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Local cortical cerebral blood flow and response to carbon dioxide during anesthesia in patients with moyamoya disease

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Abstract

Purpose. The CO_2 reactivity of cortical cerebral vessels and local cortical blood flow (l-CoBF) were evaluated during anesthesia in patients with moyamoya disease who were undergoing revascularization surgery.

Methods. Using laser–Doppler flowmetry, the CO_2 reactivity of cortical cerebral vessels and l-CoBF were measured continuously in five patients at the local surgical field of the middle cerebral artery (MCA) territory.

Results. Local-CoBF values obtained during the normocapnic condition varied from site to site of gyrus in the MCA region (0–73 $ml \cdot 100 g^{-1} \cdot min^{-1}$). Local-CoBF was maximal at 39–43 mmHg of the $PaCO_2$ range, and decreased above and below this range. The response of l-CoBF to CO_2 was larger at the sites where the maximal level was obtained during normocapnia. In two patients, l-CoBF decreased by about 50%, and remained law even 40 min after administration of acetazolamide.

Conclusion. In patients with moyamoya disease, l-CoBF values obtained during the normocapnic condition varied from site to site of gyrus, and not only hypocapnia but also hypercapnia decreased l-CoBF within the MCA region.

Key words: Moyamoya disease, Neurosurgical anesthesia, Local cortical blood flow, CBF response to CO_2, Acetazolamide

Introduction

Moyamoya disease is a rare chronic occlusive cerebrovascular disease of unknown etiology with distinct bilateral angiographic features. The typical clinical signs and symptoms include repeated transient ischemic attacks (TIAs) in children, and subarachnoid or intracerebral hemorrhage in adults [1,2].

Reconstructive vascular surgery is used to improve decreased cerebral blood flow (CBF) of patients with moyamoya disease before fixed neurologic deficits occur. A new surgical procedure, encephalo-duro-arterio-myo-synangiosis (EDAMS), involves an attempt to increase collateral circulation from both the middle meningeal artery and the stripped superficial temporal artery [3].

Normal or slightly raised arterial CO_2 tension during anesthesia is recommended in patients with moyamoya disease [4–8]. Hypocapnia decreases CBF during anesthesia, and is definitely associated with postoperative worsening of ischemia [5,6,8] because cerebrovascular CO_2 reactivity is preserved during hypocapnia in moyamoya disease [9–13]. On the other hand, the cerebrovascular response to hypercapnia induced by 5–7% CO_2 inhalation is severely impaired [9,11,14], and CBF declines during anesthesia under hypercapnia [15].

In this study, we measured local cortical cerebral blood flow (l-CoBF) continuously using the laser–Doppler method in patients undergoing EDAMS or omentum transplantation, and evaluated the CO_2 reactivity of cortical cerebral vessels in patients with moyamoya disease.

Materials and methods

Institutional Ethics Committee approval and informed consent were obtained. Five patients with moyamoya disease with ischemic cerebrovascular signs and symptoms without intracranial hemorrhage were included in the study (Table 1).

After premedication with hydroxyzine ($1 mg \cdot kg^{-1}$, i.m.) and atropine ($0.01 mg \cdot kg^{-1}$, i.m.), anesthesia was induced with enflurane, isoflurane, or sevoflurane with

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Table 1. Patients and case summaries

Patient and case No.	Age (years)/sex	Stage	Operation	Anesthetic agents
1a	4 / M	3	Lt-EDAMS	Enflurane/N_2O/O_2
1b	6 / M	4	Rt-EDAMS	Isoflurane/N_2O/O_2
2a	7 / F	3	Rt-EDAMS	Sevoflurane/N_2O/O_2
2b	8 / F	3	Lt-EDAMS	Sevoflurane/N_2O/O_2
3	17 / F	2	Lt-EDAMS	Isoflurane/N_2O/O_2
4	19 / F	4	Rt-EDAMS	Isoflurane/N_2O/O_2
5	31 / F	Infarction	Omental transplantation	Isofluran/N_2O/O_2

EDAMS, encephalo-duro-arterio-myo-synangiosis.
Stages, classified according to Suzuki and Takaku [1].

Table 2. Physiological data during the operations and measurements made

Patient and case No.	$PaCO_2$ (mmHg)	Blood pressure systolic/diastolic (mmHg)	Measurements
1a	38.8–41.0	80–90/40–50	CO_2 response
1b	38.8–47.9	80–90/40–50	l-CoBF, CO_2 response
2a	39.5–50.5	80–90/40–50	l-CoBF, CO_2 response, acetazolamide loading
2b	37.3–46.2	110–120/50–60	l-CoBF, CO_2 response
3	42.7–43.0	120–130/70–80	l-CoBF
4	34.5–36.8	100–110/60–70	l-CoBF
5	38.7–44.6	100–116/60–70	l-CoBF, CO_2 response, acetazolamide loading

l-CoBF, local cortical cerebral blood flow.

oxygen, or by intravenous thiamylal (5 mg·kg^{-1}). After tracheal intubation with vecuronium (0.1 mg·kg^{-1}, i.v.), the lungs were mechanically ventilated. Anesthesia was maintained with enflurane, isoflurane, or sevoflurane, and nitrous oxide/oxygen mixture (FiO_2 = 0.30–0.35). Additional doses of vecuronium were given when necessary. Rectal temperature, oxygen saturation (by pulse oximeter), end-tidal CO_2 ($ETCO_2$), and heart rate (by ECG) were monitored during surgery. A radial artery was cannulated for continuous blood pressure monitoring and arterial blood gas analysis (Corning 170 pH/Blood Gas Analyzer; Ciba Corning Diagnostics, Medfield, MA, USA). Rectal temperature was maintained at 35.5–36.5°C by the use of warm-water blankets.

The l-CoBF was measured by laser–Doppler flowmetry, and electrical signals from the flowmeter were continuously recorded on a polygraph. 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 g^{-1}·min^{-1} of CBF, and the response time is 10 ms.

After craniotomy (before undergoing revascularization procedures), two probes (3 mm diameter) of the laser–Doppler flowmeter were placed in gentle contact with the cortical surface by avoiding sites with visible surface vessels. In order to avoid dislocation of the probes, they were fixed by elastic rubber bands to a round surgical frame. The pulsatile variation of flow was considered as an indicator of a clean flow signal [16]. First, measurements of l-CoBF were performed at several sites on each gyrus in the surgical field of the region at the middle cerebral artery (MCA), while ventilation was controlled to maintain $PaCO_2$ at 40 ± 3 mmHg (mean ± SD) along with constant anesthetic depth, until stable values were obtained at each site for about 5 min. Sites where the maximal and minimal l-CoBF values were obtained during normocapnia were selected to evaluate the CoBF reactivity to $PaCO_2$ changes (patients 1 and 2). In an adult patient (patient 5), an infarct site and another surrounding area were selected. Arterial CO_2 tension was increased or decreased by changing the respiratory rate, while tidal volume was kept constant. Continuous measurements of l-CoBF for about 10 min were performed, and ventilation was returned to the normocapnic condition after arterial blood samples were obtained. In two patients (cases 2a and 5), the hemodynamic reserve was assessed by an acetazolamide (500 mg·60 kg^{-1}) challenge.

Results

The arterial blood pressure and $PaCO_2$ during the operation and l-CoBF measurements under normocapnia are summarized in Tables 2 and 3.

Table 3. Local cortical cerebral blood flow (l-CoBF) during normocapnia

Patient and case No.	Stage	$PaCO_2$ (mmHg)	l-CoBF of gyrus in the surgical field ($ml \cdot 100\,g^{-1} \cdot min^{-1}$)
1a	3	40.8	32
1b	4	39.6	13, 18, 16, 35, 22
2a	3	39.5	15, 60, 38, 32, 60, 58
2b	3	41.9	38, 18, 44, 24, 20, 45
3	2	42.7	22, 25, 31, 62, 36, 73, 42, 53, 35, 60, 50, 3
4	4	36.8	0, 55, 10, 58, 25, 9, 3
5		40.0	14 (site of infarction), 24 (surounding area)

Underlining indicates sites of CO_2 response measurement.

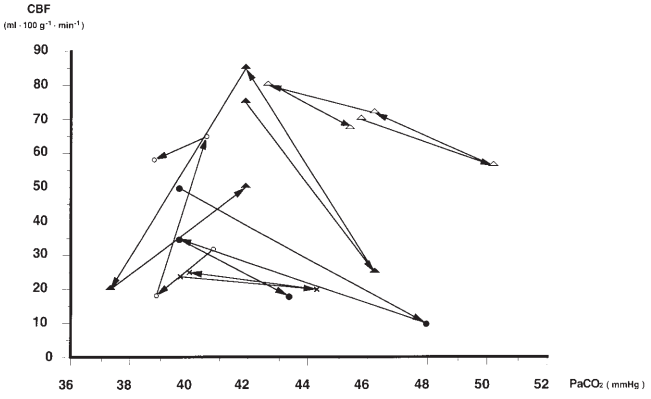

Fig. 1. Reactivity of local cortical cerebral blood flow (l-CoBF) to $PaCO_2$, measured at the high-flow site where the maximal level was obtained during normocapnia in each patient. *Open circles*, case 1a; *solid circles*, case 1b; *open triangles*, case 2a; *solid triangles*, case 2b; *crosses*, case 5

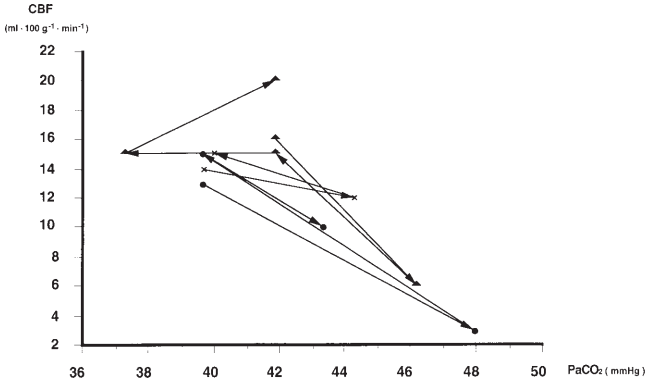

Fig. 2. Reactivity of local cortical cerebral blood flow (l-CoBF) to $PaCO_2$, measured at the low-flow site where the minimal level was obtained during normocapnia in each patient. The values for cases 1a and 2a were excluded from the data because we were unable to record the pulsatile variation of flow. *Solid circles*, case 1b; *solid triangles*, case 2b; *crosses*, case 5

Local-CoBF values obtained under normocapnic conditions varied widely from site to site of the gyrus in the MCA region (0–73 $ml \cdot 100\,g^{-1} \cdot min^{-1}$). In the adult patient, the l-CoBF value of the infarct site was half that of the surrounding area (Table 3). Local-CoBF as a function of $PaCO_2$ is shown Figs. 1 and 2. The values of cases 1a and 2a at low flow sites were excluded from the data because we were unable to record the pulsatile variation of flow. Local-CoBF was maximal at 39–43 mmHg in the $PaCO_2$ range. Above and below this range, l-CoBF decreased. The reactivity of l-CoBF to CO_2 was larger at the sites where the maximal level was obtained during normocapnia (high-flow site) than at the sites where the minimal level was obtained (low-flow site) (Figs. 1 and 2). After acetazolamide loading in patients 2 (case 2a) and 5, l-CoBF levels decreased and had not returned to their initial values after 40 min.

Surgery and anesthesia were uneventful, and there was no abnormal neurologic finding postoperatively in any patient.

Discussion

The mean hemispheric CBF was found to be lower in all children with moyamoya disease [9–12,17], and especially in children with a completed stroke compared with children with TIAs [9,18]. The regional CBF was also abnormal in patients with decreased hemispheric CBF [11]. The regional CBF was relatively low in the upper frontal region, and high in the posterotemporal and occipital regions [17], which was different from the "hyperfrontal" pattern found in healthy volunteers [12]. Since stenosis or occlusion of the internal carotid, middle, and anterior cerebral arteries precedes that of the posterior cerebral artery in moyamoya disease, the upper frontal region is fed mainly by the severely stenosed middle and anterior cerebral arteries, while the posterotemporal and occipital regions are fed by near-normal branches of the posterior cerebral artery [12,19].

In this study, we measured l-CoBF within the MCA region continuously by laser–Doppler flowmetry

(LDF). Compared with the standard methods, LDF quantitatively measures microcirculatory flow in small tissue, but not large-vessel blood flow, and allows rapid (100 ms), continuous, intraoperative measurement of l-CoBF without damaging the tissue. We have been able to obtain reproducible readings by avoiding regions with visible surface vessels and observing the pulsatile variation of flow. In experimental animals, there is a linear relationship between blood flow values measured by LDF and the hydrogen clearance method [16,20]. The limitation of this method is that LDF does not provide accurate measurements of absolute local CBF values, and measures l-CBF only in a 3.5–4.5-mm-deep layer of the cortical surface [20]. However, it does allow accurate measurements of changes in l-CBF due to the induction of focal cerebral ischemia [21], and can demonstrate disturbed cerebrovascular CO_2 reactivity at the cortical surface in moyamoya disease more clearly than other standard methods.

In this study, l-CoBF values at the surgical field in young patients supplied mainly by MCA during normocapnia were relatively low, as in previous reports, and varied from site to site in the gyrus (Table 3). Takeuchi et al. [19] studied the epicerebral microcirculation by fluorescein angiography, and found varying filling and circulation times from gyrus to gyrus, or from area to area in a gyrus. This pattern can be explained by the characteristic finding of different stages of vessel occlusion even in the same patient.

The cerebrovascular CO_2 reactivity is generally preserved during hypocapnia in moyamoya disease [9–13]. Hemispheric CBF and regional CBF were reduced evenly by hypocapnia [9,12]. Thus, hypocapnia reduces CBF directly by constricting the moyamoya vessels without inducing an inverse steal effect. This finding supports the previous reports that characteristic TIAs in children were typically precipitated by crying or exercising [9,10]. In this study, l-CoBF within the MCA region decreased markedly even when only a slight decrease in $PaCO_2$ was induced.

A recent report showed that l-CoBF measured by LDF decreased during hypercapnia in ten young patients with moyamoya disease undergoing STA–MCA anastomosis [15]. Similarly, l-CoBF decreased markedly in this study during hypercapnia (Fig. 1). In moyamoya disease, it is considered that the normal CO_2 reactivity is preserved in the temporo-occipital regions, but is impaired in the frontal region during hypercapnia [9,11–13]. The cortical and pial arteries in the frontal region seem to be in a state of full dilatation or high vascular resistance due to proximal occlusion or severe stenosis [13], so that they may no longer be able to dilate during hypercapnia. As a result, vasodilation in the CO_2-reactive temporo-occipital region may lead to intracerebral steal from the maximally dilated non-CO_2 reactive front-parietal collateral vessels. Compared with other standard methods, LDF can demonstrate this disturbed cerebrovascular CO_2 reactivity more clearly, because LDF measures l-CBF only in a 3.5–4.5 mm deep layer of the cortical surface [20]. In the hypercapnic state, cerebrovascular CO_2 reactivity was disturbed to a greater extent in this cortical surface than in the deep regions of the brain [10].

CBF measurement before and after acetazolamide injection have been performed to assess cerebral perfusion reserve prior to EC–IC bypass surgery [22]. Diminished capacity in the posterior region was demonstrated in one patient with moyamoya disease [23]. Similarly, focal decreases in the regional CBF following acetazolamide loading were noted in five of nine children. A long-lasting decrease in l-CBF has been observed by Yamada et al. [24] in two cases.

Anesthetic management may affect the outcome for patients with moyamoya disease. The deteriorative effects of hypocapnia are apparent from this and some previous reports. Thus, it is recommended that hypocapnia should be avoided in these patients. In addition, since hypercapnia also decreases CBF in patients with moyamoya disease, it would seem prudent to maintain normocapnia in these patients.

Inhalational agents might influence CBF in moyamoya disease during general anesthesia. However, because we experienced no cases with neurological deterioration, the choice of anesthetic agents might play a minor role in CBF responses during surgery as long as normocapnia is maintained.

Postoperatively, the maintenance of appropriate blood pressure, intravascular volume, oxygenation, and oxygen-carrying capacity is also important to minimize substrate supply to the brain [4]. With the exception of STA–MCA anastomosis, there is no immediate increase in perfusion following surgery. The anastomotic channels begin to develop 2 weeks after EDAMS, and well-developed anastomotic channels were observed on angiogram 3 months postoperatively. Thus, these patients should be managed in the same way for a few months following surgery until collateral circulation between the external carotid system and the brain surface is accomplished [3].

In conclusion, l-CoBF values obtained during a normocapnic condition varied from site to site of gyrus, and not only hypocapnia but also hypercapnia decreased l-CoBF within the MCA region in patients with moyamoya disease.

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