Cortical blood flow response to hypercapnia during anaesthesia in Moyamoya disease

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Cortical blood flow (CoBF) was measured continuously by the laser-Doppler method to evaluate the effect of hypercapnia on cortical blood flow during ten surgical procedures in ten young patients (mean ± SD 9.3 ± 6.4 yr) with Moyamoya disease. The CoBF was 42.8 ± 13.4 (ml· 100 g^{-1}· min^{-1}) during normocapnia ($PaCO_2$ = 39.0 ± 2.4 mmHg), and 38.7 ± 14.4 during hypercapnia ($PaCO_2$ = 47.1 ± 2.5 mmHg). There was a decrease in CoBF with hypercapnia (P < 0.05) so that the normal CoBF response to hypercapnia was impaired during surgery in the patients with Moyamoya disease. He concluded that patients with Moyamoya disease have a precarious cerebral circulation and hypercapnia may be detrimental to the cortical circulation. This suggests that normocapnia is preferable to hypercapnia in patients with Moyamoya disease during anaesthesia.

Pendant dix interventions chirurgicales pratiquées chez dix jeunes patients (âge moyen 9,3 ± 6,4 ans) souffrant de la maladie de Moyamoya, le débit sanguin cortical (DSCo) est mesuré continuellement par la méthode Laser-Doppler dans le but d'évaluer les effets de l'hypercapnie sur le débit sanguin cortical. Le DSCo (ml· 100 g^{-1}· min^{-1}) est de 42,8 ± 13,4 pendant la normocapnie ($PaCO_2$ = 39,0 ± 2,4 mmHg) et de 38,7 ± 14,4 pendant l'hypercapnie ($PaCO_2$ = 47,1 ± 2,5 mmHg). La baisse du débit pendant hypercapnie est significative (P < 0,05). Ce qui démontre que la réponse du débit sanguin cérébral est perturbée pendant la chirurgie de la maladie de Moyamoya. On conclut que cette maladie a une influence néfaste sur la circulation cérébrale pendant l'hypercapnie. Ceci suggère que dans la maladie de Moyamoya, la normocapnie est préférable à l'hypercapnie.

Key words
ANAESTHESIA: neurosurgical;
BLOOD: flow;
BRAIN: blood flow, carbon dioxide tension;
COMPLICATIONS: Moyamoya disease.

Moyamoya disease is a rare occlusive cerebrovascular disease. Angiographic findings may demonstrate progressive stenosis or occlusion of the terminal portions of the internal carotid artery and the origins of the anterior cerebral and middle cerebral arteries, abnormal vascular networks at the base of the brain, and several transdural anastomoses. The characteristic symptoms of the disease are transient ischaemic attacks (TIAs) causing hemiparesis or weakness of the limbs associated with hyperventilation when crying or exercising.[1] However, the details of the pathophysiological mechanism remain uncertain.

Several surgical approaches have been reported to increase the blood supply to the ischaemic hemispheres, such as superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis,[1] encephalo-myo-synangiosis (EMS),[2] and encephalo-duro-arterio-synangiosis (EDAS).[3] Patients with Moyamoya disease have a precarious cerebral circulation. During surgery, it is considered to be important to preserve cerebral blood flow by controlling blood pressure and arterial carbon dioxide tension ($PaCO_2$).

Several[4–7] studies have evaluated the cerebrovascular CO_2 reactivity in patients with Moyamoya disease. The CO_2 reactivity is preserved in the hypocapnic state[4–7] so that decreasing PCO_2 will reduce cerebral blood flow in Moyamoya disease. However, the effect of hypercapnia on the cerebral circulation has not been evaluated in this disease.

In this study, we measured cortical blood flow (CoBF) continuously using the laser-Doppler method during

TABLE I Patient summary

Case No.	Age/Sex (yr)	Type of onset	Clinical signs	Duration from onset to operation	Operation side
1	13/F	TIA	Mental retardation	10 yr	Rt.
2	5/F	TIA	No deficit	1 yr	Lt.
3	8/F	TIA	Rt. hemiparesis	1 yr, 2 mo	Rt.
4	16/F	TIA	No deficit	5 yr	Rt.
5	8/F	TIA	Quadriparesis	3 yr	Rt.
6	8/F	TIA	No deficit	3 yr	Lt.
7	3/M	TIA	No deficit	3 mo	Rt.
8	2/M	TIA	Rt. hemiparesis	7 mo	Rt.
9	7/F	TIA	No deficit	1 yr	Lt.
10	23/F	TIA	Lt. hemianopsia	11 yr	Rt.

F: female, M: male, TIA: transient ischaemic attack, Rt.: right, Lt.: left.

TABLE II Physiological data during normocapnia and hypercapnia

	Normocapnia	Hypercapnia
HR (bpm)	95.7 ± 18.2	96.0 ± 16.6
BP (mmHg)	99.4 ± 14.6	101.1 ± 14.5
$PaCO_2$ (mmHg)	39.0 ± 2.4	47.1 ± 2.5*
PaO_2 (mmHg)	190.8 ± 41.1	171.1 ± 19.6

HR: heart rate, BP: blood pressure.
*$P < 0.01$ versus normocapnia.

STA-MCA anastomosis, and the effect of hypercapnia on CoBF in Moyamoya disease was evaluated.

Methods

Institutional Ethics Committee approval and informed consent were obtained. Fourteen young patients (three male and seven female ranging in age from 2 to 23 year, mean ± SD 9.3 ± 6.4 yr) with Moyamoya disease were included in the study. The diagnosis had been established by bilateral carotid angiography in all patients. All patients had ischaemic cerebrovascular symptoms and signs without intracranial haemorrhage (Table I).

Ten STA-MCA anastomoses with EMSs were performed in these patients. After premedication with mono-sodium trichlorethyl phosphate (80–100 mg · kg⁻¹ po) or hydroxyzine (1 mg · kg⁻¹ im), anaesthesia was induced by inhalation of sevoflurane (4–5%) nitrous oxide, and oxygen, or by thiopentone (4–5 mg · kg⁻¹ iv). After administration of vecuronium (0.1 mg · kg⁻¹ iv), the trachea was intubated, and the lungs were mechanically ventilated. Additional doses of vecuronium or pancuronium were given when necessary. The patients received midazolam 1–2.5 mg and fentanyl 4.0–10.7 μg · kg⁻¹ in addition to oxygen and nitrous oxide 33:67. Temperature, oxygen saturation, end-tidal CO_2, blood pressure, and heart rate by ECG were monitored during the operation. A radial artery cannula was inserted for sampling of blood gases (ABL3, Radiometer, Denmark).

The CoBF was measured by the laser-Doppler method. The principles of measurement of tissue surface blood flow with a laser-Doppler flowmeter have been previously described.[8-11] In brief, the laser-Doppler method is based on the principle that light scattered by moving red blood cells experiences a frequency shift that is proportional to the mean velocity of red cells. Electrical signals generated by the photodetector contain information about the frequency, which is related to the blood cell velocity, and the power, which is related to the blood volume. Blood flow is computed as:

(blood flow) = (blood volume) · (blood velocity)

The laser-Doppler flow value is the microcirculatory blood flow within an illuminated tissue volume of about 1 mm³. The laser-Doppler flowmeter (ALF21, Advance, Tokyo) used in this study had a diode laser beam with an optical output power of 2 mW at the probe and a wavelength of 780 nm. The measurement range is 0–100 ml · 100⁻¹ · min⁻¹ of CBF.

After craniotomy, the dura was opened and the site of anastomosis was chosen. While the STA branch was harvested from the skin flap, a flat probe was placed on the cortex, avoiding surface vascular channels, for continuous monitoring of CoBF in the sampling area. Measurements were performed at eight sites in the parietal lobes, and two sites in the frontal lobes. Ventilation was controlled to maintain end-tidal CO_2 at about 40 mmHg and normocapnic CoBF was measured. After a steady state recording was obtained during normocapnia, ventilation was controlled to maintain end-tidal CO_2 at about 45–50 mmHg while monitoring oxygen saturation. Blood pressure and blood gases were measured during normocapnia and hypercapnia. Electrical signals from the laser-Doppler flowmeter were recorded continuously on a polygraph (Nihon Kohden, Tokyo).

Data analysis was performed with a computerized statistical analysis package (Stat Flex, View Flex Inc.,

TABLE III   Cortical blood flow during normocapnia and hypercapnia, and CO_2 reactivity

CoBF at normocapnia $(ml^{-1} \cdot 100\,g^{-1} \cdot min)$	CoBF at hypercapnia $(ml^{-1} \cdot 100\,g^{-1} \cdot min)$	$\Delta CoBF \cdot \Delta PCO_2^{-1}$ $(ml^{-1} \cdot 100\,g^{-1} \cdot min^{-1} \cdot mmHg)$	$\Delta\%CoBF \cdot \Delta PCO_2^{-1}$ $(\%^{-1} \cdot mmHg)$
42.8 ± 13.4	$38.7 \pm 14.4^*$	-0.64 ± 0.82	-1.57 ± 1.59

CoBF: cortical blood flow.
*$P < 0.05$ versus normocapnia.
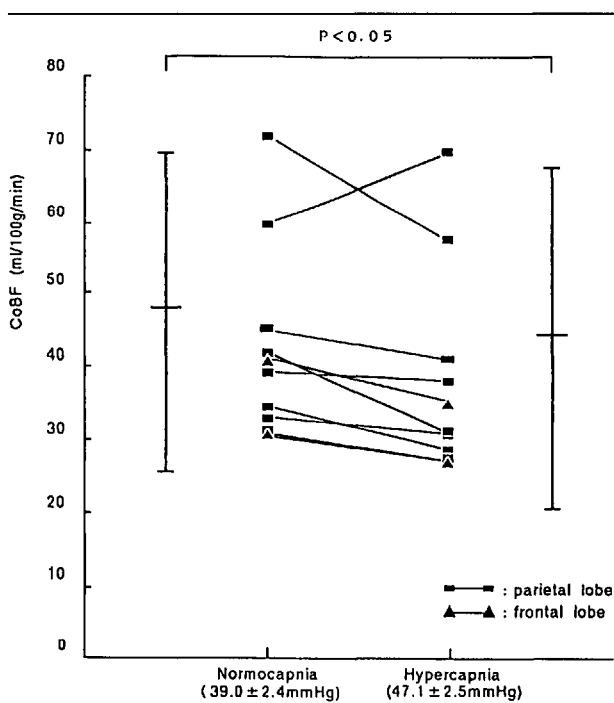
FIGURE 1   CoBF measured by the laser-Doppler method during normocapnia and hypercapnia. Measurements were performed at eight sites in the parietal lobes, and two sites in the frontal lobes. There was a decrease in CoBF during hypercapnia ($P < 0.05$).

FIGURE 2   Continuous recording of CoBF in a typical case. CoBF was gradually decreased during hypercapnia.

Tokyo). Normality of distribution of the data obtained during normocapnia and hypercapnia was analyzed. In the absence of a normal distribution the data were analyzed using the Wilcoxon test. When normal distribution was confirmed during each state, analysis was with Student's paired t test. All data were expressed as mean $\pm$ SD, a $P < 0.05$ was considered significant.

Results

The summarized data of all patients are shown in Table I. Anaesthesia and surgery were uneventful in all patients. There were no differences in blood pressure, heart rate or PaO_2 between the normocapnic and hypercapnic state (Table II). The $PaCO_2$ was 39.0 ± 2.4 mmHg during normocapnia and 47.1 ± 2.5 mmHg during hypercapnia ($P < 0.001$). The CoBF was 42.8 ± 13.4 (ml · 100 g^{-1} · min^{-1}) during normocapnia, with individ-
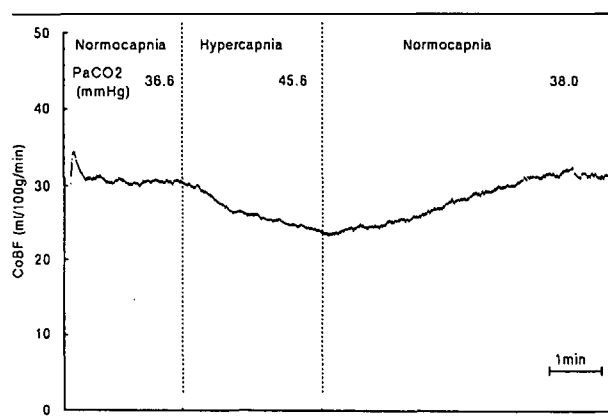
ual variations (Figure 1). During hypercapnia, CoBF decreased to 38.7 ± 14.4 ($P < 0.05$, Table III, Figure 1). The ratio of CoBF change versus change in $PaCO_2$ (CoBF· $PaCO_2^{-1}$:ml · 100 g^{-1} · min^{-1} · mmHg^{-1}) was -0.64 ± 0.82. A continuous recording of the typical case is shown in Figure 2.

Discussion

Several studies of cerebral blood flow (CBF) in Moyamoya disease have been reported[4-7,12,13] using argon inhalation,[4,12] [133]Xe clearance[5-7] and thermal diffusion methods.[13] However, many of these measurements are complicated and intermittent assessments of flow except for the thermal diffusion method.[13] In the present study, the laser-Doppler method was used for measurement of CoBF which allows continuous measurement, is noninvasive and can be performed rapidly at the time of operation. The laser-Doppler flowmeter has been used to measure local CBF both in experimental animals[8-10] and in human patients during surgery.[11] Skarphedinsson *et al.*[8] compared the laser-Doppler with the hydrogen clearance method in rats, and found a good correlation between the values of local CBF obtained. Other studies[9,10] have reported similar results. Thus, the laser-Doppler flowmeter may be used to measure microcirculatory blood flow of the cerebral cortex quantitatively.

The cerebral circulation in patients with Moyamoya

disease has been studied by various methods[4-7,12,13] and is sluggish. Karasawa et al.[12] measured CBF using argon inhalation in 17 children with Moyamoya disease, and divided them into three groups according to the neurological manifestations of transient ischaemic attack, minor and major stroke. Cerebral blood flow was decreased in all three groups, especially in the group with major strokes, compared with normal children. Takeuchi et al.[13] measured CoBF by thermal diffusion in 12 young patients with Moyamoya disease during STA-MCA anastomosis performed under neuroleptanaesthesia. They reported that the mean pre-bypass CoBF was 39.4 ± 13.0 ml · 100 g^{-1} · min^{-1} in the parieto-temporal regions during normocapnia, with individual variation. In our study, the mean CoBF was 42.8 ± 13.4 ml · 100 g^{-1} · min^{-1} by the laser-Doppler method, again with interindividual variation. The variation may be characteristic of CoBF in Moyamoya disease.

Several studies[4-7] have reported the cerebrovascular CO_2 reactivity in patients with Moyamoya disease. Carbon dioxide reactivity is preserved in the hypocapnic state.[4-7] Uemura et al.[6] measured regional cerebral blood flow in patients with Moyamoya disease using the ^{133}Xe intracarotid injection. During hypercapnia induced by 5% CO_2 inhalation, regional cerebral blood flow was unchanged or decreased slightly. Using the ^{133}Xe inhalation in patients with Moyamoya disease regional cerebral blood flow was increased in the temporo-occipital regions and was unchanged or decreased in the frontal region by 5% CO_2 inhalation.[7] In the present study, CoBF was decreased during hypercapnia. In Moyamoya disease, the cortical arteries in the fronto-parietal lobes, which are fed mainly by the severely stenosed middle and anterior cerebral arteries or collateral pathways through the abnormal vascular network, seem to be either in a state of full dilatation or high vascular resistance due to proximal occlusion or severe stenosis. Thus they may not be able to dilate further during hypercapnia.[7] Furthermore, in Moyamoya disease, stenosis or occlusion of the internal carotid, middle cerebral and anterior cerebral arteries precedes that of the posterior cerebral artery. Since the temporo-occipital regions are fed mainly by the posterior cerebral artery, CO_2 reactivity is considered to be relatively preserved in these regions. Under such conditions, greater cerebral vasodilatation in the region with relatively preserved CO_2 reactivity could divert blood away from regions with impaired CO_2 reactivity. The decrease of cerebral blood flow during hypercapnia in this study may be explained by this "intracerebral steal" effect. Thus, both hypocapnia and hypercapnia may be detrimental to the cerebral circulation in Moyamoya disease. When managing patients with Moyamoya disease during surgery, normocapnia is preferable to hypercapnia.

Increasingly, patients with Moyamoya disease are treated surgically to improve the cerebral circulation, and several cases of neurological deterioration after general anaesthesia have been reported.[14,15] According to our results in patients with Moyamoya disease, normocapnia is preferable to hypercapnia during surgery.

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