Bilateral Hemispheric Reduction of Cerebral Blood Volume and Blood Flow Immediately After Experimental Cerebral Hemorrhage in Cats

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Acute cerebral circulatory changes following experimental cerebral hemorrhage were investigated in eight cats. The cerebral hemorrhage was produced in the right basal ganglia by introducing arterial blood via a thin catheter, using the systemic arterial blood pressure of the cat as a driving force. Local cerebral blood volume was measured continuously in the bilateral parietotemporal cortices employing photoelectric apparatuses. Carbon black dilution curves were recorded from the regions, and the mean transit time of blood was calculated. Local cerebral blood flow was estimated from mean transit time and cerebral blood volume. Intracranial pressure was monitored continuously in the right parietal epidural space. Five minutes after cerebral hemorrhage, intracranial pressure increased by 24.0 ± 6.1 mm Hg, while mean arterial blood pressure increased by only 2.9 ± 2.0 mm Hg. Cerebral blood volume decreased by 1.60 ± 0.24 vol% in the hemorrhagic and 1.14 ± 0.30 vol% in the nonhemorrhagic hemisphere. Cerebral blood flow decreased by 30.0 ± 4.5 ml/100 g brain/min in the hemorrhagic (initially 64.5 ± 13.6) and by 30.3 ± 7.5 ml/100 g brain/min in the nonhemorrhagic (initially 60.9 ± 6.9) hemisphere. Increased intracranial pressure appeared to be the main cause of the observed cerebral blood volume/flow reduction shortly after experimental hemorrhage in the basal ganglia. Several other factors and mechanisms involved are discussed. (Stroke 1988;19:991–996)

Information on the cerebral hemodynamics is indispensable for the appropriate management of patients with acute cerebral hemorrhage. In contrast to cerebral ischemia, however, there have so far been few clinical1–5 or experimental6–7 studies on the cerebral circulation following cerebral hemorrhage, especially at its acute stage. The unpredictable onset and the absence of suitable methods for monitoring the cerebral circulation may have precluded a positive approach to the pathophysiology of acute cerebral hemorrhage. A decrease in cerebral blood flow (CBF) has been demonstrated in intracranial hypertension caused by brain tumor,8 an expanded intracranial balloon,9,10 and subarachnoid injection of fluids.11–13 However, cerebral hemodynamic changes following hemorrhagic assault may not be explained simply on the basis of the resultant lesion as an intracranial mass; the anatomic location and spatial evolution of the hematoma formed, its rate of expansion, and the biochemical activity of the extravasated blood must also be taken into consideration.

We recently developed a new experimental model of cerebral hemorrhage in which a moderate-sized hematoma was produced in the basal ganglia of cats using the systemic arterial blood pressure (SABP) of the cat itself as a driving force for hematoma formation. The purpose of our study was to investigate the changes in intracranial pressure (ICP), cerebral blood volume (CBV), and CBF immediately after such experimental cerebral hemorrhage by means of our photoelectric method.14–16

Materials and Methods

The experiments were carried out on eight adult cats of either sex weighing 2.7–4.5 kg. The cats were anesthetized by intraperitoneal injection of 50 mg/kg α-chloralose and 500 mg/kg urethane supple-
mented with 0.5% procaine hydrochloride for local anesthesia. After endotracheal intubation and immobilization with small amounts of alcuronium chloride, respiration was controlled with a respirator (model 662, Harvard, South Natick, Massachusetts). Rectal temperature of the cats was maintained at 37–37.5°C using a heating blanket. Thin polyethylene catheters were inserted into the right lingual and left brachial arteries. The catheters were used for injection of carbon black solution into the carotid artery and for removal of arterial blood, respectively. Another polyethylene catheter was inserted into the femoral artery and used for monitoring SABP with a pressure transducer (model 662, Harvard, South Natick, Massachusetts). The head of each cat was fixed in a stereotactic head-holder (type SN-1, Narishige, Tokyo, Japan), and the scalp was incised and reflected at the midline.

Local CBV was monitored continuously with the photoelectric apparatus developed by Tomita et al. It comprised a 1.0 mm o.d. miniature lamp (Hamai Electric, Tokyo) and a silicon photodiode (Sharp Electric, Tokyo) covered with two sheets of bandpass filter (Fuji Photo Film, Tokyo). As shown in Figure 1, the lamps were inserted with scrupulous care into the brain tissue, to a depth of approximately 5 mm from the surface, in the bilateral parietotemporal regions through a small cranial hole. The photodiodes were attached to the inner layer of the skull just above the inserted lamps. The silicon photodiodes detected the redness or intensity of the light transmitted through a thin layer of the cerebral cortex, which was continuously recorded on a DC recorder (model PG-6, Rikadenki, Tokyo). The intensity of the light was then calibrated to the CBV. To obtain tissue carbon black dilution curves from the same regions, 0.1 ml of 1:40 diluted physiological carbon black solution (Pelikan ink) was injected into the right carotid artery via the lingual artery. The tissue dilution curves were drawn, overlapping on the CBV recordings. The mean transit time of blood (MTT) was estimated from the tissue carbon black dilution curve using the conventional area-over-height method. Local CBF was calculated by adapting the Stewart-Hamilton equation.

Experimental cerebral hemorrhage was produced by the following procedure. Through a small cranial hole, a thin (0.8 mm o.d.) polyethylene catheter was inserted meticulously into the right basal ganglia using a stereotactic technique. The other end of the catheter was connected to a stopcock, which was also connected to the catheter inserted into the left brachial artery. By opening the stopcock, brachial arterial blood was introduced into the basal ganglia. Usually, blood flow through the catheter stopped spontaneously within 1 minute. ICP in the hemorrhagic hemisphere was monitored with a pressure transducer (model AA2460, Toyoda Machine Works) through a 1.0 mm o.d. polyethylene catheter inserted into the right parietal epidural space. All cranial holes were tightly plugged with dental cement (Duracron) to ensure a closed system within the cranium.

Local CBV in both hemispheres, ICP, and SABP were measured continuously during the experiment. After obtaining tissue carbon black dilution curves under steady-state conditions, experimental cerebral hemorrhage was produced, and additional tissue carbon black dilution curves were obtained approximately 5 minutes thereafter. One hour after the induction of hemorrhage, the brain of each cat was removed for pathologic examination. The tip of the catheter inserted for producing hemorrhage and the size and location of the hematoma were determined.

Data are presented as mean ± SEM. Statistical analysis was performed using Student's t test and Wilcoxon's signed rank test.

**Results**

Figure 2 shows a photograph of a coronal section of an autopsied brain, which was obtained after one of the experiments. A moderate-sized hematoma was present in the right basal ganglia, and the hemorrhagic hemisphere was slightly edematous. Similar hematomas in the basal ganglia with or without ventricular perforation were found in all eight cats. Ventricular dilatation was not observed. One cat with massive subarachnoid hemorrhage, which intrinsically prevented measurement of CBV,
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Reduced CBV in Cerebral Hemorrhage

ICP

CBV\textsubscript{h}

CBV\textsubscript{c}

SABP

FIGURE 3. Example of recordings in a cat of intracranial pressure (ICP), cerebral blood volume in hemorrhagic (CBV\textsubscript{h}) and nonhemorrhagic (CBV\textsubscript{c}) hemispheres, and systemic arterial blood pressure (SABP) during induction of basal ganglia hemorrhage. ICP increased shortly after cerebral hemorrhage, followed by reduction in CBV\textsubscript{h} and CBV\textsubscript{c}.

was excluded from the analysis. An example of the continuous recordings of ICP, CBV in the hemorrhagic and nonhemorrhagic hemispheres, and SABP before and after experimental cerebral hemorrhage is presented in Figure 3. ICP began to increase abruptly approximately 15 seconds after the induction of cerebral hemorrhage, reached a peak of approximately 30 mm Hg above the control level within 1 minute, and tended to decrease gradually thereafter. CBV in the hemorrhagic and nonhemorrhagic hemispheres began to decrease simultaneously approximately 30 seconds after the beginning of the ICP elevation, and the reduction continued throughout the observation period. The small downward arrows in Figure 3 indicate injections of carbon black solution into the carotid artery; these are followed by carbon black dilution curves overlapping on the CBV recordings. MTT calculated from the carbon black dilution curves was delayed in both hemispheres 5 minutes after cerebral hemorrhage. SABP increased minimally following cerebral hemorrhage.

ICP increased 5 minutes after the induction of hemorrhage in all seven cats. The average increase was 24.0±6.1 mm Hg \((p<0.02)\). Mean arterial blood pressure (MABP) was 131.3±11.2 mm Hg in the control state and was elevated slightly \((2.9±2.0\) mm Hg) after cerebral hemorrhage (not significant). Figure 4 summarizes the changes in local CBV in both hemispheres 5 minutes after the hemorrhagic

FIGURE 4. Changes in cerebral blood volume (\(\Delta CBV\)) in hemorrhagic and non-hemorrhagic hemispheres following cerebral hemorrhage in cats. Cerebral blood volume decreased in both hemispheres, but reduction was greater in hemorrhagic hemisphere \((p<0.05)\). *\(p<0.02\).
episode. CBV decreased by 1.60 ± 0.24 vol% in the hemorrhagic hemisphere (p<0.02) while it decreased by 1.14 ± 0.30 vol% in the nonhemorrhagic hemisphere (p<0.02); the reduction in CBV was thus greater in the hemorrhagic hemisphere (p<0.05). In the hemorrhagic hemisphere, MTT was 6.80 ± 1.01 seconds in the control state and was prolonged by 3.60 ± 0.76 seconds 5 minutes after cerebral hemorrhage (p<0.02, Figure 5). In the nonhemorrhagic hemisphere, MTT was 6.50 ± 0.50 seconds in the control state and was prolonged by 3.46 ± 1.19 seconds after cerebral hemorrhage (p<0.02); there was no significant difference in MTT prolongation between the two hemispheres. Local CBF in the hemorrhagic hemisphere was 64.5 ± 13.6 ml/100 g brain/min in the control state and, as summarized in Figure 6, was markedly decreased by 30.0 ± 4.5 ml/100 g brain/min 5 minutes after cerebral hemorrhage (p<0.02). Local CBF in the nonhemorrhagic hemisphere was 60.9 ± 6.9 ml/100 g brain/min in the control state and decreased considerably by 30.3 ± 7.5 ml/100 g brain/min following cerebral hemorrhage (p<0.02). No significant difference in CBF reduction between the two hemispheres was noted.

Discussion

The basic theory, validity, and applications of our photoelectric method have been discussed. Briefly, the characteristics of our photoelectric apparatus can be summarized as follows: 1) it ensures accurate, stable, and continuous measurement of local CBV in a thin layer of cerebral cortex, 2) it permits intermittent estimation of local CBF by concomitant use of tissue carbon black dilution curves, 3) the construction of the apparatus is extremely simple, and 4) it is inexpensive. Concerning the possible tissue damage accompanying lamp insertion into the brain tissue, we have demonstrated that the normal responsiveness of the cerebral vasculature, for example, autoregulation of CBF and CO2 reactivity, could be well preserved after the procedure. The distinctive feature of our apparatus is that it measures the local cortical blood volume represented mainly by small vessels, that is, arterioles, capillaries, and venules.

To simulate spontaneously occurring hypertensive cerebral hemorrhage in humans, we devised a new experimental model for basal ganglia hemorrhage. Hemorrhage in the basal ganglia accounts for >50% of the total hypertensive cerebral hemorrhages observed in clinical cases. Since a lesion involving a large mass should appear after cerebral hemorrhage, the cerebral circulatory changes may be deduced in part from the results obtained for cerebral neoplasms or intracranial hypertension. As indicated by Ropper and Zervas, however, the extravasating blood or its constituents also play an important role in subsequent pathophysiologic developments. Thus, arterial blood of a cat was introduced into the basal ganglia, using SABP of the cat itself as a driving force. It is a matter of dispute whether small perforating arteries, which rupture and bleed, have a high intraluminal pressure equivalent to SABP. Further, hemostasis assisted by
vasoconstriction, which may be a common reaction in arterioles in vivo, could not be expected. According to Laplace’s law, the tension developed in the wall is proportional to the intraluminal pressure and radius of the vessel. Nevertheless, the unique aspect of our model, that the hemorrhage, having occurred, ceases spontaneously by the achievement of an equilibrium between the bleeding pressure and the local tissue pressure, must be emphasized.

In our experiments, ICP began to increase shortly after the induction of cerebral hemorrhage and peaked at 24.0 ± 6.1 mm Hg above the control level within a few minutes. Based on an investigation of the time course of ICP in primary intracerebral hemorrhage, Papo et al. reported that patients with an initial ICP of approximately 30 mm Hg showed intermediate disturbance of consciousness with an inconsistent clinical course and outcome. Our postmortem findings also implied that our model would correspond to a moderate case of basal ganglia hemorrhage in humans. The gradual reduction in ICP observed after reaching a peak might be due to the compliance of the cranial cavity. The observed changes in MABP were minimal following the hemorrhage. This was in line with previous investigations that found no changes in arterial blood pressure during mild elevations of ICP. Cushing reported in 1902 that SABP increased markedly in response to prominent elevation of ICP to as high as the SABP, but this was not the case in our experiments.

In all seven cats, CBV and CBF were significantly decreased in both hemispheres 5 minutes after the induction of cerebral hemorrhage. CBV was reduced more in the hemorrhagic hemisphere, while there was no significant difference in CBF reduction between the hemispheres. These findings differed somewhat from our previous results for experimental cerebral ischemia, in which the CBV changes were confined mostly to the ipsilateral hemisphere. The reduction of CBV and CBF in both hemispheres immediately after hemorrhage may be mainly attributable to the increase in ICP. Figure 3 clearly illustrates the relation between the time course of ICP and CBV in both hemispheres. As described above, our photoelectric apparatus measures local CBV as represented by small vessels, that is, arterioles, capillaries, and venules. The precise intraluminal pressure of these vessels is unknown, but it is conceivable that they are readily compressed by an ICP elevation of as little as 24.0 mm Hg. Some authors have postulated that the cerebral venous system may be vulnerable under intracranial hypertension. However, since they did not examine the effects of ICP on the cerebral microcirculation, the primary target of ICP in the cerebral vasculature remains obscure. Figures 7 and 8 show the relation between changes in ICP and CBV and between changes in ICP and CBF following experimental stroke, respectively. No good cor-

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**Figure 7.** Relation between changes in intracranial pressure (ΔICP) and cerebral blood volume (ΔCBV) in both hemispheres 5 minutes after cerebral hemorrhage in cats. ●, hemorrhagic hemisphere; ○, nonhemorrhagic hemisphere.

**Figure 8.** Relation between changes in intracranial pressure (ΔICP) and cerebral blood flow (ΔCBF) in both hemispheres following cerebral hemorrhage in cats. ●, hemorrhagic hemisphere; ○, nonhemorrhagic hemisphere.
relation was observed between ICP and CBV or between ICP and CBF. Our results are in agreement with the clinical data of Mizukami et al,\(^5\) who failed to find any direct connection between ICP and CBF. Our findings do not exclude a causative role for ICP in CBV/CBF reduction but do suggest a difference in the degree of ICP increase and the degree of resultant CBV/CBF decrease among cats. Some other possible explanations for the CBV/CBF reduction, such as 1) dysautoregulation of CBF following cerebral hemorrhage,\(^1,2,3\) 2) brain edema, 3) disturbance of brain supply due to distortion and displacement of brain tissue,\(^4,24\) 4) effects of humoral factors (norepinephrine, etc.), and 5) transneural depression or diaschisis,\(^3-4,25\) are less likely in our experimental model.

In conclusion, it appears that an increase in ICP participates mainly in the bilateral hemispheric reduction of CBV and CBF immediately after experimental basal ganglia hemorrhage in cats. Other factors listed above may affect the process to lesser extents. Further investigations are now in progress to specify the precise underlying mechanisms.

**References**


**Key Words** • cerebral blood flow • cerebral hemorrhage • intracranial pressure • cats
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