Different methods of giving patients a drug to prevent stroke complications can lead to 'massive variation' in outcomes

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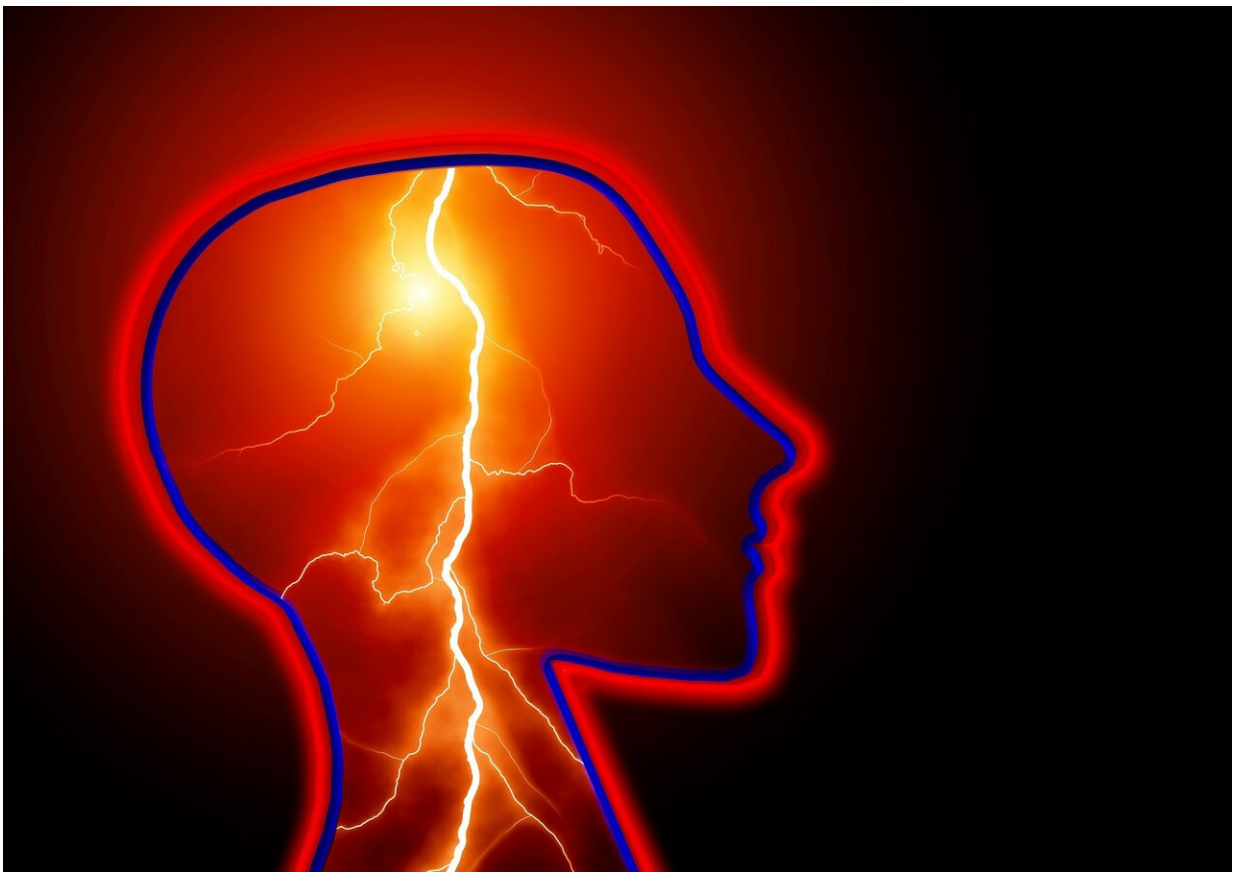

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Different methods of giving patients the same drug to prevent severe

complications after a type of stroke lead to different outcomes, according to the first study ever to compare how patients fare after being treated with each method.

Aneurysmal subarachnoid hemorrhage, a life-threatening type of stroke that happens when a ruptured aneurysm causes bleeding into the space surrounding the brain, has an average mortality rate of 30 to 50 percent. And among patients who survive the initial hemorrhage, about one-third develop severe and often debilitating disabilities because of complications in the days following the hemorrhage.

"Delayed cerebral ischemia is one of the main complications contributing significantly to disability and even death if the patient survives the initial bleed," says Sherif Mahmoud, clinical associate professor in the Faculty of Pharmacy and Pharmaceutical Sciences and lead author of the study, published in the journal *Pharmacotherapy*.

A drug called nimodipine is currently the only treatment proven to prevent this complication, which is a neurological injury caused by lack of blood flow to the brain. It's recommended that all patients recovering from a subarachnoid hemorrhage receive nimodipine for 21 days. However, there are different ways to administer the drug, and the study shows that not all these methods are equal.

The issue: How and how much

The study was the first ever to compare various nimodipine formulations and administration techniques, examining 727 patients in 21 hospitals across North America. In Canada, nimodipine is only available in tablets; in the United States, it's available as a liquid or in soft gelatin capsules taken orally.

Patients who are able to swallow tablets or capsules receive a consistent

dose. The issue arises with patients who are unable to swallow the medication.

In areas where nimodipine tablets are available, health-care professionals must crush them bedside and mix them with water to give to the patient through an enteral feeding tube. However, as Mahmoud highlights, there are no guidelines for how to crush the tablets or how soon after crushing them to give the medication to the patient.

"Nimodipine is a light-sensitive medication. If it stays in the light for a while it can actually break down," he notes.

Where gel capsules are available, the gel must be extracted from the capsules bedside, then given through a feeding tube. However, patients receiving the drug this way often don't receive the full capsule contents.

"There's a study with one of our collaborators that found drawing liquid from the capsule is very inconsistent. They're not drawing the whole drug, they're not getting all of the medication."

Dramatic difference in outcomes

Mahmoud and his collaborators compared rates of delayed cerebral ischemia in groups of patients who received each formulation.

"We found there was a massive variation. We weren't expecting to see a difference that dramatic."

Of the patients involved in the study, 31 percent experienced delayed cerebral ischemia. However, the prevalence was 59.1 percent among the patients who received crushed tablets and 45.8 percent among those who received liquid drawn from capsules at the bedside.

The lowest rate of delayed cerebral ischemia, just 13.5 percent, was observed in the group who received nimodipine that had been extracted at the hospital pharmacy rather than bedside.

Considering that the administration methods with the most potential for inconsistency were associated with the highest rates of delayed cerebral ischemia in patients, Mahmoud says the findings point to a need for standardization to ensure all patients are getting the full dosage of nimodipine—and getting the best chance of benefiting from the drug.

One solution, Mahmoud suggests, would be to have hospital pharmacies prepare the drug when a liquid formulation is needed but not commercially available, creating a standardized process.

"Before this study, we didn't know there was a difference [in outcomes]. It was thought that as long as you're giving the drug, it's fine. But now, it's not fine—we know there's a difference so it's necessary to have consistency here."

More information: Sherif Hanafy Mahmoud et al, Comparison of nimodipine formulations and administration techniques via enteral feeding tubes in patients with aneurysmal subarachnoid hemorrhage: A multicenter retrospective cohort study, *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* (2023). DOI: 10.1002/phar.2791

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