

Health Technology TRENDS

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Ultrasound may give a boost to treatment for often fatal stroke type

Combining high-frequency ultrasound with clot-busting drugs may give physicians a new therapeutic tool to treat a frequently fatal type of stroke, according to a small safety study.

In the United States, intracerebral hemorrhage (ICH) comprises about 10% of all strokes. However, ICH accounts for a larger share of stroke-related deaths than ischemic stroke, which represents approximately 85% of strokes. ICH is closely associated with poorly controlled hypertension. About half of patients with ICH die within one month of the event, and patients who survive often lose so much brain function that they can no longer care for themselves. ICH occurs when a blood vessel in the brain bursts, allowing blood to leak into surrounding brain tissue. In some cases, physicians may perform stereotactic neurosurgery to evacuate the pooled blood. However, the decision about whether or when to perform neurosurgery for ICH remains controversial.

"As the blood pools in cerebral tissue, it starts to clot and increases pressure within the brain and begins to leach out iron and other toxins that can damage surrounding brain cells," says principal investigator David Newell, M.D., executive director, Swedish Neuroscience Institute (Seattle, WA, USA). "So, the goal in treating brain hemorrhage is removing the pooled blood as soon as possible to prevent further damage," he says.

Ischemic stroke patients may receive intravenous (IV) therapy with the thrombolytic agent tissue plasminogen activator (tPA) to dissolve the blood clot or other obstruction blocking blood flow to the brain. However, tPA is contraindicated in patients with brain

hemorrhage, so patients with suspected stroke undergo computed tomography (CT) screening to rule out bleeding before treatment with IV tPA can begin.

Likewise, candidates for ultrasound-assisted thrombolysis, or sonothrombolysis, to treat ICH in the current trial were screened for active bleeding. "We purposely had a delay before starting treatment in our trial to make sure that patients did not have an aneurysm or vascular lesion; patients with active bleeds or growing hemorrhages were excluded from our trial," says Newell. "Brain hemorrhages are usually caused by small vessels deep within the brain that eventually stop bleeding due to natural clotting action," he says. "We waited at least six hours to make sure patients were stable, demonstrated over two CT scans, before we initiated thrombolysis," Newell says. "We did not see any re-bleeds in our study."

Newell says sonothrombolysis would be contraindicated in patients with blood clotting disorders that cannot be corrected.

Newell explains that as a potential treatment for ICH, tPA is delivered directly to the hemorrhage site rather than intravenously, so systemic exposure to the drugs is not an issue. In addition, "we use a dose that is approximately one-one-hundredth of the dose used for intravenous tPA therapy to treat ischemic stroke," he says.

New findings

In the current trial¹, Newell and colleagues evaluated the safety of adding

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*Ultrasound for fatal stroke type
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▶ *"The initial results from our small safety study really exceeded our expectations."*

catheter-delivered ultrasound to enhance the action of locally injected clot-dissolving drugs followed by drainage as a new treatment for ICH. Investigators screened 35 patients with ICH or intraventricular hemorrhage (IVH), a type of ICH that involves bleeding into the ventricles, the channels that contain cerebrospinal fluid. Nine patients, ages 38 to 83, met entry criteria. Investigators stereotactically delivered a ventricular drainage catheter and an ultrasound microcatheter (EkoSonic SV Endovascular System, EKOS Corporation, Bothell, WA, USA)² together directly into the ICH or IVH. Recombinant tPA was administered through the ultrasound catheter in 3 doses (IVH total dose, 3.0 mg; ICH total dose, 0.9 mg) over a 24-hour treatment period. After tPA is administered, the catheter's ultrasound pulse disperses the clot-dissolving drug throughout the hemorrhage area, and a drainage catheter collects the liquefied clot.

Newell and colleagues found that after 24 hours, ultrasound-assisted thrombolysis reduced the mean hemorrhage volume by 59.0% in ICH patients and by 45.1% in IVH patients, compared to baseline CT scans. Seven of 9 patients demonstrated clinical improvement, defined as a decrease in the National Institutes of Health Stroke Score at 30 days. One patient died within 30 days of admission. Another ICH patient was excluded from analysis due to catheter breakage. No intracranial infections or significant episodes of rebleeding on clinical or CT assessment occurred.

Investigators also compared results from current trial patients to a matched control

group of patients in the MISTIE and CLEAR trials; MISTIE and CLEAR are evaluating thrombolysis (at the same dose levels) and drainage without ultrasound assistance to treat ICH and IVH.

Implications

"The initial results from our small safety study really exceeded our expectations," Newell told *Health Technology Trends*. Newell and colleagues are currently in the early stages of planning further clinical trials of ultrasound-assisted thrombolysis to treat ICH and IVH, he notes.

Newell believes that ultrasound-assisted thrombolysis has a small learning curve that experienced neurosurgeons should be able to overcome quickly. "The neuronavigation techniques we used are fairly common, and most neurosurgeons should be quite familiar with them," he says. If the technology receives regulatory approval from the U.S. Food and Drug Administration as a treatment for ICH, the technology should probably be reserved for use at stroke centers of excellence.

Notes

1. The Washington State Life Sciences Discovery Fund supported the SLEUTH (Safety of Lysis with EKOS Ultrasound in the Treatment of Intracerebral and Intraventricular Hemorrhage) trial.
2. The EkoSonic Endovascular System currently has 510(k) marketing clearance from the U.S. Food and Drug Administration for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. ▶

*Medical device innovation post-PPACA
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nor payers "appreciate the differences [between] drugs and devices."

Change in reimbursement to come?

As Northrop interprets the legislation, "the door is still open" to public and private use of such research to inform reimbursement decisions.

Rubin reminded the panel and audience of Garber's remarks that the legislation is in its early rulemaking phase. "Now the heavy lifting begins," said Rubin.

"The rules of the game have changed a bit," Neumann told the device industry. He urged manufacturers to anticipate CER, because, "if you don't produce the evidence, others will."

Notes

1. The United Kingdom's National Institute for Health and Clinical Excellence (NICE). NICE's use of cost-effectiveness analysis is controversial in the United States.
2. Beginning in 2013, device sales will be subject to a 2.3% excise tax. ▶