Action of Vasodilators on Regional Cerebral Blood Flow in Subacute or Chronic Cerebral Ischemia

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SUMMARY Regional cerebral blood flow (bicompartmental and stochastic method) was measured in a series of 20 patients with unilateral brain softening. Measurements were repeated during the administration of a vasodilator. A detrimental effect on the perfusion of the diseased area was observed in the majority of cases. It has been shown that the chances for a vasodilator to decrease the perfusion in the diseased area were greater when the angiogram showed obstruction of an intracranial artery.

Methods

Patients

Twenty patients (11 men and nine women) aged 17 to 77 years (average 53 years) were studied. Of these, 19 had unilateral brain softening and one had diffuse arteriopathy with cerebral atrophy (Patient P4). They were investigated at least one week after the stroke except for Patient P6, who was investigated after four days. The location of the brain softening was determined by neurological examination and an EEG done by the same observer (A.C.). All patients underwent an angiographical study on the affected side (carotid angiogram alone in 17, both carotid and vertebral angiograms in three). The angiogram was never performed on the same day as the blood flow measurement.

Pharmacological Tests

The following drugs were investigated: in patient series F, halothane, 1% in O₂-N₂O gas mixture (Fluothane®, I.C.L.); in patient series P, papaverine chloridehyde, 100 mg in i.v. drip; in patient series D, methoxy-6-quinolil-4-1-vynil-2 piperidyl-5-3-propanol-1-chlorhyde, 80 mg in i.v. drip (Descidium®, S.P.R.E.T.); and in patient series V, vincamine chloridehyde, 40 mg in i.v. drip (Pervone®, Millot Laboratories, France). Each drug was administered for 30 minutes after the end of the first measurement and continued for the duration of the second measurement.

Results

Location of the Diseased Area

The location of the brain softening, as determined from clinical data, was in the territory of the anterior cerebral artery in one patient (hemiparesis prominent in lower limb), in the territory of the middle cerebral artery in 17 patients (hemiplegia and/or hemianesthesia) and in the territory of the posterior cerebral artery in one patient (hemianopia). In two patients (P4 and P6), the angiogram was normal. It showed stenosis of the internal carotid artery in two patients (P1 and P2), stenosis of the anterior cerebral artery in one (F4), displacement of some cerebral arteries (edema?).
FIGURE 1. Relative decrease in flow induced in the diseased area. Patient D1: 43-year-old woman with paresthesias in the right hand, right superior quadrantanopia, and thrombosis of the left rolandic artery. (A) Gray matter flow in 25 regions during control measurement. Flow increased (+) or decreased (−) by more than 24% (black) or by 12% to 23% (hatched) as compared to the mean of the whole hemisphere (PCO₂: 39.1 ± 0.56, BP: 84). (B) Increase in flow during perfusion of Desclidium™ by more than 4 SD (black) or between 2 and 4 SD (hatched) (PCO₂: 39.4 ± 0.79, BP: 83). (C) Regional CBF determined by the stochastic method during the control measurement (PCO₂: 39.1 ± 0.56, BP: 84). (D) Differential printout of the increases in flow (stochastic method) under the action of Desclidium™ (PCO₂: 39.4 ± 0.39, BP: 83).

in two (P5 and D2), thrombosis of the posterior cerebral artery in one (P3), and complete or partial thrombosis of the middle cerebral artery in all the other patients.

Values of Regional CBF

Individual values of the flows in the various regions of the explored hemisphere were used to establish the "mean" cerebral blood flow (table 1). With the bicompartmental method, the mean value was 44.14 ± 6.47 ml/100 gm per minute for the gray matter and 17.18 ± 2.48 ml/100 gm per minute for the white matter. With the stochastic method, the mean regional CBF was equal to 25.22 ± 5.81 ml/100 gm per minute.

CBF in the Diseased Areas

In the diseased area, the flow in the gray matter was found to be decreased in ten cases, increased in four and not significantly different from the whole of the hemisphere in four. In two cases an increased flow surrounded by ischemia was found in the diseased area. The duration of the disease was 14 ± 10 days in the series of patients with an increased flow and 37 ± 25 days in those with a decreased flow in the softened area.

Effect of the Vasodilators on CBF

The action of the various drugs on the mean blood flow of the hemisphere is shown in table 2. In the diseased area itself, the CBF was either increased or decreased (fig. 2) or relatively decreased, i.e., unmodified as opposed to an increase in flow in the surrounding normal regions (figs. 1B and D).

As shown in table 2, the results obtained by both measurement procedures were similar except for patients F3 and D1. In Patient D1, a discrepancy was noted between the clinical...
Table 1  Individual Values of Regional CBF

<table>
<thead>
<tr>
<th>Case</th>
<th>BP*</th>
<th>BP†</th>
<th>PC01</th>
<th>PC02</th>
<th>Fg†</th>
<th>Fg‡</th>
<th>ΔFg</th>
<th>FW†</th>
<th>FW‡</th>
<th>ΔFW</th>
<th>rCBF*</th>
<th>rCBF†</th>
<th>ΔrCBF</th>
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<tr>
<td>F1</td>
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<td>0.65</td>
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<td>13.4</td>
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<tr>
<td>F2</td>
<td>68</td>
<td>66</td>
<td>38.1</td>
<td>1.06</td>
<td>41.0</td>
<td>5.65</td>
<td>54.4</td>
<td>56.1</td>
<td>+3.2</td>
<td>18.6</td>
<td>16.7</td>
<td>-10.0</td>
<td>36</td>
</tr>
<tr>
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<td>80</td>
<td>80</td>
<td>34.9</td>
<td>0.14</td>
<td>34.7</td>
<td>0.92</td>
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<td>62.6</td>
<td>+13.8</td>
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<td>-4.2</td>
<td>32</td>
</tr>
<tr>
<td>F4</td>
<td>83</td>
<td>42</td>
<td>39.4</td>
<td>1.41</td>
<td>38.7</td>
<td>1.63</td>
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<td>1.63</td>
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<tr>
<td>F6</td>
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<td>15.3</td>
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BP: mean arterial blood pressure. Fg: average flow in gray matter. FW: average flow in white matter. rCBF: average flow determined by the stochastic method. ΔFg, ΔFW, ΔrCBF: variations in average flows (in percentage). † = first measurement, ‡ = second measurement.

Data which suggested a temporal lesion (superior quadrantanopia) and the angiogram which demonstrated a thrombosis of the rolandic artery. The two measuring procedures led to contradictory conclusions concerning the flow in the temporal lobe, but both agreed on a relatively decreased perfusion produced by the vasodilator in the territory of the rolandic artery (fig. 1).

Correlation With Angiographical Data

Thrombosis of one of the cerebral arteries was demonstrated by angiography in 11 patients. In the majority of these (table 2), an unfavorable effect of the drug on the diseased area was shown by the bicompartmental method (eight decreases in flow versus one increase) as well as by the stochastic method (eight decreases in flow versus two increases). In eight patients with no demonstrable arterial thrombosis, opposite proportions were observed: two decreases in flow versus six increases (bicompartmental method) and one decrease in flow versus five increases (stochastic method).

Discussion

Recording the radioactivity of the skull with a gamma camera allows the brain surface to be subdivided at will. With the data being stored in a magnetic memory, this subdivision can be modified later; new regions of interest can be chosen according to the clinical data or the results of previous measurements.

When a high resolution is desired, a maximum number of channels (600 to 800) are used. The counting rate in each channel is equal to 600/10 seconds on an average, with a standard deviation of 15%. Of course, the size of the individual areas studied in this way is smaller than the minimum authorized by the resolution of the device, which is approximately 20 × 20 mm². The image of the flow distribution has the same resolution as a static brain scan obtained with the same gamma camera. Areas of similar perfusion thus delineated are made of a certain number of unitary areas which do not differ statistically from their neighbors (fig. 1).

In order to insure precise measurement as well as a maximum discrimination of regional differences in the flows, two methods of calculation were used simultaneously in this work. The results were actually similar in all cases except two (table 2).

The bicompartmental method, yielding specific information on the flow in the gray matter, is used for the determination of abnormal perfusions in the control measurement. Although the distribution of the grey matter flows is uneven in a normal brain, it is even more so for the flows determined by the stochastic method; indeed, they depend essentially on the relative volume of the highly perfused gray matter. A high flow area is normally observed along the upper border of the brain image (corresponding to a two-fold cortical layer) and in the insular region (corresponding to the folds of the insular cortex and the basal ganglia). Nevertheless, the stochastic method, by the differential printout of the two measurements (independent of the gray matter volume) gives valuable information about the redistribution of the flows caused by the vasodilator.

General anesthesia was used to maintain a steady position of the head and stable respiratory parameters with a constant arterial Pco₂. This insures a better reproducibility of the two measurements, as shown previously in a series of six patients. According to the method of Wilkinson et al., the average standard deviation of our two measurements in the...
same region was found to be 6.2% for the flow in the gray matter and 7.7% for the flow in the white matter.  

The average values obtained for the regional cerebral blood flows (25.22 ml/100 gm per minute) are definitely lower than normal. This is not due to a reduction of brain metabolism under general anesthesia because the same method, applied under local anesthesia in a series of six patients (mean age 63 years) with a brain tumor, yielded similar values for regional CBF (28.31 ± 7.67 ml/100 gm per minute). It is more likely due to a general reduction of the perfusion of the whole hemisphere, as usually noted in regional brain ischemia.

In addition, the values obtained for the flows are lower when the duration of the washout recording is longer. This duration was 15 to 17 minutes for the bicompartmental method instead of 10 minutes or less which is commonly used by others. In a series of ten patients, Charlet and Marcel-Vergnes obtained gray matter flows of either 66 ± 7.56 ml or 45.9 ± 2.42 ml according to a recording duration of either 10 or 15.5 minutes. Our investigation was devoted to the redistribution of the flows under the action of the vasodilators and not to the absolute determination of the flows.

We are aware that the method used for localizing the lesion being based on clinical data is open to criticism. Since none of our patients died during the period of observation, no correlation has been made between clinical and pathological data.

In the control measurement, the perfusion of the diseased area was found to be decreased in ten cases and increased in four. Increased perfusion was indeed observed in cases investigated earlier after the stroke (14 ± 10 days instead of 37 ± 25 days), but our difference in delay between the two groups is not as marked as in the data published by Paulson. Halothane decreased the mean arterial blood pressure while the other drugs did not (table 1), but the four drugs had no significantly different effect on the redistribution of the flows. In the entire series of patients, the vasodilator action on the perfusion of the diseased areas was more often

![Figure 2](http://stroke.ahajournals.org/)

**Figure 2.** Absolute decrease in flow in the diseased area. Patient D6: 54-year-old woman with left hemiplegia, hemianesthesia and hemianopia, and thrombosis of the right middle cerebral artery. (A) Variations in the flow in the gray matter in 25 regions under the action of Descludium. Increase in flow (I) or decrease (D) by more than 4 SD (black) or between 2 and 4 SD (hatched) (BP: 90, mean flow in gray matter: 40.8). (B) Differential printout of the variations in regional CBF in the same conditions. Closed circles: decrease, open circles: increase in flow (BP: 90, mean regional CBF: 21).
An Unusual Etiology of Stroke

GRANULOMATOUS ANGIITIS/Burger et al.

SUMMARY A 43-year-old man, who died five months after the onset of left-sided sensory deficit, had angiographical and pathological evidence of an angiitis confined largely to the distribution of the right middle cerebral artery. Histological examination identified this process to be intracranial noninfectious granulomatous angiitis. Although certain clinical and pathological features of this disorder overlap with other vasculitides which affect the central nervous system, the disease nevertheless retains sufficient individuality to warrant status as an entity, and should be considered in the differential diagnosis in adults with lesions which produce focal neurological deficits and signs of increased intracranial pressure.

The definitive answer regarding an infectious etiology will come only from detailed culture studies of the affected vessels.

Introduction

GRANULOMATOUS ANGIITIS is an inflammatory disorder of unknown etiology whose curious preference for vessels of the central nervous system may be expressed clinically as stroke. This report describes the clinical and pathological manifestations of this disorder and considers its nosological position among the other vasculitides which may affect the central nervous system.

Report of a Case

Clinical History

The patient was a 43-year-old black man who was first admitted to Duke University Medical Center on November 9, 1970, for evaluation of repetitive attacks of numbness of the left side of the body which had begun two months previously. The initial attack of 20 minutes' duration was characterized by numbness of the left foot, staggering gait, difficulty with speech, and decreased use of the left arm and leg. Within a week the numbness extended to the entire left side of the body, at which time there was urinary urgency with precipitate micturation, anorexia, and a six-pound weight loss. The patient denied seizure activity, headache, visual disturbance, or loss of consciousness. The past medical history contained no relevant illnesses. Specifically, there was no history of asthma, allergies, sinusitis, or lesions of the skin.

The patient was well developed and cooperative, and did not appear ill. The blood pressure was normal. Decreased deep tendon reflexes and plantar responses were normal. A Hoffmann response was present on the left. There was...

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