Regional Cerebral Blood Flow in Patients With Hypertensive Intracerebral Hemorrhage

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Abstract:
Regional cerebral blood flow was measured by $^{133}$Xe clearance method in 44 patients with hypertensive intracerebral hemorrhage (HIH) within three weeks from attack. Mean CBF in cases with the more disturbed consciousness was the lower value. There was no definite relationship between mean CBF and the duration from last stroke to measurement. In 44 cases, 35 showed hematoma of so-called “lateral type” and nine showed a “mesial type.” There was no difference of mean CBF between these two groups. In the group with lateral-type hematoma, 14 cases were thought to show large space-occupying signs, and their mean CBF was significantly lower than that of the other 21 cases.

In 16 cases, relative hyperemic regions were observed in both the focal and nonfocal areas. In seven cases, relative ischemic regions were frequently in nonfocus rather than focus.

Response of hyperemic region to carbon dioxide was good in seven and poor in three regions in focal area, and was good in three and poor in two regions in nonfocus.

Early venous filling (EVF) was observed in 13 cases and all of them were with lateral-type hematomas. Only four out of 13 cases showed good correlation between angiographical findings and cerebral circulation.

Additional Key Words
- cerebrovascular diseases
- CO$_2$ response
- $^{133}$Xe clearance method
- early venous filling

The development of an isotope clearance method to measure regional cerebral blood flow has added new information to studies of the cerebral circulation.$^{1-4}$ Thereafter, this method has been used for the estimation of regional cerebral circulation in patients with cerebrovascular diseases by many workers.$^{5-14}$ However, most of the reports have been concerned mainly with occlusive cerebrovascular disease.

In this study, regional cerebral blood flow was measured simultaneously on six regions in patients with hypertensive intracerebral hemorrhage (HIH), and a functional test was made using 5% CO$_2$ inhalation at the same time. The purpose of this work was to evaluate the local disturbance of cerebral circulation induced by cerebral hemorrhage and to observe the relationship between cerebral circulation and clinical features.

Methods
This paper presents the results obtained by measuring the regional cerebral blood flow in 44 patients with hypertensive intracerebral hemorrhage. The patients were divided into two groups according to angiographical appearance of the lenticulostriate arteries:$^6$: (1) 35 patients with lateral-type hematoma showing medial displacements of the lenticulostriate arteries, and (2) nine patients with mesial-type hematoma showing lateral displacements of the lenticulostriate arteries. In the former group, the age range was 35 to 71 years with an average age of 51 years; days after the onset of symptoms to time of measurement ranged from three hours to 19 days. In the latter group, the age range was from 40 to 67 years, with an average age of 56 years, and the days after onset of symptoms to time of measurement was six hours to eight days.

The method consisted of a slug injection, lasting one to two seconds, of about 1 mc of $^{18}$Xe dissolved in about 1 ml of sterile saline into the internal carotid artery. The internal carotid artery of the diseased side of a patient was cannulated with a thin polyethylene catheter percutaneously through the common carotid artery using the Seldinger technique under local anesthesia with Procaine hydrochloride without any other premedication. The correct position of the catheter was ascertained by noting visualization of the internal carotid artery after a rapid injection of radiopaque contrast media fluoroscopically. Samples of arterial blood for P$_{CO_2}$ determination were taken through the catheter. The intracarotid blood pressure was continuously measured with an electric manometer.

Each scintillation detector had 1 by 1-inch NaI crystal
and was lodged in a lead collimator block (17 × 12 × 24.5 cm), which had six holes placed 2 cm apart from one another. Each hole constituted a cylindrical collimator which measured 3 cm in diameter and 10.7 cm in length.

The counting areas of the six probes were the upper part of frontal region (channel 1), the lower part of frontal region (channel 2), parietal (channel 3), temporal (channel 4), parieto-occipital (channel 5), and occipital regions (channel 6). The positions of the six probes were assessed by taking x-ray film of the cranium.

The clearance curves were analyzed by Digital computer JEC-7 type. Usually the regional cerebral blood flow was measured two times, that is, two injections of 133Xe were made at intervals of about 15 minutes. The first clearance curves were obtained in the "resting state" and the rCBF values were calculated from the stochastic analysis (rCBFl0) as well as from the initial slope analysis (rCBF initial).

The next set of curves was obtained after the arterial Pco2 had been altered by inhalation of air mixed with carbon dioxide in a concentration of 5 vol %. In the functional test, rCBF was calculated only from the initial part of the logarithmic-recorded clearance curves.

Results

The average value of cerebral blood flow of six regions was 49.3 ml/100 gm brain per minute with SD of ± 6.1 in six normal subjects. The average interregional coefficient of cerebral blood flow was ± 7.2%. Therefore, a finding of an interregional difference exceeding 15% may be thought to be abnormal, as reported by Høedt-Rasmussen et al.,7 and the region with the abnormal interregional difference was designated as the relative hyperemic region or the relative ischemic region.

Interregional difference was expressed as percentage difference between individual mean cerebral blood flow of the six regions and the values for each region.

The reproducibility of rCBF initial was assed in five subjects by two successive measurements of regional cerebral blood flow. The second measurement was carried out about five minutes after the first measurement was completed.

The average difference of rCBF initial between first and second measurements was 4.5% and its standard deviation was 3.3%. Therefore, the region which showed difference exceeding 15% may be thought to have shown significant increase or decrease of rCBF initial during 5% CO2 inhalation.

MEAN CBF OF THE DISEASED HEMISPHERE

It would be said that one of the most important indicators of clinical signs was the state of consciousness after the stroke. Consciousness observed in 44 cases at measurements was as follows: six cases in the state of coma, six cases in stupor, 20 cases in somnolence, and 13 cases in clear consciousness.

The average of mean CBF for each group was: 26.8 ± 5.3, 34.3 ± 3.5, 32.0 ± 5.5, and 36.2 ± 4.8 ml/100 gm brain per minute, respectively. The average of mean CBF of six cases in coma was significantly lower than those of the other three groups (P < 0.05) (fig. 1).

Twenty-four cases had their rCBF measured within two days after the onset of the stroke, and 20 cases were measured from three to 19 days after the episode. The average value of mean CBF of the former was 32.2 ± 5.1, and of the latter was 33.7 ± 6.5 ml/100 gm brain per minute. This result showed no significant difference of mean CBF between these two groups (fig. 2).

Thirty-five cases showed the lateral-type hematoma and nine cases showed the mesial-type hematoma angiographically. The average of mean CBF in the group with the lateral-type hematoma was 33.3 ± 5.8 ml/100 gm brain per minute and that in the group with the mesial-type hematoma was 31.2 ± 5.1 ml/100 gm brain per minute. There was no difference between these results (fig. 3).

It is difficult to assess the size of hematoma in a patient with an intracerebral hemorrhage by findings of carotid angiography. However, we tried to measure the shift of arteries and to appreciate the space-occupying signs in the cerebral angiogram which showed the lateral-type hematoma. In 35 cases with the lateral-type hematoma, 14 cases were evaluated to show the large mass signs angiographically. The average of mean CBF of them was 29.1 ± 6.3 ml/100 gm brain per minute and of the 21 cases without large mass signs was 36.0 ± 3.7 ml/100 gm brain per minute. Mean CBF of the patients with large mass signs was significantly lower than that of the other 21 cases (P < 0.01) (fig. 4).

LOCAL ABNORMALITIES

In this study, rCBF was estimated in six regions on the diseased hemisphere of the patient's head, and three channels (Nos. 2, 3, and 4) were thought to be nearest
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FIGURE 2
Correlation between mean CBF and the interval from onset to test: mean CBF ± SD (ml/100 gm brain per minute).

FIGURE 3
Difference of mean CBF between patients with lateral-type and those with mesial-type hematomas: mean CBF ± SD (ml/100 gm brain per minute).

to the hematoma and to show the changes influenced by the damage of the cerebral hemorrhage. Therefore, channels 2, 3, and 4 were designated as focal area or focus and the others as nonfocal area or nonfocus.

In 16 cases, 11 relative hyperemic regions were observed in the focal area and nine relative hyperemic regions were in the nonfocal area. There was no difference in the interval from onset to the state of consciousness between cases with the hyperemic region in focus and those with hyperemic region in nonfocus.

In seven cases, three relative ischemic regions were observed in focus and five relative ischemic regions were in nonfocus.

There was no difference in the interval from onset to the state of consciousness between cases with the ischemic region in focus and those with the ischemic region in nonfocus (fig. 5).

pCBF CHANGES INDUCED BY 5% CO2 INHALATION
The response to hypercapnia was appreciated in 37 out of 44 cases. Global loss of response to hypercapnia was observed in four patients with the lateral-type hematoma (cases 5, 36, 43, and 45) and in two patients with the mesial type of hematoma (cases 25 and 29). All but one of the patients measured their cerebral circulation within five days after the onset of the stroke. They all showed no focal abnormalities. But, there was no coincidence concerning the state of consciousness at measurements and space-occupying signs in these six cases.

Response of hyperemic region to carbon dioxide was good in seven and poor in three regions in focal area, and was good in eight and poor in one region in nonfocal area.

Reactivity of ischemic region to 5% CO2 inhalation was good in three and poor in zero regions in focus, and was good in three and poor in two regions in nonfocus (fig. 6).

EARLY VENOUS FILLING
Early venous filling (EVF) could be observed in 13 cases, and all of them were with lateral-type hematomas. All but one of the cases were examined within three days after their last episodes of cerebrovascular disease. Six cases had large space-occupying signs. Consciousness was variable in 13 cases but motor disturbance was severe in most cases.
Five cases had EVF of the internal cerebral vein (ICV), three cases had EVF of the deep veins, two cases had EVF of both deep veins and sylvian veins, two cases had EVF of sylvian veins, and one case had EVF of the sylvian vein and parieto-occipital vein. Six of 13 cases had the relative hyperemic regions in their diseased hemispheres, but only four cases showed good correlation between angiographical findings and cerebral circulation. Two of four cases had EVF of ICV or deep veins, one case had EVF of ICV and sylvian vein, and the remaining case had EVF of the sylvian vein and parieto-occipital vein. This last case had two relative hyperemic regions and these findings corresponded with each other very well. Response to CO$_2$ inhalation was kept well at the relative hyperemic regions in three out of four cases (one case was not tested for CO$_2$ reactivity).

**Discussion**

A few cases with large space-occupying signs did not show the lower mean CBF. This was due perhaps to the difficulty in assessments of hematomas in cerebral angiograms. On the other hand, the hematomas could not be sufficiently reflected in some cases, as the shifting of arteries or sometimes the size of hematoma would not agree with the extent and degree of damage in the hemisphere. Most cases showed lower values of mean CBF, that is, cerebral damage should be more severe and cerebral perfusion more decreased in most cases with acute cerebral hemorrhage than in cases with occlusive cerebrovascular disease, and this hypoperfusion might be kept longer during the acute stage of cerebral hemorrhage. There was no difference between mean CBF of cases with lateral-type hematoma and those with mesial-type hematoma, although clinical signs and symptoms were more marked in the latter than in the former. This means that cerebral circulation may be disturbed similarly in most cases with cerebral hemorrhage, regardless of the location of lesions, or this clearance method would...
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FIGURE 6

Cerebrovascular response to hypercapnia observed in the abnormal regions.

not be able to notice the decreased cerebral blood flow in patients with mesial-type hematoma. It seems likely that this measurement could detect the relatively superficial changes but could not reflect sufficiently the disarrangements located in the deeper layers of the diseased hemispheres.

Ekberg et al.⁶ and Ingvar¹⁷ found that a generalized decrease of rCBF was measured in all regions, and especially a marked decrease in rCBF over the region corresponding to the hematoma.

Jaffe et al.¹² reported that decreases in blood flow had been correlated with the angiographical area of vascularity and displacements of vessels and marked decreases in hemispheric mean CBF had been associated with severe clinical features in six cases of intracerebral hemorrhage. On the contrary, Agnoli et al.¹⁸ found that focal hyperemia was never in the cortical portions of the lesion, but rather in the neighboring regions (such as the frontal, parietal and occipital) in four out of seven cases with cerebral hemorrhage. They also observed that cases with marked brain edema had a diffusely low blood flow while cases without brain edema showed hyperemic foci.

In this series, the region with abnormal value could be found, even if it had been the relative hyperemic region or the relative ischemic region, not only in the neighboring area but also in the remote area of hematoma. Abnormal foci were observed in all regions of the diseased hemispheres and did not show the definite location in patients with cerebral hematomas; this would be appreciably different from the regional circulation disclosed both in patients with occlusive cerebrovascular disease and in patients with hemorrhagic lesions reported previously. In cerebral hemorrhage it seems likely that regional circulation was influenced not only by the location and size of the lesion but also by its extent and direction of hematoma. At the same time, secondary changes, that is, cerebral edema of surrounding area and elevation of intracranial pressure, would cause damage in other areas and make the derangement of cerebral circulation more complex.

Hjøedt-Rasmussen et al.⁷ reported that focal hyperemia in acute apoplexy was caused by the "luxury perfusion syndrome," which was first discussed by Lassen,,¹⁹ and vasomotor paralysis in focal hyperemic area might be considered as a basic abnormality of the local circulation in apoplexy. In the present study, cerebrovascular reactivity was examined by using a mixture of 5% CO₂ and air and the global loss of response to hypercapnia was observed in six cases tested within five days from stroke. This time interval was similar to that verified in cases with cerebral hemorrhage reported previously.⁵ Consciousness and space-occupying signs were different among these six cases as Fieschi et al.²⁰ found no definite correlation with the severity of the clinical features. In 16 cases with relative hyperemic region, four regions showed poor response to hypercapnia induced by 5% CO₂ inhalation and three of them were adjacent to the lesions. This finding means that some cerebral vessels surrounding the hematoma would be in a state of maximal dilatation, perhaps due to local tissue acidosis.¹⁹ However, some cases showed abnormal regions without response to CO₂ in the area located far from the hematoma and demonstrated the complexity of local cerebral circulation.

All the 13 cases showing EVF had the lateral-type hematoma. Similar findings were observed in cases with occlusive cerebrovascular disease in all but one of
the cases with EVF examined within three days from onset.7

Cronqvist et al.,21 Cronqvist and Laroche,22 Hjødt-Rasmussen et al.,7 and Cronqvist22 reported that angiographical findings, such as early venous filling or capillary blush, were often correlated with hyperemic region. However, only four of these 13 cases showed good correlation between cerebral angiographical findings and regional circulation. EVF observed in cases with occlusive disease would be relatively superficial and those changes could be detected by the clearance method. On the other hand, in patients with cerebral hemorrhage, their lesions were located in the deeper parts of the brain and hyperemia could not be easily verified. The detector unit used in this series had only six probes and the crystals were the larger ones, so we were unable to verify the complex changes in many cases.

Relative ischemic regions were found much less frequently than relative hyperemic regions in patients with cerebral hemorrhage. This is due perhaps to the number of probes and size of crystal in the detector unit used for this study. But, the reason is uncertain why most of the relative ischemic regions showed good response to hypercapnia.

References