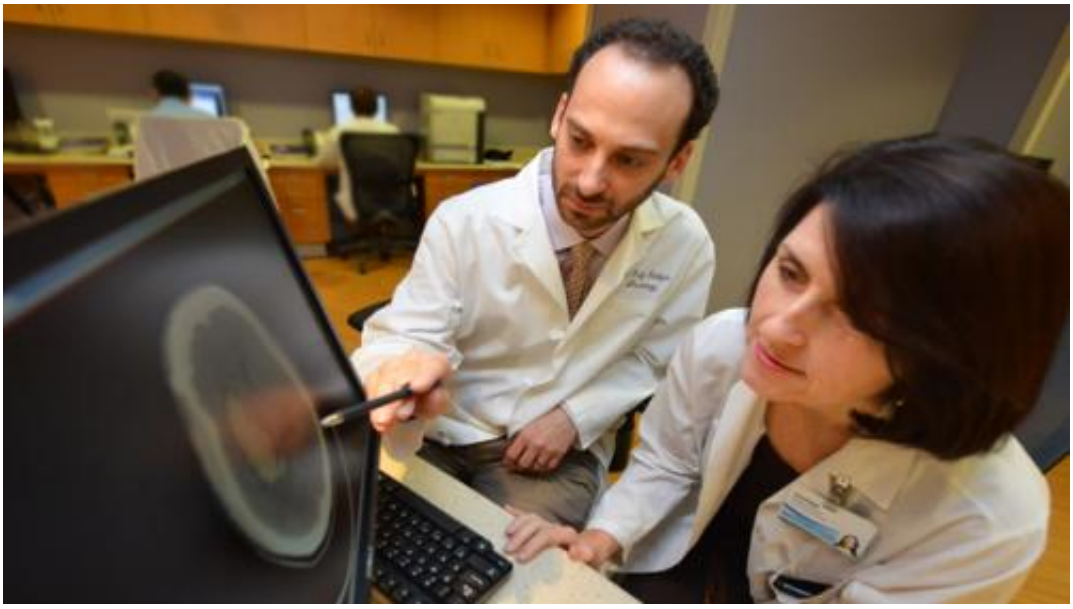
Antibiotic studied to reduce hemorrhagic stroke damage

April 1 2013



This is Dr. Jeffrey A. Switzer, stroke specialist at the Medical College of Georgia at Georgia Regents University, and Dr. Susan C. Fagan, Assistant Dean of the University of Georgia College of Pharmacy. Credit: Phil Jones

A new study will help determine if an antibiotic is a partial antidote for the poisonous effect blood has on the brain following a hemorrhagic stroke, researchers say.

They want to know if minocycline, a broad-spectrum antibiotic, can reduce high rates of disability from this comparatively rare stroke type characterized by spontaneous bleeds into the brain, said Dr. Jeffrey A.

Switzer, stroke specialist at the Medical College of Georgia at Georgia Regents University.

"We hope that, given early, minocycline can help reduce the damage of a type of stroke for which there is currently no proven therapy," Switzer said. He is principal investigator on an American Heart Association grant funding a trial enrolling 24 patients over two years, half of whom will get minocycline.

Dr. David Hess, Chair of the MCG Department of Neurology, and Dr. Susan C. Fagan, Assistant Dean of the University of Georgia College of Pharmacy, have shown minocycline is safe and potentially effective at combating some collateral damage of the more common clot-based strokes.

In a follow-up analysis, minocycline also appeared to reduce the inflammation that follows the initial stroke as well as levels of matrix metalloproteinases, or MMPs, a family of enzymes that destroys the basement membrane of blood vessels, making rupture more likely.

Elevated levels of MMPs and inflammatory cells have been found in the blood of both kinds of stroke patients and high levels correlate with poor outcomes. Minocycline also is known as a powerful collector of iron, a vital blood component that helps transport oxygen inside blood vessels but poisons brain tissue upon direct contact.

Switzer hopes minocycline will reduce levels of all three in hemorrhagic stroke, reducing bleeding and the size and impact of the stroke. Nearly 40 percent of hemorrhagic strokes increase in size during the first 24 hours. Most of the growth occurs within the first few hours, so timely intervention could reduce brain tissue loss, he said.

In fact, if minocycline proves safe in hemorrhagic strokes, the

researchers believe the best place to give it would be in an ambulance on the way to the hospital. Minocycline may be able to expand the window during which the clot buster tPA can be given to ischemic stroke patients. Switzer and his colleagues have first-hand experience that the earlier the better with stroke intervention. "If we could give something in the field before we can confirm the type of stroke because we know it's safe for both, that would be a novel strategy to help patients," he said.

For the study, they will use computerized tomography, or CT, to confirm a hemorrhagic stroke then get baseline assessments of blood levels of agents of interest, such as MMPs, as well as the patient's cognitive and physical abilities before giving the first dose of minocycline intravenously. Subsequent doses will be given orally, if the patient can swallow, over the next four days. Measures of outcomes and biomarkers will be reassessed at 24 hours, seven days or at time of hospital discharge and again at 90 days post-stroke.

They hope that decreasing blood levels of MMPs will serve as an indicator of how well the therapy works.

Risk factors for hemorrhagic stroke include uncontrolled hypertension; use of older blood thinners commonly prescribed for conditions such as heart disease and clots in the legs; and amyloid angiopathy, a deposit of Alzheimer's-like plaque that weakens the walls of blood vessels on the brain surface, typically in older individuals.

In addition to the substances in the blood that do harm, the physical mass created by bleeding causes damage. "It's tearing and pushing on structures in the brain and can cause a shifting of tissue that can be fatal in the closed chamber of the skull," Switzer said. "However, for those with smaller bleeds, better treatments, such as perhaps minocycline, are needed to combat the toxic effects of blood on brain tissue."

Provided by Medical College of Georgia