Blood Pressure Lowering and Acute Perihematomal Brain Edema After Intracerebral Hemorrhage

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See related article, p 1292.

Intracerebral hemorrhage (ICH) is a common and often fatal subtype of stroke that produces severe neurological deficits in survivors.1 There are still no proven therapeutic interventions for ICH, but there has been much interest in the potential use of acutely reducing blood pressure to limit hematoma expansion. A key factor affecting ICH outcome is hematoma size, and hematoma expansion occurs in about one third of patients with ICH.2 This has led to 3 clinical trials: Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT), Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH), and The Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial (ICH ADAPT).3–5 INTERACT 2 reported last year6 and suggested an improvement in outcome although this did not reach statistical significance. Understanding the importance of those results requires determination of whether acute blood pressure reductions may have detrimental and beneficial effects in patients with ICH. In this issue of Stroke, McCourt et al7 from the ICH ADAPT study, report findings on the effect of acutely reducing blood pressure in patients with ICH on cerebral perfusion and perihematomal edema growth. They report that neither parameter was affected, suggesting that blood pressure intervention is safe in this patient population.

Although death may occur acutely after an ICH, delayed neurological decline often occurs in patients with a large hematoma. Edema development elevates intracranial pressure and can cause herniation and death.2,8 Perihematomal edema is commonly observed during the acute and subacute stage, and it may be more accountable for the poor neurological outcome than the hematoma mass itself.9,10 Therefore, it is important that McCourt et al7 found no effect of blood pressure lowering on perihematomal edema growth after ICH.

One potential concern of reducing blood pressure is that it might decrease blood flow to ischemic tissue enhancing brain damage. Whether such tissue exists after ICH is controversial with a number of studies, suggesting that secondary ischemic/reperfusion injury is not a major component of ICH-induced brain damage.2,11 In their study, McCourt et al7 only found a modest reduction in perihematomal cerebral blood flow in control patients (≈12%), and this reduction was not significantly changed by acute blood pressure lowering. The reductions in flow in both sets of patients were above what is normally considered the threshold for ischemic brain damage. Thus, an effect on cerebral blood flow does not seem to be a concern in using agents to reduce blood pressure (at least for the hematoma sizes in this trial).

Several mechanisms of edema formation other than ischemia have been identified as underlying ICH-induced edema during the past decade.2,11 These include hydrostatic pressure during the clot formation, clot retraction, coagulation cascade activation with thrombin production, red blood cell lysis, complement cascade activation in the brain parenchyma, and inflammation.2,11 There seems to be several phases of edema formation related to underlying mechanism. There is an early phase (first several hours), involving hydrostatic pressure and clot retraction with movement of serum from the clot into the surrounding tissue. There is then a second phase (first 2 days) related to the coagulation cascade and thrombin production, and a third phase related to red blood cell lysis.11 Future studies should develop effective therapies to reduce perihematomal brain edema.

Although the results of the McCourt et al7 study support the thesis that acutely lowering blood pressure does not have detrimental effects on perihematomal cerebral blood flow and edema growth, a concern about that study is that there is no evidence that the blood pressure reduction affected hematoma expansion. This may reflect the relatively small number of patients in this subset of the ICH ADAPT trial. However, it should be noted that in the INTERACT 2 trial, the reduction in hematoma expansion with blood pressure lowering did not reach significance.5 It may be that to have a major effect on hematoma expansion and perhaps clinical outcome, blood pressure lowering may need to be instituted earlier after ICH (the median time to randomization was 7.4 hours after onset in the McCourt et al7 study) when a greater percentage of patients are undergoing expansion. The demonstration by McCourt et al7 that ischemia is apparently not a concern with blood pressure reduction will help facilitate such early interventions.

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References


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