Cerebrovascular CO₂ reactivity in elderly and younger adult patients during sevoflurane anaesthesia

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Purpose: General anaesthetic agents and aging affect cerebrovascular CO₂ reactivity (CCO₂R). The purpose of this study was to investigate the effect of aging on CCO₂R in patients during sevoflurane anaesthesia.

Methods: Twenty-four patients were divided into two groups of 12 according to age; 20–40 yr and 50–70 yr. Anaesthesia was induced with 5 mg·kg⁻¹ thiopentone and maintained with sevoflurane 1.0 to 1.5% (end-tidal) and nitrous oxide 66% in oxygen to maintain anaesthesia. End-tidal CO₂ tension (P_{ET}CO₂) was altered from 20 to 50 mmHg in 5 mmHg steps by changing the respiratory rate. Middle cerebral blood flow velocity (CBFV) and pulsatility index (PI) were measured by transcranial Doppler (TCD) at each step change in P_{ET}CO₂. The CCO₂R was calculated as the change of CBFV per mmHg at each 5 mmHg interval.

Results: In each group, there were no changes in blood pressure, heart rate, end-tidal sevoflurane concentration, or PI as the P_{ET}CO₂ was increased from 20 to 50 mmHg. The CCO₂R at P_{ET}CO₂ of 35 to 50 mmHg in the younger group (0.80 ± 0.27 (SD) cm·sec⁻¹·mmHg⁻¹) was larger than that in the elderly group (0.31 ± 0.16 cm·sec⁻¹·mmHg⁻¹) (P < 0.01).

Conclusion: It is concluded that, during sevoflurane anaesthesia, CCO₂R is well preserved, and that the CCO₂R at P_{ET}CO₂ of 35 to 50 mmHg in the 20 to 40 yr age group is greater than that in the 50 to 70 yr age group.

Objectif : L'anesthésie générale et le vieillissement affectent la réactivité cérébrovasculaire au CO₂ (CCO₂R). Ce travail visait à étudier l'effet du vieillissement sur la CCO₂R pendant l'anesthésie au sévoflurane.

Méthodes : Vingt-quatre patients étaient répartis en deux groupes de 12 selon leur âge: 20 à 40 ans et 50 à 70 ans. L'anesthésie était induite avec du thiopentone 5 mg·kg⁻¹ et maintenue avec du sévoflurane 1,0 à 1,5% (télé-expiratoire) et du protoxyde d'azote 66% en oxygène. La P_{ET}CO₂ était modifiée de 20 à 50 mmHg par échelons de 5 mmHg en changeant la fréquence respiratoire. La vélocité du débit sanguin cérébral (CBFV) et l'index de pulsatilité (PI) étaient mesurés à l'aide d'un Doppler transcrânien à chaque changement d'échelon de la P_{ET}CO₂. La CCO₂R était calculée comme le changement du CBFV par mmHg à chaque intervalle de 5 mmHg.

Résultats : Dans chacun des groupes, la pression artérielle, la fréquence cardiaque, la concentration télé-expiratoire en sévoflurane n'ont pas changé, ainsi que le PI lorsque la P_{ET}CO₂ augmentait de 20 à 50 mmHg. Dans le groupe le plus jeune, aux P_{ET}CO₂ de 35 à 50 mmHg, la CCO₂R était plus élevée (0,80 ± 0,27 (ET) cm·s⁻¹·mmHg) que dans le groupe plus âgé (0,31 ± 0,16 cm·s⁻¹·mmHg, P < 0,01).

Conclusion : Pendant l'anesthésie au sévoflurane, la CCO₂R est bien préservée et aux P_{ET}CO₂ de 35 à 50 mmHg, la CCO₂R est plus élevée dans le groupe d'âge de 20 à 40 ans que dans celui de 50 à 70 ans.

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THE measurement of cerebral blood flow velocity (CBFV) by transcranial Doppler ultrasound flowmetry (TCD) is a useful non-invasive method of assessing cerebral haemodynamics.¹ It is reported that CBFV does not directly indicate cerebral blood flow (CBF), but the changes of CBFV correlate well with the changes of CBF if end-tidal carbon dioxide tension ($P_{ET}CO_2$) is not influenced by changes in arterial blood pressure and if $P_{ET}CO_2$ closely reflects arterial CO₂ tension ($PaCO_2$).²

It is well established that an increase in $PaCO_2$ causes an increase in CBF and a decrease in $PaCO_2$ has the opposite effect.³ The change of cerebrovascular resistance or CBF in response to changes of $PaCO_2$ is termed cerebrovascular CO₂ reactivity (CCO₂R). In some situations in neuroanaesthesia or in neurological patients, it is important to decrease intracranial pressure and this achieved by a decrease of CBF induced by reduced $PaCO_2$. In this respect, it is also important to know the effects of anaesthetic agents and patient age on the CCO₂R. In the present study, CCO₂R is defined as the change in mean CBFV per mmHg change in $P_{ET}CO_2$ (cm·sec⁻¹·mmHg⁻¹).

Thiopentone anaesthesia has been reported to decrease CCO₂R but aging does not.⁴ Isoflurane enhances CCO₂R more than do nitrous oxide or halothane.⁵ Desflurane,⁶ sevoflurane,⁷ propofol and midazolam are reported not to decrease CCO₂R.⁸ However, there have been no studies concerning the effects of aging on the CCO₂R in patients during sevoflurane anaesthesia. In the present study, we investigated the effects of aging on CCO₂R during sevoflurane anaesthesia.

Methods

The protocol was approved by the ethics committee of our institution and informed consent was obtained from each subject. Twenty-four patients of ASA physical status 1 or 2 (aged from 20–40 yr, or from 50–70 yr, with no cerebral or general vascular, respiratory, renal or liver disease) and who were undergoing lower abdominal surgery for colon or uterine cancer in the supine position in our hospital were included. Those taking drugs other than premedication before surgery were excluded. Patients were divided into two groups of 12 according to age.

Non-invasive arterial blood pressure, heart rate, arterial O₂ saturation (SpO₂) by pulse oximetry (UltimaTM, Datex, Finland), rectal temperature (oesophageal temperature in sigmoidectomy), airway pressure, and end-tidal CO₂ tension ($P_{ET}CO_2$) and sevoflurane concentration (S_{ET}) (UltimaTM) were mon-

itored. Rectal or oesophageal temperature was maintained between 36.0 and 36.5°C using a warming blanket during the operation.

Atropine 0.5 mg and hydroxyzine 50 mg *im* were administered 30 min before patients entered the operating room. After inserting an epidural catheter into a single interspace between T12–L4, anaesthesia was induced with 5 mg·kg⁻¹ thiopentone and sevoflurane 2% (S_{ET}) and tracheal intubation was facilitated with 0.15 mg·kg⁻¹ vecuronium. Anaesthesia was maintained with sevoflurane 1.0 to 1.5% (S_{ET}), nitrous oxide 66% in oxygen and epidural block using 3–6 ml mepivacaine 1% to maintain systolic blood pressure within 20% of the pre-anaesthesia value. Measurements were performed during surgery. During the measurement no drugs such as vasoconstrictors, vasodilators or epidural mepivacaine were administered.

The cerebrovascular blood flow velocity (CBFV) and pulsatility index (PI) of the left middle cerebral artery were monitored continuously with TCD (TC2-64TM, EME, Germany). A Doppler probe (IMP2TM, EME) was fixed by means of a specially designed holder over the left temporal bone window in a position providing the best signal (depth 50 to 60 mm). Mean CBFV was measured directly by TCD. The PI was calculated automatically using the formula: $PI = (\text{peak systolic velocity} - \text{end diastolic velocity}) / (\text{mean velocity})$ and is an approximate indicator of cerebrovascular resistance.⁹ The $P_{ET}CO_2$ was increased stepwise from 20 to 50 mmHg by changing the respiratory rate with a constant tidal volume. At every 5 mmHg stepwise change in $P_{ET}CO_2$, CBFV and PI were recorded for one minute by maintaining the $P_{ET}CO_2$ at the same level for at least two minutes. The value at which the best signal was obtained was used. The CCO₂R was calculated at each 5 mmHg interval in $P_{ET}CO_2$ as the change of CBFV per mmHg $P_{ET}CO_2$ and is expressed as cm·sec⁻¹·mmHg⁻¹.

Statistical analysis was performed using the chi-square test and Mann-Whitney U test for demographic data and with repeated measured analysis of variance followed by Fisher's PLSD for the measured variables. *P* values < 0.05 were considered statistically significant.

Results

There were no demographic differences except for age (Table I). No patient showed SpO₂ < 98%. In every patient, airway pressure was in the range 18–22 cm H₂O. Blood pressure (100–132 mmHg systolic and 56–81 mmHg diastolic), heart rate (75–88 beats·min⁻¹) and S_{ET} (1.0–1.5% in both groups; (1 MAC sevoflurane in 66% nitrous oxide = 1.25% in the younger group, and 0.9% in the elderly group). The

TABLE I Demographic data

	Younger group	Elderly group
Age (yr)	31 ± 2 (20–40)	62 ± 4 (50–70)*
Sex (Male/Female)	6/6	8/4
Body weight (kg)	58.5 ± 3.6 (45.0–71.0)	53.4 ± 2.9 (47.5–65.0)
Type of surgery		
Hemicolectomy	5	4
Sigmoidectomy	3	5
Hysterectomy	4	3
Anaesthesia duration (min)	235 ± 39 (115–425)	256 ± 30 (135–370)
Blood loss (ml)	205 ± 42 (30–320)	241 ± 62 (20–550)
Crystalloid infusion (ml)	1996 ± 354 (930–3800)	2352 ± 396 (850–3600)

mean ± SD (range), *: $P < 0.05$ vs younger group

mean CBFV increased with increasing $P_{ET}CO_2$; 42.2 ± 5.8 cm·sec⁻¹ at 20 mmHg to 64.9 ± 8.7 cm·sec⁻¹ at 50 mmHg in the younger group ($P < 0.01$), 38.7 ± 3.9 cm·sec⁻¹ at 20 mmHg to 52.9 ± 4.6 cm·sec⁻¹ at 50 mmHg in the elderly group ($P < 0.01$). The younger group showed higher CBFV than the elderly group at $P_{ET}CO_2$ of 40 mmHg (60.2 ± 5.2 cm·sec⁻¹ vs 49.4 ± 5.6 cm·sec⁻¹, respectively, $P = 0.02$) to 50 mmHg (64.9 ± 8.7 cm·sec⁻¹ vs 52.9 ± 4.6 cm·sec⁻¹, respectively, $P = 0.0496$) (Figure). During the study, PI showed no change in either group and no differences between groups (Figure). The CCO_2R is shown in Table II and the slope of CBFV change in the Figure. The younger group showed greater CCO_2R than did the elderly group at $P_{ET}CO_2$ of 35 to 50 mmHg (Table II).

Discussion

In the present study, CBFV increased with increasing $P_{ET}CO_2$ and CBFV was greater in younger than in elderly patients at $P_{ET}CO_2$ of 40 to 50 mmHg. The CCO_2R , represented as CBFV change per mmHg $P_{ET}CO_2$ was greater in younger than in elderly patients at $P_{ET}CO_2$ of 35 to 50 mmHg. However, there were no changes in PI in either group and no differences in PI between the two groups.

TABLE II Cerebrovascular CO_2 reactivity

$P_{ET}CO_2$ (mmHg)	20–25	25–30	30–35	35–40	40–45	45–50
Young 20–40 yr	0.48 ± 0.19	0.34 ± 0.15	0.32 ± 0.17	1.01 ± 0.30	0.70 ± 0.22	0.66 ± 0.24
Elderly 50–70 yr (cm·sec ⁻¹ ·mmHg ⁻¹)	0.49 ± 0.20	0.41 ± 0.18	0.29 ± 0.15	0.31 ± 0.17* ¹	0.28 ± 0.13* ²	0.33 ± 0.14* ³

*: $P < 0.05$ vs the younger group

1): $P < 0.05$ vs the value at 20–25 mmHg

2): $P < 0.05$ vs the value at 25–30 mmHg

3): $P < 0.05$ vs the value at 30–35 mmHg

FIGURE Mean middle cerebral arterial blood flow velocity (mV) and pulsatility index (PI) during change in $P_{ET}CO_2$. Closed circles: younger group; open circles: elderly group. mean ± SD. 1): $P < 0.05$ vs the value at 20 mmHg. 2): $P < 0.05$ vs the value at 25 mmHg. 3): $P < 0.05$ vs the value at 30 mmHg. 4): $P < 0.05$ vs the value at 35 mmHg. *: $P < 0.05$ vs the younger group

To examine CCO_2R , $P_{ET}CO_2$ was used instead of $PaCO_2$. However, in the present study, $P_{ET}CO_2$ was considered to have changed in parallel with $PaCO_2$, because the subjects had no pulmonary or vascular disease.

The CBF change has been reported to correlate well with the rate of change of CBFV but not with the absolute value of CBFV.¹⁰ However, Sueyoshi *et al.*¹¹ reported that CCO_2R measured using absolute values of CBFV correlated well with CCO_2R measured with

CBF using an argon inhalation method. In the present study, all the absolute values of mean CBFV at 35 and 40 mmHg P_{ET}CO₂ were within the range reported previously (33–90 cm·sec⁻¹).¹ Therefore, it seems reasonable to consider that the CCO₂R is related to the absolute value of CBFV.

The CBF may be altered by changes not only of PaCO₂, but of other variables such as blood pressure, cardiac output, body temperature,¹² intrathoracic pressure or depth of anaesthesia. Although cardiac output was not measured in the present study, absence of changes in blood pressure and heart rate suggests haemodynamic stability. Body temperature, intrathoracic pressure reflected by the airway pressure, and depth of anaesthesia represented by S_{ET}, were unchanged. Therefore, changes in CBFV, in this study, are largely the results of changes in P_{ET}CO₂.

Huber *et al.*¹³ reported that it was not the large arteries but the arterioles that reacted to the change in PaCO₂. It is said that PI is an approximate indicator of cerebrovascular resistance.⁹ The stable PI in the present study suggests that the resistance of the middle cerebral artery is unchanged by changing P_{ET}CO₂. Therefore, one may assume that CBFV correlates with CBF.

During general anaesthesia using halothane,⁵ isoflurane,¹⁴ desflurane,⁶ sevoflurane⁷ or intravenous anaesthetics such as propofol or midazolam,⁸ CCO₂R was preserved. However, the CCO₂R during sevoflurane anaesthesia was tested only in patients with cerebrovascular diseases.⁷ The present study showed that CCO₂R was also well preserved during sevoflurane anaesthesia in patients with normal cerebral circulation. Inhalation anaesthetics are reported to increase CCO₂R.⁵ Isoflurane increases CCO₂R more than halothane.⁵ It seems that no other study has been performed to compare the CCO₂R with different anaesthetic methods. Therefore, it was impossible to compare CCO₂R during sevoflurane anaesthesia with that with other anaesthetic methods.

It has been reported that the CCO₂R in the awake state is less in elderly than in younger subjects.² Schieve also showed a tendency for lower CCO₂R in the elderly.⁴ The lower CCO₂R in the elderly was also observed during sevoflurane anaesthesia in the present study. Another possibility is that, in the elderly group, cerebrovascular dilatation by sevoflurane is large enough so that there is no further dilatation at higher CO₂ concentrations.

The decreased CCO₂R in the elderly during sevoflurane anaesthesia at high P_{ET}CO₂ makes an increase of intracranial pressure less likely than in younger patients. However, in neuroanaesthesia, such high P_{ET}CO₂ levels are not recommended. Therefore, the difference in CCO₂R is of little clinical importance.

In conclusion, during sevoflurane anaesthesia, CBFV increased as the P_{ET}CO₂ was increased from 20 to 50 mmHg, and CCO₂R was greater in patients aged 20–40 yr than in those of 50–70 yr at P_{ET}CO₂ of 35–50 mmHg.

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