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Advances in Stroke

Critical Care and Emergency Medicine

Wade S. Smith, MD, PhD; Stefan Schwab, MD

The science of neurocritical care and emergency medicine has advanced in several areas over the last year, particularly in the management of acute hypertension during neurological emergencies.

Intracerebral Hemorrhage

Early ascription of do-not-resuscitate status to patients with intracerebral hemorrhage (ICH) has been previously shown to correlate with in-hospital mortality raising concerns over a self-fulfilling prophecy in clinical care. This has been replicated by a large observational study in Seattle, whereby the presence of a do-not-resuscitate order altered the multivariate predictive model of outcomes.¹ In exploration of potential treatments for ICH, use of do-not-resuscitate should be investigated prospectively because this simple change in practice (ie, not de-escalating care for the first several days in all patients with ICH) could positively affect outcomes. In regard to blood pressure management, a multimodality monitoring study this year using invasive brain tissue oxygen and cerebral microdialysis in 18 patients with ICH showed less brain tissue hypoxia and lower lactate/pyruvate ratios in patients with higher cerebral perfusion pressures.² Current ICH guidelines recommend blood pressure modification based on absolute blood pressure value and intracranial pressure alone³; customizing this recommendation based on real-time feedback from measures of brain physiology makes sense but should still be considered investigational.

Intraventricular Hemorrhage

The Combined Approach to Lysis Utilizing Eptifibatide and rt-PA in Acute Ischemic Stroke (CLEAR) intraventricular hemorrhage trial was a randomized trial of intraventricular tissue plasminogen activator versus medical therapy for intraventricular hemorrhage.⁴ The trial showed that intraventricular hemorrhage was more rapidly cleared in the treatment arm (7.5 versus 12 days) but there was no clinical impact of this therapy. However, this may be an important finding because prolonged use of external ventricular drains expends healthcare resources (eg, physician effort in flushing and manipulating the drain, extended time in an intensive care unit) and can lead to complications such as infection.

Subarachnoid Hemorrhage

Guidelines for the management of subarachnoid hemorrhage from the Neurocritical Care Society were published.⁵ Several practical recommendations are made including discouraging the routine use of pulmonary artery catheters, prophylactic phenytoin, hypervolemia, and use of albumin; the guidelines encourage the use of antifibrinolytic agents if surgical or endovascular treatment is to be delayed, electroencephalographic monitoring for poor-grade patients who fail to improve over time, and euvolemia with saline and use of fludrocortisone for negative fluid balance.

A major randomized, Phase III trial of clazosentan in 764 patients found no benefit for this endothelin receptor antagonist in reducing morbidity or mortality from vasospasm, a disappointing result.⁶ This leaves only oral nimodipine as the standard drug for the prevention of vasospasm.

Multimodality monitoring in a large cohort of patients with poor-grade subarachnoid hemorrhage found results similar to such monitoring in patients with ICH. In this study, 30 patients with poor-grade subarachnoid hemorrhage were monitored with invasive brain oxygen probes and cerebral microdialysis.⁷ The investigators found a threshold of cerebral perfusion pressure ≤ 70 mm Hg for which mortality and poor outcome rose in the lower blood pressure cohort. This too should be considered investigational but underscores the value that multimodality monitoring may provide to the brain-injured patient.

Ischemic Stroke

The Scandinavian Candesartan Acute Stroke Trial (SCAST) randomized 2029 patients with ischemic stroke within 7 days to candesartan versus placebo and found no benefit and potential harm.⁸ Blood pressure was lower in the treated group (147/82 versus 152/84 mm Hg, $P < 0.0001$) and improved clinical outcome favored placebo when 6-month Rankin scores were analyzed (OR, 1.17; $P = 0.048$). Adverse events were no different in the 2 cohorts suggesting that the relative hypotension created by candesartan is significant and physicians should continue to avoid even modest attempts to lower blood pressure in patients with ischemic stroke unless blood pressure is excessive ($> 220/120$ mm Hg). In a differ-

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ent observational study of patients arriving to an emergency department with severe hypertension ($>180/110$ mm Hg), 30% had neurological diagnosis (18% stroke, 31% ICH, 38% subarachnoid hemorrhage).⁹ Of these patients, mortality was associated with larger drops in blood pressure. Translating these findings and reiterating American Heart Association guidelines on acute blood pressure management in acute ischemic stroke appears to be necessary because a recent study on antihypertensive use in 16 emergency departments raises concern.¹⁰ In this study, antihypertensives were administered against guidelines 70% of the time, and to those who medications are administered, the fall in blood pressure was often excessive. Despite emergency medical providers' awareness of these guidelines, the largest barrier appears to be adherence suggesting that stronger focus on implementation of guidelines should be the focus.¹¹

Traumatic Brain Injury

A randomized trial of bifrontal hemicraniectomy for 155 adults with severe traumatic brain injury was undertaken in Australia and New Zealand.¹² Hemicraniectomy reduced intracranial pressure and shortened intensive care unit stay but was associated with worse outcome in the surgical arm compared with medical therapy alone (70% versus 51%, $P=0.02$). Despite attempting to control for baseline imbalances in patient cohorts (27% of the surgical group had unreactive pupils versus 12% in the medical group, $P=0.04$), such imbalances may have accounted for the differences in clinical outcomes. In addition, the trial excluded patients who needed evacuation of mass lesions (subdural and parenchymal hematoma) so generalizing these results to such patients is not warranted. The investigators used "refractory intracranial pressure" as a trigger to randomize, yet nearly all of the medical therapy patients postrandomization had intracranial pressures below this trigger. So, were the right patients selected? This trial is important because it is the first randomized trial of bilateral hemicraniectomy in traumatic brain injury and likely should give pause to the routine use of hemicraniectomy for cerebral swelling alone, but physicians should be careful to not extrapolate these findings to patients with mass lesions who also have brain swelling in whom hemicraniectomy may be lifesaving. Furthermore, this trial provides no additional insight into the use of hemicraniectomy for ischemic stroke, a practice that is well established with a reasonable evidence basis.

Disclosures

None.

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