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**Transcranial near-infrared light therapy improves motor function following embolic strokes in rabbits: an extended therapeutic window study using continuous and pulse frequency delivery modes.**

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Photon or near-infrared light therapy (NILT) may be an effective neuroprotective method to reduce behavioral dysfunction following an acute ischemic stroke. We evaluated the effects of continuous wave (CW) or pulse wave (P) NILT administered transcranially either 6 or 12 h following embolization, on behavioral outcome. For the studies, we used the rabbit small clot embolic stroke model (RSCEM) using three different treatment regimens: 1) CW power density of 7.5 mW/cm<sup>2</sup>; 2) P1 using a frequency of 300  $\mu$ s pulse at 1 kHz or 3) P2 using a frequency of 2 ms pulse at 100 Hz.

Behavioral analysis was conducted 48 h 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. Quantal dose-response analysis showed that the control group P(50) value was 1.01 $\pm$ 0.25 mg (n=31). NILT initiated 6 h following embolization resulted in the following P(50) values: (CW) 2.06 $\pm$ 0.59 mg (n=29, P=0.099); (P1) 1.89 $\pm$ 0.29 mg (n=25, P=0.0248) and (P2) 1.92 $\pm$ 0.15 mg (n=33, P=0.0024). NILT started 12 h following embolization resulted in the following P(50) values: (CW) 2.89 $\pm$ 1.76 mg (n=29, P=0.279); (P1) 2.40 $\pm$ 0.99 mg (n=24, P=0.134). At the 6-h post-embolization treatment time, there was a statistically significant increase in P(50) values compared with control for both pulse P1 and P2 modes, but not the CW mode. At the 12-h post-embolization treatment time, neither the CW nor the P1 regimens resulted in statistically significant effect, although there was a trend for an improvement.

The results show that P mode NILT can result in significant clinical improvement when administered 6 h following embolic strokes in rabbits and should be considered for clinical development.

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