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Researchers fine-tune clot-busting treatment for bleeding in brain

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A multicenter study led by Johns Hopkins doctors has fine-tuned the dosage and timing for administering clot-busting tissue plasminogen activator (tPA) to patients with strokes caused by bleeding within the brain. The treatment, as reported this week at the European Stroke Conference in Nice, France, has been shown to dramatically decrease death and disability in patients with this typically lethal subset of stroke.

"We've gone from what's usually an 80 percent death rate in patients with this condition to an 80 percent survival rate," says study leader Daniel Hanley, M.D., professor of neurology at the Johns Hopkins University School of Medicine.

This condition, known as intracerebral hemorrhage (ICH), causes blood to clot inside the brain's interior cavities, building up pressure within the brain. The higher pressure, along with inflammation caused by chemicals in the trapped blood, can irreversibly damage the brain, usually leading to death or extreme disability. Until recently, Hanley notes, no treatment existed for this subset of stroke.

The new research builds on a series of previous studies designed to test the safety and efficacy of clot-busting drugs in patients with ICH. This treatment, developed by Hanley and his colleagues, clears the trapped blood out of the brain by bathing-and dissolving-the clot directly in tPA. This drug normally isn't recommended for conditions that involve bleeding, such as ICH, because it can increase the risk of further hemorrhage. However, since high-dose (80 to 100 mg) tPA is effective

at breaking up clots in other conditions, such as heart attacks and other types of strokes, Hanley and his colleagues wondered whether very low doses of the drug might be a safe and effective way to treat ICH.

The previous studies showed that giving tPA to ICH patients hadn't significantly increased bleeding or death, so in the latest study, Hanley and his colleagues sought to determine the safest and most effective treatment regimen using this drug.

At 20 hospitals located across the United States, Canada, Great Britain, and Germany, the researchers recruited 52 patients recently diagnosed with ICH. All of the patients had received the usual treatment for this condition, placing a catheter inside the brain to release the trapped blood. Using the same catheter as a conduit for flooding tPA directly onto the clot, the researchers put each patient on one of three treatment regimens: 0.3 milligrams of the drug every 12 hours, 1 milligram of the drug every 12 hours, or 1 milligram of the drug every 8 hours.

Tracking patients' progress with daily CT scans, the researchers found that the clots dissolved within three to four days on average, with patients on 1 milligram of tPA every 8 hours dissolving their clots about a day faster than those on the other treatment regimens. This timing is about two to three times faster than that of previous patients who didn't receive tPA. Hanley notes that additional bleeding among all the patients was minimal; those treated with tPA weren't any more likely to have additional hemorrhaging than those past patients who didn't receive the drug.

One month after treatment, more than 80 percent of the patients were alive, and 10 percent of these had recovered enough to return to their jobs, the researchers report.

"We think that this treatment is the most promising story in brain

hemorrhage in many years," says Hanley. "We've taken a condition that used to have an extremely high rate of death and disability and turned it around."

Source: Johns Hopkins Medical Institutions