determination of the effective stroke dose (P_{50}) or clot amount (mg) that produces neurological deficits in 50% of the rabbits. Using the RSCEM, a treatment is considered beneficial if it significantly increases the P_{50} compared with the control group.

Results—In the present study, the P_{50} value for controls were 0.97±0.19 mg to 1.10±0.17 mg; this was increased by 100% to 195% (P_{50}=2.02±0.46 to 2.98±0.65 mg) if laser treatment was initiated up to 6 hours, but not 24 hours, postembolization (P_{50}=1.23±0.15 mg). Laser treatment also produced a durable effect that was measurable 21 days after embolization. Laser treatment (25 mW/cm^2) did not affect the physiological variables that were measured.

Conclusions—This study shows that laser treatment improved behavioral performance if initiated within 6 hours of an embolic stroke and the effect of laser treatment is durable. Therefore, transcranial laser treatment may be useful to treat human stroke patients and should be further developed. **(*Stroke*. 2004;35:1985-1988.)**

Key Words: laser ■ neuroprotection ■ embolism ■ stroke, acute ■ stroke, ischemic ■ clinical trials

Laser therapy has been shown to be effective in a variety of settings, including treating lymphoedema and muscular trauma, and it is now approved by the Food and Drug Administration for the treatment of carpal tunnel syndrome.[1,2] Recent studies have shown that laser-generated infrared radiation (ie, photon or light energy) is able to penetrate various tissues, including the brain, and modify function. Laser-generated infrared radiation (ie, photon energy) can penetrate various tissues, including the brain,[3–6] and can induce angiogenesis,[3] modify growth factor (transforming growth factor-β) signaling pathways,[4] and enhance protein synthesis.[7] Of importance to the current study are recent reports showing that laser treatment could reduce lesion size in the rat heart after myocardial infarction.[5,6,8] Because there are similarities between cardiac and cerebral ischemia, we investigated whether laser treatment reduces stroke-induced behavioral deficits. For these studies, we used the rabbit small clot embolic stroke model (RSCEM),[9–12] which is produced by injection of blood clots into the cerebral vasculature, resulting in ischemia-induced behavioral deficits that can be measured quantitatively with a dichotomous rating scale.[9–12]

Materials and Methods

Male New Zealand White rabbits (Irish Farms, Norco, Calif) were anesthetized and a catheter was inserted into the common carotid artery, through which microclots were injected, as described in detail previously.[9–12] The procedures used in this study were approved by the Department of Veterans Affairs and the Veterans Administration San Diego Healthcare System (VASDHS).

Embolic Strokes

For the RSCEM, microclots were prepared from blood drawn from a donor rabbit and allowed to clot at 37°C, as described in detail previously.[9–12] The microclots were resuspended in phosphate-buffered saline, then washed and allowed to settle, followed by aspiration of the supernatant and spiking of the particles with tracer quantities of 15-μm radiolabeled microspheres. The specific activity of the particles was determined by removing an aliquot, after which appropriate volumes of phosphate-buffered saline solution were added so that a predetermined weight of clot could be rapidly injected through the catheter. After the injection, the syringe and catheter were flushed with normal saline.

Quantal Dose–Response Analysis

To evaluate the quantitative relationship between clot dose and behavioral deficits, logistic (S-shaped) curves are fitted by computer to the quantal dose–response data as described in detail previous-

Received February 4, 2004; final revision received April 14, 2004; accepted April 22, 2004.

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***Stroke* is available at http://www.strokeaha.org** **DOI: 10.1161/01.STR.0000131808.69640.b7**