J Anesth (2011) 25:409–414
DOI 10.1007/s00540-011-1131-6

CLINICAL REPORT

Time course of changes in cerebral blood flow velocity after tourniquet deflation in patients with diabetes mellitus or previous stroke under sevoflurane anesthesia

Hiroshi Hinohara · Yuji Kadoi · Kenichiro Takahashi · Shigeru Saito · Chikara Kawauchi · Akio Mizutani

Received: 9 November 2010 / Accepted: 14 March 2011 / Published online: 7 April 2011

Abstract We observed an increase in mean middle cerebral artery blood flow velocity (V_{mca}) after tourniquet deflation during orthopedic surgery under sevoflurane anesthesia in patients with diabetes mellitus or previous stroke. Eight controls, seven insulin-treated diabetic patients, and eight previous stroke patients were studied. Arterial blood pressure, heart rate, V_{mca}, arterial blood gases, and plasma lactate levels were measured every minute for 10 min after tourniquet release in all patients. V_{mca} was measured using a transcranial Doppler probe. V_{mca} in all three groups increased after tourniquet deflation, the increase lasting for 4 or 5 min. However, the degree of increase in V_{mca} in the diabetic patients was smaller than that in the other two groups after tourniquet deflation (at 2 min after tourniquet deflation: control 58.5 ± 3.3, previous stroke 58.4 ± 4.6, diabetes 51.7 ± 2.3; $P < 0.05$ compared with the other two groups). In conclusion, the degree of increase in V_{mca} in diabetic patients is smaller than that in controls and patients with previous stroke.

Keywords Tourniquet · Orthopedic · Cerebral blood flow velocity · Diabetes · Stroke

H. Hinohara
Division of Intensive Care,
Gunma University Hospital,
Maebashi, Japan

Y. Kadoi (✉) · K. Takahashi · S. Saito
Department of Anesthesiology,
Gunma University Hospital,
3-39-22 Showa-machi, Maebashi,
Gunma 371-8511, Japan
e-mail: kadoi@med.gunma-u.ac.jp

C. Kawauchi
Department of Anesthesiology,
Gyoda General Hospital,
Gyoda, Japan

A. Mizutani
Department of Anesthesiology,
School of Medicine, Oita University,
Oita, Japan

Introduction

Although the pneumatic tourniquet is a beneficial tool for obtaining a bloodless surgical field during orthopedic surgery, ischemic metabolites released after tourniquet deflation provoke several physiological alterations [1, 2]. Rapid decreases in arterial pH and increases in $PaCO_2$ and lactate are known to occur immediately after tourniquet deflation [1–4]. The rapid elevation in $PaCO_2$ reported after tourniquet deflation [5, 6] would consequently result in a corresponding increase in cerebral blood flow (CBF). The study by Hirst et al. [7] and our previous reports [3, 4] showed that a transient increase in CBF, indicated by middle cerebral artery (MCA) blood flow velocity, does occur after tourniquet deflation.

Reportedly, the vasodilatory or vasoconstrictive responses of the cerebral arteries to changes in $PaCO_2$ are different in patients with diabetes mellitus or previous stroke compared with those in patients without these diseases [8, 9]. Thus, we hypothesized that the increase in MCA blood flow after tourniquet deflation would have a different time course in patients with diabetes mellitus or previous stroke.

Therefore, in this study, we analyzed the increase in MCA blood flow velocity after tourniquet deflation in patients with diabetes mellitus or previous stroke undergoing orthopedic surgery under sevoflurane anesthesia.

Case report

After obtaining the approval of the ethics committee of our institution and Institutional Review Board, written informed consent was obtained from all patients. Patients undergoing elective orthopedic surgery requiring the use of a tourniquet on the lower extremity were studied. Patients with previous stroke were defined as those having a history of ischemic cerebrovascular disease and symptoms of a neurological disorder. This status was confirmed by preoperative brain computed tomography (CT) scan or magnetic resonance imaging (MRI). Diabetic patients were defined as those receiving insulin therapy.

A three-lead electrocardiography and noninvasive blood pressure monitors were attached to all patients (Hewlett Packard, Andover, MA, USA). Anesthesia was induced with 2 mg/kg propofol, 5 μg/kg fentanyl, and 0.1 mg/kg vecuronium, followed by endotracheal intubation. Muscle relaxation was achieved by intermittent administration of vecuronium. The left radial artery was cannulated with a 22-gauge indwelling catheter to monitor arterial blood pressure and to measure arterial blood gas and plasma lactate levels.

All patients were mechanically ventilated, with continuous monitoring of end-tidal carbon dioxide (pressure of end-tidal CO_2, $PetCO_2$) (Hewlett Packard). Anesthesia was maintained with sevoflurane (from 1.5% to 2.5%) in 33% oxygen and 67% nitrous oxide. Bispectral index (BIS) monitoring (A-2000; ASPECT Medical Systems, Natick, MA, USA) was used to maintain BIS levels between 45 and 50.

A 2.0-MHz transcranial Doppler probe (TC2-64; EME, Uberlingen, Germany) was attached to the patient's head at the right temporal window and mean blood flow velocity in the middle cerebral artery (V_{mca}), as an index of CBF, was measured continuously. In patients with previous stroke, the measurement of V_{mca} was performed at the same site as that of the previous stroke. Signal quality was determined by the characteristic high-pitched sound and the waveform of the sonogram display. After the signals were identified at a depth of 45–60 mm, the probe was fixed using a probe holder so as not to change the insonating angle.

Study protocol

The lower extremity being operated on was exsanguinated with an Esmarch bandage and the pneumatic tourniquet was inflated to a pressure of 450 mmHg. Lactated Ringer's solution was infused throughout the surgery at a rate of 5 ml/kg/h. After anesthetic induction, ventilation was controlled with a tidal volume of 8–10 ml/kg body weight and a respiratory rate of 8–12 breaths per minute, to maintain $PetCO_2$ at 35 mmHg. In addition, 2–3 min before release of the tourniquet, ventilatory rate or tidal volume was adjusted to tightly maintain $PetCO_2$ at 35 mmHg. Thereafter, respiratory rate and tidal volume were maintained unchanged throughout the rest of the study period.

Noninvasive blood pressure, heart rate, V_{mca}, arterial blood gases, and plasma lactate levels were measured every minute for 10 min after tourniquet release in all patients, using a Stat Profile Ultima (NOVA Biomedical, Boston, MA, USA).

All data are expressed as mean ± SD. Following the confirmation of equal variance among groups by the Bartlett test, the χ^2 test or one-way factorial or repeated-measures analysis of variance was performed with multiple comparisons. When the F value was significant, the Bonferroni method was used to make multiple comparisons. Statistical significance was set at $P < 0.05$. All calculations were performed on a Windows computer with SPSS (SPSS, Chicago, IL, USA) and Stat View 5.0 software packages (Abacus Concepts, Berkeley, CA, USA).

Table 1 shows the demographic data of the three groups. There were no significant differences among the groups. All patients had easily detectable MCA flow velocities.

Table 2 shows the time course of changes in physiological variables in the three groups. Mean arterial pressure (MAP) in all three groups decreased for 3 min after tourniquet deflation, the decrease in diabetic patients at 1 min after deflation being greater than in the other two groups.

Heart rates (HR) in all three groups increased after tourniquet deflation, the increase lasting for 1–2 min. The HR increase in controls and previous stroke patients at 1 min after deflation was greater than that in diabetic patients. Plasma pH levels in the three groups decreased after tourniquet deflation, the decrease lasting for 7 min. Plasma lactate levels in the three groups increased for 10 min after tourniquet deflation. Also, there was a significant difference in plasma lactate level in the diabetic group at 2, 3, and 4 min after tourniquet deflation, compared with that in the other two groups. $PaCO_2$ in the three groups increased after tourniquet deflation; the increase lasted for 3 min.

Table 3 and Fig. 1 show the time course of changes in V_{mca} in the three groups. V_{mca} in the three groups increased after tourniquet deflation, the increase lasting for 4–5 min. The degree of increase in V_{mca} in the diabetic patients, however, was smaller than that in the other two groups after tourniquet deflation.

Discussion

In the present study, V_{mca} increased in all three groups after tourniquet deflation, although the degree of V_{mca} increase

Table 1 Demographic data of the three groups

Factor	Control	Previous stroke	Diabetes	*P* value
Number	8	7	7	
Age (years)	62 ± 8	61 ± 5	61 ± 6	0.96
Weight (kg)	56 ± 3	55 ± 5	59 ± 5	0.23
Height (cm)	161 ± 4	160 ± 4	163 ± 4	0.64
Anesthetic time (min)	198 ± 33	206 ± 26	198 ± 41	0.88
Operation time (min)	127 ± 14	139 ± 18	134 ± 18	0.42
Tourniquet time (min)	101 ± 13	99 ± 17	105 ± 9	0.75
Types of surgery				
Knee surgery	4	5	4	
Lower leg fracture	4	3	3	
End-tidal sevoflurane concentration (%)	1.93 ± 0.13	1.84 ± 0.12	1.94 ± 0.11	0.25
BIS	44 ± 1	44 ± 2	43 ± 2	0.98

Data are expressed as mean ± SD

BIS bispectral index

in diabetic patients was smaller than that in controls and patients with previous stroke.

The number of patients with coexisting diseases, such as diabetes mellitus or previous stroke, undergoing orthopedic surgery has been steadily rising [10]. This situation has led to a heightened interest in the anesthetic implications of intraoperative changes in systemic hemodynamics and cerebral circulation in these patients. Thus, it is important for anesthesiologists to know whether cerebral circulation during anesthesia in patients with diabetes mellitus or previous stroke is different from that in patients without such diseases.

Some previous reports have described cerebrovascular CO_2 reactivity in diabetic patients under anesthesia. Previously, we examined cerebrovascular CO_2 reactivity in diabetic patients under propofol anesthesia and showed that diabetic patients receiving insulin therapy had impaired cerebrovascular CO_2 reactivity [9]. In contrast, Kawata et al. [11] found no impaired cerebrovascular CO_2 reactivity in diabetic patients under isoflurane–nitrous oxide anesthesia. There have been few reports describing cerebrovascular CO_2 reactivity in patients with previous stroke under anesthesia [8, 12]. Kitaguchi et al. [12] reported that both CO_2 reactivity and cerebral autoregulation were well maintained during the inhalation of 33% nitrous oxide, 33% argon, and oxygen with 1.5% sevoflurane [0.88 minimum alveolar concentration (MAC)] in patients with ischemic cerebrovascular disease. In a previous study, we also showed that CO_2 reactivity in patients with previous stroke was not different from that in control patients during anesthesia with 1.0 MAC sevoflurane in 33% nitrous oxide and 67% nitrous oxide [8]. In the same previous study, we found that cerebrovascular CO_2 reactivity differed between sevoflurane and isoflurane anesthesia [8]; cerebrovascular CO_2 reactivity under sevoflurane anesthesia was lower than that under isoflurane anesthesia at equipotent anesthetic doses. Thus, different anesthetic agents or different concentrations of the same anesthetic agent could have differential effects on cerebrovascular CO_2 reactivity. The differing results in diabetic patients, as well, may in part be attributable to the different anesthetic agents used.

There have been some reports examining changes in CBF or MCA velocity after tourniquet deflation. Hirst et al. [7], examining the effects of intraoperative release of a thigh tourniquet on MCA blood flow using transcranial Doppler sonography, found that MCA flow velocity increased significantly from 52 ± 6 to 82 ± 24 cm/s (an increase of 58% ± 13%) within 4 ± 1 min after tourniquet release and remained elevated for 7 min. Fujii et al. [5] examined the effects on MCA flow velocity of release of tourniquets on the upper and lower extremities and found that the increase in MCA blood flow velocity was greater in patients requiring lower extremity tourniquets than in those with upper extremity tourniquets. These two studies demonstrated that increased MCA flow velocity after tourniquet deflation was mainly attributable to an increase in $PaCO_2$. Our study indicates that the degree of change in CBF after tourniquet deflation under sevoflurane anesthesia could depend on the patient's underlying medical condition, such as the presence of diabetes mellitus. The possible cause of the differential changes in MCA flow in diabetic patients may be an impaired vasodilatory response to hypercapnia in diabetic patients treated with insulin [9].

In diabetic patients, more profound increases in lactate, more profound decreases in MAP, and small changes in HR and MCA flow after tourniquet deflation were observed

Table 2 Time course of changes in physiological variables in the three groups

Variable	Group	Predeflation	Time from tourniquet deflation (min)									
			1	2	3	4	5	6	7	8	9	10
MAP (mmHg)	Control	111 ± 10	89 ± 10*	88 ± 9*	88 ± 8*	94 ± 10	99 ± 7	103 ± 9	104 ± 10	106 ± 11	107 ± 10	110 ± 10
	Stroke	109 ± 9	87 ± 11*	88 ± 10*	91 ± 8*	97 ± 7	99 ± 10	101 ± 6	103 ± 11	104 ± 8	105 ± 10	109 ± 10
	Diabetes	106 ± 8	79 ± 6*#	83 ± 11*	87 ± 11*	91 ± 12	95 ± 8	100 ± 7	106 ± 9	104 ± 11	104 ± 9	107 ± 10
HR (beats/min)	Control	75 ± 5	94 ± 5*	88 ± 8*	81 ± 7	79 ± 6	79 ± 5	80 ± 6	79 ± 6	78 ± 6	77 ± 6	78 ± 6
	Stroke	75 ± 5	94 ± 7*	89 ± 7*	83 ± 7	79 ± 6	78 ± 6	79 ± 6	77 ± 6	79 ± 8	78 ± 4	79 ± 5
	Diabetes	77 ± 6	85 ± 5*#	84 ± 7	80 ± 6	77 ± 7	79 ± 6	78 ± 6	79 ± 8	78 ± 8	78 ± 6	77 ± 7
pH	Control	7.445 ± 0.05	7.399 ± 0.07*	7.405 ± 0.04*	7.389 ± 0.04*	7.403 ± 0.04*	7.409 ± 0.05*	7.415 ± 0.05*	7.427 ± 0.03*	7.431 ± 0.08	7.442 ± 0.04	7.447 ± 0.03
	Stroke	7.446 ± 0.07	7.395 ± 0.06*	7.398 ± 0.04*	7.391 ± 0.05*	7.405 ± 0.04*	7.410 ± 0.06*	7.413 ± 0.05*	7.423 ± 0.06*	7.434 ± 0.06	7.444 ± 0.05	7.446 ± 0.04
	Diabetes	7.448 ± 0.06	7.400 ± 0.05*	7.391 ± 0.05*#	7.390 ± 0.04*	7.403 ± 0.05*	7.410 ± 0.05*	7.411 ± 0.05*	7.422 ± 0.06*	7.429 ± 0.07	7.441 ± 0.04	7.445 ± 0.04
$PaCO_2$ (mmHg)	Control	36 ± 2	46 ± 2*	49 ± 2*	45 ± 3*	42 ± 3	39 ± 2	37 ± 2	37 ± 2	35 ± 2	35 ± 2	35 ± 2
	Stroke	36 ± 1	47 ± 3*	49 ± 3*	46 ± 2*	41 ± 2	39 ± 3	37 ± 3	37 ± 3	36 ± 1	35 ± 2	35 ± 2
	Diabetes	36 ± 2	48 ± 3*	50 ± 3*	45 ± 2*	40 ± 3	40 ± 2	38 ± 2	37 ± 3	36 ± 2	35 ± 2	36 ± 1
PaO_2 (mmHg)	Control	168 ± 16	175 ± 21	170 ± 21	165 ± 19	166 ± 20	166 ± 18	161 ± 22	163 ± 19	165 ± 18	163 ± 16	165 ± 18
	Stroke	177 ± 25	172 ± 16	165 ± 20	163 ± 18	166 ± 19	166 ± 20	163 ± 20	165 ± 19	164 ± 19	160 ± 19	165 ± 16
	Diabetes	170 ± 21	166 ± 20	159 ± 22	160 ± 22	161 ± 19	164 ± 19	160 ± 20	164 ± 17	166 ± 17	160 ± 21	161 ± 17
Lactate (mmol/l)	Control	1.1 ± 0.2	2.5 ± 0.5*	2.5 ± 0.3*	2.7 ± 0.3*	2.4 ± 0.3*	2.2 ± 0.4*	2.2 ± 0.3*	2.1 ± 0.3*	2.1 ± 0.4*	2.0 ± 0.4*	2.1 ± 0.2*
	Stroke	1.1 ± 0.3	2.7 ± 0.5*	2.5 ± 0.4*	2.7 ± 0.3*	2.4 ± 0.4*	2.2 ± 0.4*	2.3 ± 0.4*	2.2 ± 0.4*	2.1 ± 0.3*	2.1 ± 0.3*	2.1 ± 0.2*
	Diabetes	1.0 ± 0.2	2.8 ± 0.3*	3.1 ± 0.4*#	3.3 ± 0.5*#	2.9 ± 0.4*#	2.6 ± 0.5*	2.4 ± 0.4*	2.3 ± 0.4*	2.1 ± 0.4*	2.1 ± 0.3*	2.0 ± 0.4*

Data are expressed as mean ± SD

MAP mean arterial pressure; *HR* heart rate

*$P < 0.05$ compared with predeflation period

# $P < 0.05$ compared with the other two groups at the same time point

Table 3 Time course of changes in mean blood flow velocity in the middle cerebral artery (V_{mca}) in the three groups

	Group	Predeflation	Time from tourniquet deflation (min)									
			1	2	3	4	5	6	7	8	9	10
Vmca (cm/s)	Control	48.8 ± 2.7	56.6 ± 4.6*	58.5 ± 3.3*	58.1 ± 4.0*	54.0 ± 2.2*	51.2 ± 1.9	50.2 ± 1.8	47.3 ± 2.2	46.0 ± 2.5	45.7 ± 1.8	46.3 ± 1.5
	Stroke	46.2 ± 1.9	54.0 ± 4.3*	58.4 ± 4.6*	56.4 ± 2.6*	52.7 ± 2.0*	49.5 ± 1.7	47.5 ± 2.3	47.7 ± 2.6	45.1 ± 2.1	44.5 ± 3.9	43.7 ± 3.7
	Diabetes	47.4 ± 3.3	51.1 ± 4.6*	51.7 ± 2.3*#	49.8 ± 1.0*#	48.5 ± 1.2*#	46.8 ± 1.2#	46.2 ± 1.3	45.2 ± 1.2	45.0 ± 1.2	45.1 ± 1.5	45.5 ± 1.5

Data are expressed as mean ± SD

*$P < 0.05$ compared with predeflation period

# $P < 0.05$ compared with the other two groups at the same time point

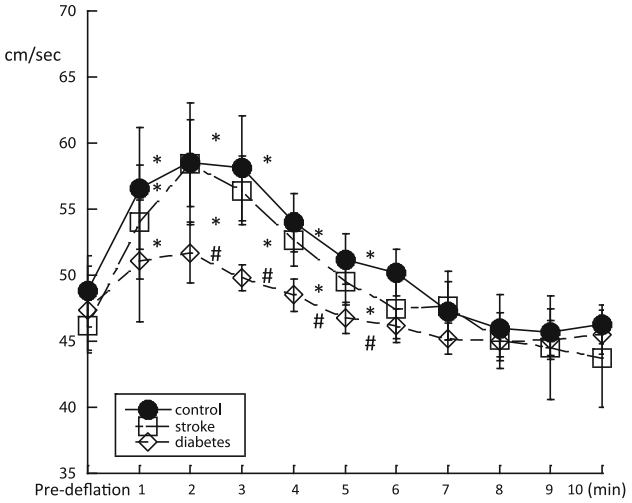

Fig. 1 Time course of changes in mean blood flow velocity in middle cerebral artery (V_{mca}) in the three groups. *$P< 0.05$ compared with predeflation period; #$P< 0.05$ compared with the other two groups at the same time point

compared with the other groups. Although we did not examine whether diabetic neuropathy was present in the diabetic patients included in this study, the specific observations in diabetic patients may be partly associated with impairment of the autonomic nervous system. It is widely reported that diabetic neuropathy is related to hemodynamic instability during anesthesia in diabetic patients [13]. Hence, it is possible that compensatory mechanisms, in the form of adaptations to maintain CBP in case of a decrease in MAP, do not occur quickly after tourniquet deflation in diabetic patients because of their impaired autonomic nervous system.

In this study, we examined V_{mca} alteration during sevoflurane anesthesia together with nitrous oxide. In clinical practice in our institute, a combination of nitrous oxide and volatile/intravenous anesthetics is sometimes used. However, it is reported that the combination of nitrous oxide and volatile anesthetics has a more potent cerebral vasodilatory effect than an equipotent dose of volatile anesthetics alone [14]. We cannot rule out the possibility, therefore, that different results may be observed in anesthesia without nitrous oxide.

In conclusion, the degree of V_{mca} increase after tourniquet deflation in diabetic patients under sevoflurane anesthesia is smaller than that in control patients and those with previous stroke. The difference may be attributable to the impaired vasodilatory response to hypercapnia in diabetic patients treated with insulin.

Acknowledgments The authors wish to thank Forte (Tokyo, Japan) for assistance with manuscript preparation in English. This study was supported in part by grants to Dr. Kadoi (No. 21591998) from the Japanese Ministry of Education, Culture, Sports, Science and Technology.

References

1. Lynn AM, Fischer T, Brandford HG, Pendergrass TW. Systemic responses to tourniquet release in children. Anesth Analg. 1986; 65:865–72.
2. Tsuchiya M, Ueda W, Tomoda M, Mokudai Y, Takeda A, Hirakawa M. The hemodynamic and metabolic changes following tourniquet release during halothane anesthesia. Masui (Jpn J Anesthesiol). 1991;40:540–3. (in Japanese with English abstract).
3. Kadoi Y, Ide M, Saito S, Shiga T, Ishizaki K, Goto F. Hyperventilation after tourniquet deflation prevents an increase in cerebral blood flow velocity. Can J Anesth. 1999;46:259–64.
4. Kadoi Y, Kawauchi C, Ide M, Saito S, Mizutani A. Differential increases in blood flow velocity in the middle cerebral artery after tourniquet deflation during sevoflurane, isoflurane or propofol anesthesia. Anaesth Intensive Care. 2009;35:598–603.
5. Fujii Y, Toyooka H, Ishikawa E, Kato N. Blood flow velocity in the middle cerebral artery response to tourniquet release. Anaesth Intensive Care. 1999;27:253–6.
6. Akata T, Tominaga M, Sagiyama M, Taniyama T, Inaba S, Takahashi S, Yoshitake J. Changes in end-tidal CO_2 level following tourniquet deflation during orthopedic surgery. J Anesth. 1992;6:9–15.
7. Hirst RP, Slee TA, Lam AM. Changes in cerebral blood flow velocity after release of intraoperative tourniquets in humans: a transcranial Doppler study. Anesth Analg. 1990;71:503–10.
8. Kadoi Y, Saito S, Takahashi K. The comparative effects of sevoflurane versus isoflurane on cerebrovascular carbon dioxide reactivity in patients with previous stroke. J Anesth. 2008; 22:135–9.
9. Kadoi Y, Hinohara H, Kunimoto F, Saito S, Ide M, Hiraoka H, Kawahara F, Goto F. Diabetic patients have an impaired cerebral vasodilatory response to hypercapnia under propofol anesthesia. Stroke. 2003;34:2399–403.
10. Kadoi Y. Anesthetic considerations in diabetic patients. Part I. Preoperative considerations of patients with diabetes mellitus. J Anesth. 2010;24:739–47.
11. Kawata R, Nakakimura K, Matsumoto M, Kawai K, Kunihiro M, Sakabe T. Cerebrovascular CO_2 reactivity during anesthesia in patients with diabetes mellitus and peripheral vascular disease. Anesthesiology. 1998;89:887–93.
12. Kitaguchi K, Ohsumi H, Kuro M, Nakajima T, Hayashi Y. Effects of sevoflurane on cerebral circulation and metabolism in patients with ischemic cerebrovascular disease. Anesthesiology. 1993;79:704–9.
13. Kadoi Y. Anesthetic considerations in diabetic patients. Part II. Intraoperative and postoperative management of patients with diabetes mellitus. J Anesth. 2010;24:748–56.
14. Lam AM, Mayberg TS, Eng CC, Cooper JO, Bachenberg KL, Mathisen TL. Nitrous oxide-isoflurane anesthesia causes more cerebral vasodilation than an equipotent dose of isoflurane in humans. Anesth Analg. 1994;78:462–8.