Recent Advances in the Acute Management of Intracerebral Hemorrhage

Joseph D. Burns, MD[a,*], Jennifer L. Fisher, MSN, ANCP-BC[a], Anna M. Cervantes-Arslanian, MD[b]

KEYWORDS

• Intracerebral hemorrhage • Hypertension • Prothrombin complex concentrate
• Minimally invasive surgery

KEY POINTS

- Aggressive antihypertensive treatment in acute intracerebral hemorrhage (ICH) is not associated with better outcomes than more moderate control and may be associated with increased rates of acute renal dysfunction. Therefore, a reasonable systolic blood pressure goal may be 140 to 160 mm Hg.
- Prothrombin complex concentrate is recommended over fresh frozen plasma for reversal of vitamin K antagonists in ICH.
- Platelet transfusion appears harmful in nonsurgical antiplatelet-associated ICH.
- Minimally invasive surgery has shown promising results in early-phase trials and multiple studies are ongoing.

INTRODUCTION

Primary intracerebral hemorrhage (ICH) is a common, devastating disease that lacks an effective specific treatment. Mortality is high, functional outcomes are poor, and these have not substantially changed for decades.[1,2] There is, therefore, considerable opportunity for advancement in the management of ICH. A significant amount of research has recently begun to address this gap. This article is aimed at updating neurologists on the most clinically relevant contemporary research. Comprehensive reviews of and guidelines for the management of ICH are outside the scope of this review and can be found elsewhere.[3]

ANTIHYPERTENSIVE TREATMENT

Acute hypertension is common after ICH[4] and is associated with larger hematoma volumes and worse outcomes.[5–7] Three recently published randomized control trials (RCTs) investigated the hypothesis that aggressive control of acute hypertension, as compared with moderate control, would lead to decreased hematoma expansion, lower mortality, and improved functional outcomes (**Table 1**).[8–10] The phase 2 trial INTERACT produced neutral, albeit somewhat equivocal, results regarding the effect of aggressive hypertension control on hematoma expansion.[9] The results of the phase 3 INTERACT2 on clinical outcomes were similarly equivocal. Although there

This article originally appeared in *Neurologic Clinics*, Volume 35, Issue 4, November 2017.
Disclosure Statement: The authors have nothing to disclose.
[a] Neurocritical Care, Department of Neurology, Lahey Hospital and Medical Center, 41 Mall Road, Burlington, MA 01805, USA; [b] Neurocritical Care, Department of Neurology, Boston Medical Center, Boston University School of Medicine, Collamore Building, C-3, 72 East Concord Street, Boston, MA 02118, USA
* Corresponding author.
E-mail address: joseph.d.burns@lahey.org

Neurosurg Clin N Am 29 (2018) 263–272
https://doi.org/10.1016/j.nec.2017.11.005

Table 1
Comparison of key elements of clinical trials of antihypertensive treatment in intracerebral hemorrhage

Variable	INTERACT[9]	INTERACT 2[8]	ATACH2[10]
Number of subjects	404	2839	1000[a]
Selected inclusion criteria			
Time from symptom onset to randomization, h	6	6	4.5[b]
SBP, mm Hg	150–220	150–220	180–240
SBP treatment goals			
Intensive, mm Hg	<140	<140	120–139
Guideline/Standard, mm Hg	<180	<180	140–179
Medication regimen	Protocol based on local availability (urapidil most common)	Protocol based on local availability (urapidil most common)	Nicardipine
Blood pressure separation (intensive vs guideline, time frame)	146 vs 157, mean of hours 1–24	150 vs 164, 1st hour; 139 vs 153, 6th hour	129 vs 141, mean minimum for first 2 h
Primary outcome (results, guideline/standard vs intensive)	Proportional hematoma growth over 1st 24 h (16.2 vs 6.2%, $P = .06$)	Proportion of subjects with 90-d mRS 3–6 (55.6 vs 52%, $P = .06$, adjusted $P = .12$)	Proportion of subjects with 90-d mRS 4–6 (37.7% standard vs 38.7% intensive, $P = .72$)
Adverse event rates	No difference	No difference	Adverse renal events higher in intensive group (9% vs 4%, $P = .002$)

Abbreviations: ATACH, Antihypertensive Treatment of Acute Cerebral Hemorrhage; INTERACT, Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage trial; mRS, modified Rankin scale; SBP, systolic blood pressure.
[a] Planned sample size n = 1280, but trial stopped for futility at n = 1000 after second preplanned interim analysis.
[b] Originally 3.0 h, extended to 4.5 h midtrial.

was no difference in the dichotomized modified Rankin score (mRS) primary outcome, a secondary ordinal analysis demonstrated a possible shift in favor of the intensive group (odds ratio 0.87 for shift to higher mRS, 95% confidence interval 0.77–1.00, $P = .04$, adjusted $P = .10$). In the one-third of patients who had sufficient radiographic data, there was no difference between groups in relative or absolute hematoma growth. ATACH 2 was more definitively negative, showing no beneficial effect of intensive antihypertensive treatment in any clinical or radiographic outcomes reported. Additionally, a higher rate of renal adverse events within 7 days of randomization in the intensive group was detected in post hoc analysis.

The main caveat in applying results of these trials at the bedside is the unexpectedly small systolic blood pressure (SBP) difference between treatment groups, driven by SBP control to the low end of the specified rage in the standard treatment groups acting as controls. Considered together, then, these trials indicate that SBP control to 120 to 140 mm Hg does not lead to improved outcomes compared with 140 to 160 mm Hg, and may be associated with an increased risk of acute renal dysfunction, supporting an SBP goal of 140 to 160 mm Hg in acute ICH.

COAGULOPATHY CORRECTION

Vitamin K Antagonists

Vitamin K antagonists (VKAs) considerably increase the frequency and severity of ICH,[11–14] making rapid reversal of VKA coagulopathy in patients with ICH crucial (**Box 1**). In a recent large, multicenter, retrospective cohort study, patients who had the international normalized ratio (INR) corrected to less than 1.3 within 4 hours of admission had lower rates of significant hematoma