Study: Preventive use of one form of natural vitamin E may reduce stroke damage

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Ten weeks of preventive supplementation with a natural form of vitamin E called tocotrienol in dogs that later had strokes reduced overall brain tissue damage, prevented loss of neural connections and helped sustain blood flow in the animals' brains, a new study shows.

Researchers say the findings suggest that preventive, or prophylactic, use of this natural form of vitamin E could be particularly helpful to people considered at highest risk for a major stroke: those who have previously suffered a ministroke, or a temporary stoppage of blood flow in the brain.

Of the almost 800,000 strokes in the United States each year, an estimated 25 percent are repeat events, according to the American Heart Association.

Vitamin E occurs naturally in eight different forms, and this work led by Ohio State University scientists is focused on the tocotrienol form, also known as TCT. The commonly known form of vitamin E belongs to a variety called tocopherols. TCT is not abundant in the American diet but is available as a nutritional supplement. It is a common component of a typical Southeast Asian diet.

In the study, 24 hours after a stroke, lesions indicating brain tissue damage were about 80 percent smaller in dogs that received supplementation than were the lesions in dogs that received no intervention. Imaging tests showed that the treated animals' brains had

better blood flow at the stroke site as compared to untreated dogs' brains, a difference attributed to tiny collateral blood vessels' ability to improve circulation in the brain when blood flow stopped in more substantial vessels.

"For the first time, in this pre-clinical large-animal model, we were able to see something that we were never able to see in the mouse or the rat: that if you had a stroke and you had prophylactically taken tocotrienol, the area of the brain affected by the stroke received blood flow from the collaterals," said Chandan Sen, professor and vice chair for research in Ohio State's Department of Surgery and senior author of the study. "These collaterals, which are an emergency response system, wake up when the blood circulation in the brain is challenged."

Sen and colleagues have spent the past 10 years documenting in cell cultures and rodents how this form of vitamin E protects brain cells from dying after the insult of a stroke. They say that the results of this large-animal study offer the last piece of evidence needed to validate testing the nutritional supplement's protection against stroke in humans. A phase II trial of its effectiveness in humans is in the planning stages.

The research is published online and is scheduled for future print publication in the *Journal of Cerebral Blood Flow & Metabolism.*

In the study, 20 dogs were randomly assigned to one of two groups: those receiving a placebo pill, and those receiving 200 milligrams of mixed tocotrienols. Though alpha-tocotrienol is the form of the vitamin known for its protection of brain cells, the supplement for this study contained a mix of tocotrienols to make it more accessible and affordable.

The dogs ate regular food and received two supplement pills per day for 10 weeks. At this point, scientists induced stroke by blocking the middle cerebral artery in the animals' brains for one hour while the animals were

under anesthesia.

The researchers used a variety of imaging techniques to examine the effects of the stroke on the two groups. Magnetic resonance imaging (MRI) showed the differences in the volume of tissue damaged by the stroke. One hour after the stroke, the lesions in the treated dogs' brains were about 60 percent smaller than the size of the lesions in the untreated brains. Twenty-four hours after the stroke, the lesions were 80 percent smaller in treated animals compared to untreated animals.

In collaboration with the Ohio Supercomputer Center, the scientists mapped the brain's communication network, represented by white matter fiber pathways. The sophisticated video images of the stroke-affected brain showed major gaps in this fiber network in the brains of animals that received no supplementation. The fiber connections were protected in the brains of dogs that received TCT.

Images of the blood vessels in the animals' brains showed different responses in the brain blood circulation based on whether or not they had received preventive treatment. The researchers used a scoring system to determine how much of the collateral circulatory system was activated in response to the blocked blood flow associated with the stroke. The score in treated dogs was almost twice as high as that in untreated animals.

"This function in the brain is similar in humans and large mammals, which underscores the significance of these findings," said Cameron Rink, first author of the study and an assistant professor of vascular surgery at Ohio State.

Additional examination of the affected brain tissue showed that the TCT supplementation appeared to support arteriogenesis, a process by which collateral arteries remodel themselves into larger vessels so they can bypass the site of blockage. Genes associated with this process were

more active in the affected brain tissue from treated animals than were those from untreated dogs.

Preventive use of TCT, a natural vitamin, is safe and should be embraced as a preventive therapy along with aspirin, a commonly prescribed medicine to prevent a stroke, said Sen, who is also a deputy director of Ohio State's Davis Heart and Lung Research Institute.

"Though most of us have no idea if we are at risk for stroke, a sizable population has had a ministroke and is therefore at high risk for a large stroke. If I had a ministroke, why would I not take something that would minimize my damage during a stroke?" Sen said. "And this is not a drug; it is a nutritional countermeasure. So there are no worries about side effects. Therefore I see it as having prophylactic value."

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