Cerebral Blood Flow Reserve Assessment in Symptomatic Versus Asymptomatic High-Grade Internal Carotid Artery Stenosis

N. Nighoghossian, MD; P. Trouillas, MD; B. Philippon, PhD; R. Itti, PhD; P. Adeleine, PhD

Background and Purpose  Thromboembolic stroke is likely to occur in patients with a restricted cerebral blood flow reserve. Our aims were to determine (1) whether symptomatic patients had any significant hemodynamic restriction ipsilateral to carotid occlusive disease compared with patients whose carotid stenosis is asymptomatic and (2) whether patients with carotid occlusive disease have impaired cerebral perfusion reserve compared with control subjects.

Methods  We compared cerebral blood flow and collateral capacity using the \(^{133}\)Xe inhalation method and acetazolamide test in symptomatic (n=10) and asymptomatic (n=10) patients who had a high-grade internal carotid artery stenosis (range, 70% to 99%). Results were compared with those from 10 healthy control subjects.

Results  Mean baseline cerebral blood flow was 40.29±1.38 mL/100 g per minute on the symptomatic side in symptomatic patients versus 45.20±2.53 mL/100 g per minute on the lesion side in asymptomatic patients (control subjects, 46.91±2.11 mL/100 g per minute in the right hemisphere versus 46.17±1.93 mL/100 g per minute in the left). There was no statistical difference between patients in symptomatic and asymptomatic groups versus control subjects (P>.10). Mean cerebral blood flow increase after acetazolamide was in the same range in symptomatic (52.89±2.54 mL/100 g per minute) and asymptomatic (56.22±3.35 mL/100 g per minute) patients (P>.10), and no difference was observed regarding control subjects (54.25±2.94 mL/100 g per minute; P>.10). Three asymptomatic and two symptomatic patients and three control subjects had no significant cerebral blood flow increase after acetazolamide.

Conclusions  An additional hemodynamic factor in thromboembolic ischemia related to severe unilateral carotid stenosis might be an unusual finding in patients without apparent hemodynamic induction of symptoms. The lack of significant variation in postacetazolamide cerebral blood flow in some patients and control subjects implies that this procedure may be inconsistent in assessing the cerebral perfusion reserve in the individual case. (Stroke. 1994;25:1010-1013.)

Key Words  • acetazolamide  • carotid artery diseases  • cerebral blood flow

The importance of hemodynamic factors in the pathogenesis of focal cerebral ischemia remains unclear, whereas embolic risk increases with severe internal carotid artery (ICA) stenosis.1 The degree of vessel occlusion correlates poorly with the hemodynamic status of the ipsilateral cerebral circulation.3 Previous studies4,5 have demonstrated a poor outcome after ICA occlusion in patients having an insufficient collateral circulation via the circle of Willis. There is also evidence suggesting that areas of brain tissue with marginal perfusion may be more susceptible to the effect of microemboli.9 Accordingly, thromboembolic transient ischemic attacks (TIAs) or reversible ischemic neurological deficit (RIND) might be expected in patients with a restricted collateral capacity. The usefulness of an acetazolamide test in assessing the cerebral perfusion reserve7 has been well established. Reduced cerebral vasoreactivity may be an early indication of a reduced collateral potential and a subsequently greater risk of developing an ischemic stroke.8 The adverse effects of extracranial arterial occlusive disease on cerebral blood flow (CBF) reserve have previously been somewhat overestimated, as postmortem studies9,10 showed that ICA occlusion frequently remains asymptomatic.

In the present study our aims were to determine first whether symptomatic patients had any significant hemodynamic restriction ipsilateral to carotid occlusive disease compared with patients whose carotid stenosis is asymptomatic and second whether patients with carotid occlusive disease have impaired cerebral perfusion reserve compared with control subjects.

Subjects and Methods  From August 1989 to June 1993, we prospectively studied 20 patients (17 men and 3 women aged 52 to 78 years; mean, 64±14 years) referred to our stroke unit and in whom documented obstructive disease of the ICA was found. Ten patients were asymptomatic (mean age, 65±13 years), and 10 patients (mean age, 63±12 years) experienced either TIAs (n=4) or RIND (n=6). Head computed tomographic (CT) scan was performed in a mean of 2 days (range, 12 hours to 5 days) after the last ischemic event. Patients who had a history of stroke or cerebral CT evidence of recent or old infarct were excluded. The patients had experienced no symptoms from the contralateral cerebral hemisphere or the brain stem. This selection was made to avoid the effects of cerebral infarction on the CBF studies. No patient had orthostatic provoked symptoms that suggested a hemodynamic mechanism. Electrocardiography and transthoracic echocardiography ruled out any cardioem-
bolic cause of cerebral ischemia. Stenosis was assessed using conventional arteriography and pulsed Doppler ultrasound studies. In asymptomatic patients angiography was done before coronary artery bypass surgery (7 patients) or followed by neck ultrasound when a carotid bruit was heard (3 patients). In symptomatic patients angiography was performed between the fourth and sixth day after the last ischemic event. The degree of stenosis was expressed as the maximum percentage reduction in the diameter of the carotid artery according to the criteria of the European Carotid Surgery Trialists.11

CBF estimation was carried out 4 to 10 (median, 7) days after angiography. A double-headed camera (Rota camera, Siemens-France) equipped with two low-resolution (maximum, 15 mm), high-efficiency collimators was used to estimate CBF during a period of 2 minutes after 1.5 minutes of inhalation of $^{133}$Xe. Count rates ranged between $3 \times 10^4$ to $4 \times 10^4$ detected within 4 minutes over each hemisphere. The inhalation gas mixture contained approximately 50 to 70 mBq/L $^{133}$Xe at the time of differences between sides, before and after acetazolamide, and groups were assessed with repeated-measures ANOVA with two within factors, side and acetazolamide, and one grouping factor. Computations were performed with the ssr statistical software package.

**Results**

In the symptomatic group, 8 patients had a unilateral ICA stenosis ranging between 90% to 99%, and 2 had stenosis ranging between 80% to 90%. In asymptomatic patients, ICA stenosis was estimated between 80% to 90% in 3 patients and between 90% to 99% in 7. Intracranial vessel study did not show any stenosis on carotid siphon or middle cerebral artery. All asymptomatic patients versus 9 in the symptomatic group had collateral flow through the anterior or posterior communicating arteries. Extracranial-intracranial collateral flow through the ophthalmic artery was depicted in 1 asymptomatic patient. Table 1 and 2 summarize clinical, CBF, and angiographic data, respectively, in asymptomatic and symptomatic patients. Table 3 compares CBF

**Statistical Analysis**

The results are presented as mean±SEM. The significances of differences between sides, before and after acetazolamide, and groups were assessed with repeated-measures ANOVA with two within factors, side and acetazolamide, and one grouping factor. Computations were performed with the ssr statistical software package.
versus 3 of the control subjects. No side effects occurred after the administration of acetazolamide.

ACZ indicates acetazolamide. Data are mean ± SEM mL/100 g per minute.

Discussion

Hemodynamic compromise in occlusive cerebrovascular disease can be estimated by the response to acetazolamide.8 CBF hyporeactivity to acetazolamide is generally accepted as a method for identifying patients with a restricted collateral capacity in whom carotid endarterectomy could be useful.14-15 A recent study16 showed that surgery restored baseline CBF values and cerebral vasoreactivity in patients with symptomatic ICA. Nevertheless, patients with convincing signs of carotid distribution "insufficiency" in the hemodynamic sense are rare.17,18

Powers3 has suggested that patients with impaired perfusion reserve may be more likely to have stagnant flow close to the carotid lesion, which would increase their risk of artery-to-artery thromboembolism. Though the limited number of subjects in each group might prevent the assessment of any difference, no statistically significant difference was found between CBF of symptomatic and asymptomatic patients after the acetazolamide test. Therefore, we can anticipate that an additional hemodynamic factor in thromboembolic ischemia related to severe high-grade ICA stenosis might be lacking. However, cerebrovascular reserve impairment that is often detectable in restricted areas2 could have been missed, as our estimation of CBF was made over the whole hemisphere.

The lack of hemodynamic factors such as arterial hypotension, positional changes, or exertion might explain these results because an abnormal vasodilatory response is usually expected in patients who have...
TABLE 4. Analysis of Differences in Cerebral Blood Flow Between Patients and Control Subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients (n=20)</th>
<th>Control Subjects (n=10)</th>
<th>Difference (Patients—Control Subjects)</th>
<th>95% Confidence Interval of Mean Difference</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF Before ACZ</td>
<td>42.71±1.51</td>
<td>46.54±1.99</td>
<td>-3.83±2.56</td>
<td>-9.08, 1.42</td>
<td>.15</td>
</tr>
<tr>
<td>CBF After ACZ</td>
<td>54.87±2.14</td>
<td>54.77±2.78</td>
<td>0.11±3.61</td>
<td>-7.29, 7.51</td>
<td>.98</td>
</tr>
<tr>
<td>CBF After—before</td>
<td>12.60±1.92</td>
<td>8.23±1.20</td>
<td>3.93±2.27</td>
<td>-0.70, 8.57</td>
<td>.09</td>
</tr>
</tbody>
</table>

CBF indicates cerebral blood flow; CI, confidence interval; and ACZ, acetazolamide. CBF is the average value of both sides, mean±SEM.

*Student's two-tailed test.

References


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