New clue to brain bleeding after stroke treatment

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The only medication currently approved for stroke treatment – tissue plasminogen activator (tPA), which dissolves blood clots – is associated with an increased risk of bleeding in the brain, particularly among patients with hyperglycemia (high blood sugar). A study led by Raymond A. Swanson, MD, chief of the neurology and rehabilitation service at the San Francisco VA Medical Center, provides a possible reason: high blood sugar fuels the formation of superoxide, a toxic form of oxygen, which in turn damages tissues, weakens blood vessels and promotes excess bleeding.

The study, which used an animal model of stroke, was published on October 14 in the online Early View section of *Annals of Neurology.*

“A stroke is usually caused by a blood clot lodging in a brain artery and cutting off blood flow,” said Swanson, who is also professor and vice chair of neurology at the University of California, San Francisco (UCSF). “If you can administer tPA in time and dissolve the clot, then blood flow is restored.” However, he said, “there’s a risk that when the clot is dissolved and blood suddenly flows back into the affected area of the brain, there will be bleeding. And that is a huge problem, because the bleeding can cause more damage, or even death.”

The risk of bleeding after tPA treatment increases in patients with hyperglycemia, Swanson said, “but whether this increase is actually caused by the hyperglycemia has been difficult to ascertain.”

To investigate the question, Swanson and his research team mimicked strokes in two groups of rats by temporarily stopping blood flow to a section of their brains. They then gave the rats tPA as blood flow was restored. One group of rats was hyperglycemic. That group had bleeding in the brain at three to five times the rate of the non-hyperglycemic rats, at rates directly proportional to blood sugar level.

“I think this supports the idea that hyperglycemia contributes to bleeding in the brains of stroke patients who have been given tPA,” Swanson said.

Swanson suspected that the bleeding was caused by superoxide, the production of which is fueled by blood sugar. To test that hypothesis, the scientists blocked superoxide production in a subset of the hyperglycemic rats. Those rats did not show excess bleeding or brain damage.

Based on their findings, the authors suggest that clinical guidelines for tPA be reconsidered. “We should ask whether stroke patients who are hyperglycemic should be excluded from tPA treatment,” said Swanson.

The authors also suggest that treatment targeting the production of superoxide could potentially negate the harmful effects of hyperglycemia in stroke patients.

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