Laser treatment clinical trial misses primary endpoint

February 23 2009

Using a laser to treat cells in the brain did not significantly reduce stroke disability, according to results of the first major clinical trial of laser therapy presented at the American Stroke Association's International Stroke Conference 2009.

The full study will be simultaneously published in Stroke: Journal of the American Heart Association and is presented in the "Sample of the Best Science of the ISC" session during the conference.

Researchers said the laser's impact on stroke disability did not reach statistical significance for the overall group of stroke patients. However, it appeared that laser therapy did provide some improvement in those experiencing moderate to moderately severe strokes.

"Although our primary endpoint of improvement for overall stroke disability missed reaching statistical significance, we saw no ill effects from the laser treatment. And, in fact, there was a strong signal that this treatment actually offered some improvement for patients with moderate to moderately severe strokes, even in the presence of prior risk factors such as previous stroke, heart disease and diabetes," said Justin Zivin, M.D. Ph.D., principal investigator of the study and a professor of neurosciences at the University of California San Diego.

The NeuroThera Effectivess and Safety Trial (NEST-2) was a prospective, double-blind, randomized and sham (inactive procedure) controlled study of the safety and effectiveness of a device called the

NeuroThera® Laser System. NEST-2, which included 660 patients and 53 researchers in four countries, is the largest human trial and the first Phase III (large randomized trial of effectiveness) of transcranial laser therapy to date. Researchers found:

• Overall, 36.3 percent of patients who received laser therapy improved to mild or none on a disability rating scale within 90 days compared to 30.9 percent of patients receiving (non-laser) inactive therapy. This difference of 5.4 percent did not reach statistical significance.

• However, of the patients considered to have moderate to moderately severe stroke impairment, 51.6 percent in the laser-treated group improved to mild or no disability range in 90 days compared to 41.9 percent of the control group. That represents a 9.7 percent absolute improvement in treated patients, which is statistically significant, Zivin said.

"For a trial that 'failed,' this one was reasonably encouraging," Zivin said, a staff neurologist at the San Diego Veterans Administration (VA) Medical Center. "Laser therapy is unlike most treatments that have been tried for acute stroke."

The only FDA-approved treatment for a stroke caused by a blood clot (an ischemic stroke) is an intravenous clot-busting drug called tissue plasminogen activator or tPA and it must be given within three hours of symptom onset. Other treatments include delivering clot-busters directly to the arteries and mechanical clot removal.

In this trial, the laser was used within 24 hours of stroke onset, with the average time to treatment being 14.6 hours. The device uses low-energy infrared radiation to painlessly penetrate several centimeters into the skull.

"We're not mechanically injuring the brain at all," Zivin said. "We shave off the patient's hair and aim the laser at 20 points around the head so that the beam can cause a reaction in or around the damaged tissue."

While the mechanisms of laser therapy are unknown, earlier animal studies indicated that spacing the laser therapy at 20 points around the skull was more effective that targeting one point. That may be because the 20-point approach allows infrared beams to cover the area of brain damage from many different angles, he said.

In the trial, researchers used two well-known scales to measure laser effectiveness on stroke disability and neurological improvement 90 days after stroke. The modified Rankin Scale (mRS) is a seven-point (0 to 6) scale of stroke disability and dependence in which "0" represents no disability; "1" refers to deficits so slight only a neurologist would notice them; "2" is slight disability such as the inability to conduct previous activities, but able to care for own affairs without assistance; and "6" is death. The mRS was used as the trial endpoint, which is the number of patients in each group who had improved to the 0-2 range on the mRS 90 days after the procedure or sham procedure, he said.

The 42-point National Institutes of Health Stroke Scale (NIHSS) is a simplified neurologic exam that measures stroke-related neurologic deficits such as extremity strength, sensory function, coordination and language ability. A higher number means more impairment.

Earlier studies have shown that stroke patients who score 7 or below on the NIHSS tend to recover to the range of 0 to 2 on the Rankin Scale on their own without any treatment. Here, researchers focused on patients who scored 7 to 22 on the NIHSS when they arrived at the hospital.

Although this study excluded stroke patients who received tPA, Zivin said he hopes to explore combination treatment with laser therapy and

tPA in the future, he said.

Source: American Heart Association