Novel celery seed-derived medicine given after clot treatment may improve stroke outcomes

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People who had an ischemic (clot-caused) stroke and were treated with a clot-busting medication and/or mechanical clot removal and also

received butylphthalide, a medication initially compounded from celery seed, experienced milder neurological symptoms with better functioning at three months after the stroke, compared to stroke patients who had their clots treated but received a placebo medication, according to preliminary research to be presented at the American Stroke Association's International Stroke Conference 2023. The meeting, to be held in person in Dallas and virtually Feb. 8-10, 2023, is a world premier meeting for researchers and clinicians dedicated to the science of stroke and brain health.

In previous studies in China, butylphthalide has shown the potential to safely protect and preserve the brain from possible damage related to stroke in animal models with a clot-caused stroke. The current study evaluated whether treatment with butylphthalide may improve the outcomes of people who initially received the intravenous clot-busting medication tissue plasminogen activator (tPA) and/or a mechanical clot removal procedure to physically remove the clot plus butylphthalide. In China, butylphthalide is licensed for use in treating ischemic stroke; however, it is not currently approved by the U. S. Food and Drug Administration.

"This is the first trial to show the benefit of using a medication that protects the brain from damage caused by a lack of oxygen to brain tissue. The medication was given to patients with acute ischemic stroke who were also receiving treatment to restore blood flow to the brain," said Baixue Jia, M.D., co-author of the study, an attending physician in interventional neuroradiology in the department of neurology in the Beijing Tiantan Hospital of Capital Medical University and a faculty member at the China National Clinical Research Center for Neurological Diseases, both in Beijing.

The researchers studied 90-day outcomes in 1,216 adults (average age of 66 years; 68% men) after they suffered a stroke that was initially treated

with tPA or mechanical clot removal therapy. The participants were treated between 2018 and 2022 at one of 59 medical centers in China. People who had minimal stroke symptoms on their initial exam (defined as 0-3 on the National Institutes of Health Stroke Scale, or NIHSS) or had severe stroke symptoms (defined as >26 on the NIHSS) were excluded from this study.

Along with their physician-chosen initial treatment, participants were randomly selected to receive either butylphthalide or a look-alike placebo administered by daily intravenous injection for the first 14 days, followed by 76 days of oral capsules. The patients were randomly assigned to the butylphthalide treatment group (607 adults) or the placebo group (609 adults). Neither the patients nor the research team knew which participants were assigned to which treatment.

Outcomes were deemed favorable if an individual had the following markers at 90-days post-stroke:

- an initially mild to moderate stroke (4-7 on the NIHSS) and had no symptoms (0 on the modified Rankin Scale, a scale that measures disability and dependence) after treatment;
- an initially moderate to serious stroke (8-14 on the NIHSS) and had no residual symptoms or mild symptoms that did not impair their ability to perform routine activities of daily living without assistance (0-1 on the disability scale); or
- an initially serious to severe stroke (15-25 on the NIHSS) had no remaining symptoms or a slight disability that impaired some activities yet still allowed a person to conduct their own affairs without assistance (0-2 on the disability scale).

The study found:

- Participants in the butylphthalide group were 70% more likely to

have a favorable 90-day outcome compared to the placebo group.
- Butylphthalide improved function equally well in the subsets of patients who initially received tPA, those who received endovascular therapy or those who received both tPA and endovascular treatment.
- Secondary events, such as recurrent stroke and intracranial hemorrhage (brain bleeds), were not significantly different between the butylphthalide and placebo groups.

"Patients who received butylphthalide had less severe neurological symptoms and a better living status at 90-days post-stroke compared to those who received the placebo. If the results are confirmed in other trials, this may lead to more options to treat strokes caused by clots," Jia said.

How butylphthalide works isn't clear, with animal studies suggesting various possible mechanisms. "The next step should be investigating the exact mechanisms of butylphthalide in humans," Jia said.

The study is limited by being based on participants who all received initial treatment with clot-busting intravenous medication or a procedure to remove the clot or both, so the results may not be generalizable to stroke patients who received other treatments. Results from this trial conducted in China may not be generalizable to other populations. In addition, butylphthalide is not approved by the FDA for any use in the U.S.

"While these are interesting results, this is only one relatively small study on a fairly select population in China. Butylphthalide, a medication initially compounded from celery seed, is not ready for use in standard stroke treatment; however, these results warrant further study consideration," said American Stroke Association volunteer expert and EPI and Stroke Council member Daniel T. Lackland, Dr.P.H., FAHA,

professor and director, in the Division of Translational Neurosciences and Population Studies and the department of neurology at the Medical University of South Carolina in Charleston, South Carolina. "The medication used in this study is not the same as celery seed or celery seed extract supplements. Stroke survivors should always consult with their neurologist or health care professional regarding diet after a stroke ." Dr. Lackland was not involved in this study.

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More information: professional.heart.org/en/meet … al-stroke-conference

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