Autoregulation of Cerebral Blood Flow Is Preserved in Primary Intracerebral Hemorrhage

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Background and Purpose—Treatment of acute hypertension after intracerebral hemorrhage (ICH) is controversial. In the context of disrupted cerebral autoregulation, blood pressure (BP) reduction may cause decreased cerebral blood flow (CBF). We used serial computed tomography perfusion to test the hypothesis that CBF remains stable after BP reduction.

Methods—Patients recruited within 72 hours of ICH were imaged with computed tomography perfusion before and after BP treatment. Change in perihematoma relative (r) CBF after BP treatment was the primary end point.

Results—Twenty patients were imaged with computed tomography perfusion at a median (interquartile range) time from onset of 20.2 (25.7) hours and reimaged 2.1 (0.5) hours later, after BP reduction. Mean systolic BP in treated patients (n=16; 4 untreated as BP<target at baseline) decreased significantly between the first (168±21 mm Hg) and second (141±19 mm Hg; P<0.0001) computed tomography perfusion scans. The primary end point of rCBF was not affected by BP reduction (pretreatment=0.89±0.11; post-treatment=0.87±0.11 mL/100 g per minute; P=0.37). Linear regression showed no relationship between changes in systolic BP and perihematoma rCBF (β=0.001 [−0.002 to 0.003]; P=0.63).

Conclusions—CBF remained stable after acute BP reduction, suggesting some preservation of cerebral autoregulation. (Stroke. 2013;00:00-00.)

Key Words: cerebral blood flow ● hypertension ● intracerebral hemorrhage

Management of hypertension during acute intracerebral hemorrhage (ICH) is controversial. Hematoma expansion may be attenuated by acute blood pressure (BP) reduction, but concern persists that cerebral autoregulation may be impaired after ICH, making perfusion of the brain passively dependent on BP.1,2 Perihematoma tissue is moderately hypoperfused3–7 and, therefore, may be vulnerable to BP reduction.

In the Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial (ICH ADAPT), BP reduction did not affect post-treatment cerebral blood flow (CBF).8 In this substudy, we assessed cerebral autoregulation with before and after BP treatment CBF measurements. We hypothesized that CBF would remain stable.

Methods

The ICH ADAPT protocol (clinicaltrials.gov NCT00963976) has been described previously.9 Briefly, patients with ICH presenting within 24 hours of onset were randomized to a target systolic BP (SBP) of <150 or <180 mm Hg within 24 hours of onset were randomized to a target systolic BP (SBP) of <150 or <180 mm Hg, followed by computed tomography perfusion (CTP) imaging 2 hours later. Patients in this observational substudy underwent additional CTP scanning before BP treatment. Each CTP was acquired with 40 mL of iodinated contrast, given over 10 seconds, with computed tomography images acquired every second for 50 seconds (80 kvp, 200 mA per image). Patients were not enrolled consecutively. Only those with normal renal function and stable neurological status underwent 2 CTP scans. Another 5 patients were studied 24 to 72 hours after onset. Those with baseline SBP >150 mm Hg were treated to a SBP target of <150 mm Hg. Patients with SBP of 120 to 150 mm Hg were treated to a target reduction of 10% of baseline. Patients with baseline SBP <120 mm Hg were not treated.

Image postprocessing and region of interest analysis were completed as described previously.10 The primary end point was the change in relative (r) CBF between baseline and 2-hour scans. Changes in relative and absolute cerebral blood volume, mean transit time, and impulse response time to peak were also measured.

Results

Twenty patients were imaged a median (interquartile range) of 20.2 (25.7; range, 1.5–72.2) hours after onset (Table 1). Four patients were below target at baseline (SBP<180 mm Hg, n=3; <120 mm Hg, n=1) and were not treated with antihypertensive medication. Mean SBP in treated patients decreased...
significantly between the first (168±21 mm Hg) and second CTP scans (141±19 mm Hg; P<0.001).

Mean perihematoma rCBF was unchanged after BP reduction (pre=0.89±0.11, post=0.87±0.11; P=0.37; Figure). Adjustment for baseline SBP and hematoma volume did not affect this result. The mean change in absolute CBF was 2.78±11.20 mL/100 g per minute (95% confidence interval, −3.19 to 8.74). Ipsilateral hemispheric rCBF remained stable (pre=0.99±0.07, post=0.96±0.06; P=0.14). Neither perihematoma (pre=37.69±14.40, post=34.91±11.37 mL/100 g per minute; P=0.34) nor ipsilateral hemispheric absolute CBF (pre=40.65±13.10, post=38.85±12.22 mL/100 g per minute; P=0.47) were affected by BP reduction (Table 2).

Perihematoma rCBF decreased in 7/16 (44%) treated and 3/4 (75%) untreated patients (Fisher exact test; P=0.58). Linear regression in all patients (n=20) indicated no relationship between change in SBP and perihematoma rCBF (β=0.001 [-0.002 to 0.003]; see the online-only Data Supplement).

Discussion
Our results indicate that BP reduction after ICH does not affect cerebral perfusion. The lack of relationship between BP change and CBF over time suggests preserved autoregulation. Two studies of cerebral autoregulation in patients with ICH have been published.10,11 A oxygen-15 positron emission tomography study in 14 patients with ICH 6 to 22 hours after onset indicated that a reduction in mean arterial pressure was not associated with changes in CBF, suggesting preservation of autoregulation.11 A single photon emission computed tomography study in 68 sub-acute (<1 week after onset) patients with ICH indicated that hemispheric CBF fell modestly with mean arterial pressure reduction, but the effect was seen primarily in those treated with the nonspecific ganglionic blocker trimetaphan.10 The same fall in CBF was not seen in patients treated with diltiazem, despite a similar BP drop, suggesting a drug-specific effect.

Although we have not assessed the upper and lower limits of cerebral autoregulation in ICH, we have shown that BP reduction does not exacerbate perihematoma hypoperfusion, which is most relevant clinically. Importantly, we have demonstrated that the CBF response to antihypertensive therapy does not vary with baseline BP or magnitude of the pressure change.

The primary limitation of this study is the small sample size, which includes a heterogeneous group of patients with respect to hematoma volume, location (lobar/deep), and time to treatment (2 to 72 hours). Ideally, autoregulation should be studied <6 hours from onset, the period where BP treatment is most likely to be beneficial. A second limitation is selection bias related to neurological stability and renal function. Nonetheless, CBF remains stable in this heterogeneous group of patients with ICH. These findings add further support to the safety of early BP reduction after ICH.
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=20)</th>
<th>Treated Patients (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>13 (65%)</td>
<td>11 (69%)</td>
</tr>
<tr>
<td>Age, y</td>
<td>73±11</td>
<td>73±13</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (75%)</td>
<td>13 (81%)</td>
</tr>
<tr>
<td>Previous ICH</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>4 (20%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Medication history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>11 (55%)</td>
<td>10 (63%)</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>4 (20%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>4 (20%)</td>
<td>3 (19%)</td>
</tr>
<tr>
<td>GCS</td>
<td>15 (2)</td>
<td>15 (2)</td>
</tr>
<tr>
<td>NIHSS</td>
<td>9 (10)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>177±31</td>
<td>180±31</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>96±19</td>
<td>97±19</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>123±21</td>
<td>124±21</td>
</tr>
<tr>
<td>Time from symptom onset to first CTP, h</td>
<td>20.2 (25.7)</td>
<td>21.7 (25.7)</td>
</tr>
<tr>
<td>Time between CTP scans, h</td>
<td>2.1 (0.50)</td>
<td>2.1 (0.59)</td>
</tr>
<tr>
<td>Hemorrhage location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar</td>
<td>7 (35%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>6 (30%)</td>
<td>5 (31%)</td>
</tr>
<tr>
<td>Lentiform</td>
<td>5 (25%)</td>
<td>5 (31%)</td>
</tr>
<tr>
<td>Caudate</td>
<td>1 (5%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>1 (5%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhage volume, mL</td>
<td>21.1±12.9</td>
<td>15.1±14.1</td>
</tr>
<tr>
<td>Intraventricular extension</td>
<td>8 (40%)</td>
<td>6 (38%)</td>
</tr>
<tr>
<td>Intraventricular hemorrhage volume, mL</td>
<td>3.0±5.9</td>
<td>3±2.65</td>
</tr>
<tr>
<td>Total intracranial hemorrhage volume, mL</td>
<td>24.1±20.4</td>
<td>18.3±17.9</td>
</tr>
</tbody>
</table>

Mean=standard deviation; median (interquartile range).

CTP indicates CT perfusion; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; and NIHSS, NIH Stroke Scale.

Table 2. Effects of Blood Pressure Management

<table>
<thead>
<tr>
<th></th>
<th>Treated Patients (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of First CTP</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>168±21</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>90±15</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>116±15</td>
</tr>
<tr>
<td>Relative perfusion measures</td>
<td></td>
</tr>
<tr>
<td>Perihematoma rCBF</td>
<td>0.89±0.11</td>
</tr>
<tr>
<td>Hemispheric rCBF</td>
<td>0.99±0.07</td>
</tr>
<tr>
<td>Perihematoma rCBV</td>
<td>0.94±0.12</td>
</tr>
<tr>
<td>Hemispheric rCBV</td>
<td>1.04±0.09</td>
</tr>
<tr>
<td>Perihematoma rMTT, s</td>
<td>−0.09±0.76</td>
</tr>
<tr>
<td>Hemispheric rMTT, s</td>
<td>0.30±0.71</td>
</tr>
<tr>
<td>Perihematoma rTmax, s</td>
<td>0.91±0.84</td>
</tr>
<tr>
<td>Hemispheric rTmax, s</td>
<td>0.21±0.43</td>
</tr>
</tbody>
</table>

CBF indicates cerebral blood flow; CBV, cerebral blood volume; CTP, CT perfusion; MTT, mean transit time; r, relative; and Tmax, impulse response time to peak.

Sources of Funding

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Disclosures

None.

References


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Figure S1. Linear regression demonstrated no relationship between changes in systolic blood pressure (BP) and perihematoma relative cerebral blood flow (rCBF) ($\beta=0.001$, [-0.002, 0.003], $P=0.63$).