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Computer-Supervised EVD Raises Safety Questions in ICU Care of IVH
Humans—1, Computers—0

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The safety trial by Haldrup et al[1] addresses blood clots from intraventricular bleeding, an anatomical subset of intracerebral hemorrhage stroke with particularly severe outcomes. The excellent, detailed phase 2 trial report of interim safety issues leading to a decision to stop the ACTIVE study demonstrates that successful management of this problem is complex and requires human oversight of a multimodal intervention, most likely a drug-device combination. Results did not endorse an advance by this technique for either clot removal or safety of intensive care unit (ICU) care of intraventricular hemorrhage (IVH).

Brain bleeding represents 15% of stroke in high-income countries and at least 30% in low-income countries, affecting 3 to 4 million adults per year.[2] Additionally, brain bleeding complicates stroke prevention in atrial fibrillation, an otherwise treatable cause of ischemic stroke. Blood in the brain injures tissue and destroys brain functions. While progress has been made in removing clots from brain bleeds with minimally invasive techniques, a strategy of primary removal of the injurious clot has not yet been successful in phase 3 trials. Importantly, we do have class IIa, level A evidence that combining fibrinolysis and a simple external ventricular drainage (EVD) device saves lives and probably improves long-term survivor function in severe IVH.[3]

Precision surgery with minimal tissue disruption is the key to promising device-supported strategies.[4] By comparison, traditional craniotomy involves a bone flap, tissue incisions, electrocautery of brain tissue, and the application of toxic blood clotting factors directly on brain tissue. The craniotomy approach has been tested multiple times and is not successful in improving outcomes, and it is particularly invasive for IVH. This led to exploration of tissue-sparing, minimally invasive approaches. The IRRA*flow* device is a ventricular drainage catheter performing active ventricular irrigation with computer-controlled perfusion capabilities that are designed to enhance 2-way flow in a specialized EVD with the goal to control intracranial pressure (ICP) and efficiently remove cerebrospinal fluid (CSF) and blood from the ventricles.[5] The device strategy is to manage catheter flow with puffs of fluid to minimize the impact of catheter obstruction on the treatment of IVH. It is one of several promising device developments applicable to the intracerebral hemorrhage/IVH blood clot removal problem.

The established evidence for IVH treatment currently requires a complex acute care management program overseen by well-trained, vigilant human observation of ICP using EVD(s) for clot and CSF removal.[3,6,7] Management includes (1) rapid and full control of ICP using an EVD, (2) use of the correct number and size of catheters, (3) proper catheter(s) location based on the anatomic configuration/size of the bleed, and (4) an ICU program that stringently avoids infections,[8] maintains catheter location, avoids catheter replacement, and sets a goal for a short time frame to removal of blood and blood products from the ventricular system.[9,10]

Importantly, new analyses of 1501 individuals combining trial and epidemiologic data suggest a robust 10% to 15% absolute treatment effect for the use of interventricular fibrinolytics in patients with IVH.[9] A phase 3 trial using combined therapy with fibrinolytics and EVDs for such a precisely defined IVH population is going to be important to the future evidence basis of IVH management. It is in this setting that the safety concerns of the ACTIVE study should be viewed.

As a recent technology meeting an unmet clinical need in IVH management, the opportunity for further innovation of the IRRA*flow* device is apparent. Most catheter occlusions were attributed to

design-related issues, including a small inner lumen relative to a standard EVD, separation of drainage and irrigation lines with unclear protocols for drainage line manipulation, a standard practice for routine EVD use, and the need for liquid (CSF) around the side holes of the catheter tip, making placement directly into a hematoma problematic without the use of thrombolytics.

The ACTIVE study results reported by Haldrup and colleagues[1] demonstrate that the singular use of the currently applied computer-controlled catheter fluid infusion strategy is insufficient to keep catheters open and remove clot. This failure to improve blood clearance, complicated by increased ICP risks to the patient, make clear the complexity of a clinician-supervised management program needed for rapid and effective minimally invasive clot removal. As we increase efforts to automate human roles in health care, it is good news that human oversight is still the criterion standard. The ACTIVE study shows us that more passive strategies may be superior to more inventive ones where stringent monitoring is required. In our opinion, IVH treatments require thrombolytics and safe drainage.

ARTICLE INFORMATION

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