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Graded Hypercapnia and Cerebral Autoregulation during Sevoflurane or Propofol Anesthesia

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Background: **Hypercapnia abolishes cerebral autoregulation, but little is known about the interaction between hypercapnia and autoregulation during general anesthesia. With normocapnia, sevoflurane (up to 1.5 minimum alveolar concentration) and propofol do not impair cerebral autoregulation. This study aimed to document the level of hypercapnia required to impair cerebral autoregulation during propofol or sevoflurane anesthesia.**

Methods: **Eight healthy subjects received a remifentanil infusion and were anesthetized with propofol (140 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and sevoflurane (1.0–1.1% end tidal) in a randomized crossover study. Ventilation was adjusted to achieve incremental increases in arterial carbon dioxide partial pressure ($Paco_2$) until autoregulation was impaired. Cerebral autoregulation was tested by increasing the mean arterial pressure (MAP) from 80 to 100 mmHg with phenylephrine while measuring middle cerebral artery flow velocity by transcranial Doppler. The autoregulation index, which has a value ranging from 0 to 1, representing absent to perfect autoregulation, was calculated, and an autoregulation index of 0.4 or less represented significantly impaired autoregulation.**

Results: **The threshold $Paco_2$ to significantly impair cerebral autoregulation ranged from 50 to 66 mmHg. The threshold averaged 56 ± 4 mmHg (mean ± SD) during sevoflurane anesthesia and 61 ± 4 mmHg during propofol anesthesia ($P = 0.03$). Carbon dioxide reactivity measured at a MAP of 100 mmHg was 30% greater than that at a MAP of 80 mmHg.**

Conclusions: **Even mild hypercapnia can significantly impair cerebral autoregulation during general anesthesia. There is a significant difference between propofol anesthesia and sevoflurane anesthesia with respect to the effect of hypercapnia on cerebral autoregulation. This difference occurs at clinically relevant levels of $Paco_2$. When inducing hypercapnia, carbon dioxide reactivity is significantly affected by the MAP. (Key words: Cerebral blood flow; inhalation anesthetics; intravenous anesthetics; transcranial Doppler.)**

CEREBRAL autoregulation refers to the process by which the brain maintains nearly constant cerebral blood flow despite variations in cerebral perfusion pressure within the range of 50 to 150 mmHg. It is known that hypercapnia abolishes this pressure autoregulation of cerebral blood flow,[1–4] but little is known about the interaction between hypercapnia and cerebral autoregulation during general anesthesia. The aim of this study was to document the level of arterial carbon dioxide partial pressure ($Paco_2$) at which cerebral autoregulation is impaired in healthy adults during general anesthesia.

With general anesthesia in normal subjects, cerebral autoregulation may be intact or abolished depending on both the anesthetic agent chosen and the dose given. In this study, two different anesthetics were administered—propofol and sevoflurane—that were expected to leave autoregulation intact at normocapnia. Most volatile anesthetics abolish cerebral autoregulation at higher doses,[5] but sevoflurane, at doses as high as 1.5 minimum alveolar concentration (MAC), is associated with intact autoregulation in normocapnic humans.[6] Propofol is associated with intact cerebral autoregulation,[5] even at doses high enough to cause electrical silence on the electroencephalogram.[7] We hypothesized that the threshold level of $Paco_2$ at which cerebral autoregulation becomes impaired is anesthetic agent–dependent, and the aim of this study was to compare the threshold between these two anesthetic agents.

Materials and Methods

After obtaining institutional ethics committee approval, written informed consent was obtained from eight adults scheduled to undergo general anesthesia for lower-limb orthopedic procedures expected to last more than 4 h. We chose procedures associated with a low level of surgical stimulation (*e.g.*, fixation of calcaneal fractures). Patients were excluded if they had active respiratory disease, any cardiovascular disease (including hypertension), and any neurologic disease or recent head injury.

Subjects received 1–2 mg of midazolam intravenously before induction of general anesthesia with thiopentone (4–5 mg/kg). The trachea was intubated after paralysis with vecuronium, and the lungs were ventilated with a mixture of air and oxygen (fraction of inspired oxygen, 0.3–0.4).

Experimental Protocol

Sevoflurane and propofol were compared in a nonblinded, randomized, crossover fashion. The study was performed twice in each subject: once with maintenance of anesthesia by infusion of propofol (140 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and once with maintenance by inhalation of sevoflurane (1.0–1.1% end-tidal concentration). The order of the two anesthetic agents was randomized. A

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minimum of 30–60 min elapsed between commencing the anesthetic maintenance agent and commencing autoregulation testing. When crossing over from one agent to the other, a minimum of 30 min was allowed for anesthetic equilibration.

An infusion of remifentanil was commenced with induction and continued throughout the study (0.125–0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Remifentanil was used to provide a rapidly variable level of opioid activity to control arterial blood pressure in the face of any variation in surgical stimulation. The dose of remifentanil was titrated to achieve a baseline blood pressure before each autoregulation test. The infusion rate was then kept constant during each test.

After induction of anesthesia, a 20-gauge catheter was inserted into a radial artery for pressure monitoring and arterial blood sampling. Transcranial Doppler (TCD) probes were adjusted to obtain signals from the middle cerebral arteries bilaterally and were held in constant position by a frame.[8] During autoregulation testing, mean arterial pressure (MAP) and middle cerebral artery flow velocity (Vmca) were continuously recorded and saved for later analysis. Temperature was monitored by an esophageal temperature probe. Hematocrit and blood gasses were measured with an automated blood gas analyzer (Novo Stat II, Waltham, MA). The study began after commencement of surgery and during steady state conditions as indicated by a stable cerebral blood flow velocity.

Cerebral Autoregulation Testing

Cerebral autoregulation was tested in the following manner. MAP was adjusted to between 75 and 80 mmHg by titration of the remifentanil infusion. An infusion of phenylephrine was then commenced and titrated to increase the MAP to 100 mmHg over a period of 2–5 min. From the recorded data, Vmca at mean arterial pressures of 80 and 100 mmHg were noted. Vmca data from the two sides were averaged. From these data, the autoregulation index (ARI) was calculated according to a previously published formula.[5]§ An ARI of 1.0 indicates no change in Vmca despite the increase in MAP. (Occasionally, Vmca decreases and ARI may exceed 1.) An ARI of zero indicates totally pressure-passive cerebral blood flow, *i.e.*, absent autoregulation with Vmca increasing in direct proportion to MAP. Autoregulation was considered to be significantly impaired when the ARI was 0.4 or less.

Testing was performed at $Paco_2$ targets of 40 mmHg and 50 mmHg, and then in 5-mmHg increments until autoregulation was impaired (ARI = 0.4). Tidal volume or respiratory rate were adjusted to achieve the target levels of $Paco_2$. End-tidal carbon dioxide was monitored and used as a guide to adjust ventilation. Once end-tidal carbon dioxide had stabilized, arterial blood was sampled for gas analysis before each autoregulation test. A further arterial blood gas analysis was performed at the completion of each autoregulation test. Data were rejected and the autoregulation test repeated if the $Paco_2$ differed by more than 2 mmHg from the target or if the $Paco_2$ changed by more than 2 mmHg during the test.

Statistical Analysis

The Wilcoxon signed rank test was used to compare the threshold $Paco_2$ at which autoregulation was first found to be impaired. Carbon dioxide reactivity for each of the two drugs was compared at two different blood pressures. For this analysis, the Wilcoxon signed rank test was applied to data from each of the drugs, and the Bonferroni correction was applied for dual comparisons.

Results

Eight subjects (five men and three women; age, 22–52 yr) participated in the study, and no subject suffered any complication. In one subject, TCD signals could be obtained from one side only. Bilateral recordings were obtained from the remaining subjects. The duration of the study was between 4 and 5 h. There was no significant change in hematocrit or temperature during the studies.

Each subject demonstrated a linear increase in Vmca with increasing $Paco_2$. At each of the four study conditions (propofol at MAP 80 or 100 mmHg and sevoflurane at MAP 80 or 100 mmHg), the correlation coefficient was > 0.9 in all subjects. With normocapnia, all subjects had an ARI of 0.6 or more, indicating intact autoregulation (defined as ARI > 0.4). Hypercapnia impaired autoregulation in all subjects.

The threshold $Paco_2$ at which significantly impaired autoregulation was first recorded ranged from 50 to 66 mmHg (table 1). The threshold averaged 56 ± 4 mmHg (mean ± SD) during sevoflurane anesthesia and 61 ± 4 mmHg during propofol anesthesia ($P = 0.03$). Figure 1 presents the number of subjects with autoregulation intact at each $Paco_2$ range. Carbon dioxide reactivity data are shown in table 2. Figure 2 presents the data from a representative subject exhibiting a linear increase in Vmca with increasing $Paco_2$, but with the slope influenced by MAP.

Discussion

The main finding of this study is that, with general anesthesia in normal humans, cerebral autoregulation is readily impaired at clinically relevant levels of hypercapnia. At the anesthetic doses studied, the degree of hy-

§ $ARI = [(R_2 - R_1)/R_1]/[(MAP_2 - MAP_1)/MAP_1]$, where R = MAP/Vmca. R is an index of cerebral vascular resistance (ignoring the contribution of intracranial pressure to cerebral perfusion pressure). Subscripts 1 and 2 refer to measurements at the lower and higher MAP, respectively.

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Table 1. Individual Data and Autoregulation Index

	Sevoflurane						Propofol					
Subject No.	$Paco_2$	MAP_1	$Vmca_1$	MAP_2	$Vmca_2$	ARI	$Paco_2$	MAP_1	$Vmca_1$	MAP_2	$Vmca_2$	ARI
1	38	81	33	101	30	1.2	41	79	33	100	35	0.7
	52	81	54	95	55	0.9	48	80	61	100	65	0.7
	55	80	79	102	93	0.3	54	80	68	102	75	0.6
	58	80	79	101	91	0.4	**62**	81	102	103	123	0.2
2	41	82	38	101	40	0.7	39	86	29	105	30	0.8
	49	82	42	95	44	0.6	51	81	42	102	42	1.0
	54	81	62	103	68	0.6	54	82	43	105	45	0.8
	60	82	73	104	84	0.4	**60**	80	58	101	69	0.3
3	40	79	49	96	47	1.2	39	81	36	100	39	0.7
	50	80	100	101	98	1.1	50	79	77	98	84	0.5
	56	81	118	96	133	0.3	55	80	83	95	83	1.0
							59	78	113	95	130	0.3
4	39	82	29	101	30	0.9	41	80	26	95	27	0.7
	50	80	47	102	50	0.7	49	78	42	105	43	0.9
	55	80	75	100	77	0.9	57	80	75	102	82	0.6
	59	81	94	103	112	0.3	62	85	73	102	77	0.7
	66	79	91	99	107	0.2	**64**	81	78	101	91	0.3
5	39	79	49	101	47	1.0	39	79	27	101	30	0.6
	48	80	74	101	78	0.8	50	77	49	102	53	0.6
	54	82	90	100	104	0.3	57	79	66	100	73	0.6
	62	81	106	101	130	0.1	**61**	79	73	100	92	0.6
6	40	79	36	101	38	0.8	43	78	50	103	53	0.8
	50	78	59	98	61	0.9	50	83	60	101	60	1.0
	55	79	97	103	101	0.8	55	83	82	100	88	0.6
	61	81	95	101	114	0.1	62	82	82	99	86	0.7
							66	80	95	101	108	0.4
							70	81	99	101	117	0.3
7	42	80	37	100	40	0.6	40	80	40	100	40	1.0
	50	80	60	100	66	0.6	51	80	66	100	72	0.6
	55	80	83	100	97	0.3	**54**	80	71	100	82	0.3
							59	80	81	100	95	0.2
8	40	80	41	100	43	0.8	39	81	27	100	28	0.8
	50	80	50	100	59	0.2	52	80	40	101	43	0.7
	56	80	68	100	81	0.2	56	80	53	100	55	0.8
							61	80	68	100	76	0.5
							65	80	76	100	90	0.2
		80 ± 1		100 ± 2				80 ± 2		101 ± 2		

In bold are the threshold arterial carbon dioxide (mmHg) ($Paco_2$) values, *i.e.*, the lowest $Paco_2$ at which significantly impaired autoregulation was recorded. Subscripts 1 and 2 refer to measurements taken at the lower and higher mean arterial pressure (mmHg; MAP), respectively.

Vmca = mean of bilateral middle cerebral arterial flow velocities (cm/s); ARI = Autoregulation Index (unitless), calculated as described in Methods.

percapnia required to impair autoregulation is significantly less with sevoflurane compared with propofol.

It is of note that, with low-dose sevoflurane, hypercapnia can impair autoregulation at a $Paco_2$ of only 50 mmHg. This degree of hypercapnia is well within the range commonly seen with spontaneous ventilation during general anesthesia. Even in mechanically ventilated patients, severe lung pathology sometimes makes it difficult to avoid a $Paco_2$ above the normal range. Our results indicate that cerebral autoregulation may frequently be impaired in these situations.

Autoregulation tests performed in this study were classified as showing either autoregulation intact (ARI $>$ 0.4) or impaired (ARI $\leq$ 0.4). The choice of this arbitrary ARI to indicate intact or impaired autoregulation was made before commencing the study and was based on our previous experience, which is that normal subjects never have an ARI of 0.4. The method used in this study tests cerebral autoregulation over a narrow range of MAP (80–100 mmHg). We chose this range of MAP because it allows autoregulation testing while imposing minimal physiological disturbance in healthy volunteers. The effect of hypercapnia is first seen at the lower extreme of the autoregulatory range[3,9]; therefore, it is possible that cerebral autoregulation would be even more sensitive to hypercapnia in patients who are hypotensive during general anesthesia.

Hypercapnia probably impairs autoregulation because of its vasodilating effect on cerebral vasculature. Propofol is not a cerebral vasodilator and does not impair cerebral autoregulation.[5,7] Although most volatile anesthetics cause cerebral vasodilation,[10] 1.2–1.5 MAC sevoflurane decreases cerebral blood flow to less than awake values.[6,11] However, it has been reported that increasing sevoflurane concentration from 1.5% to 2.5% in patients with supratentorial tumors causes a modest

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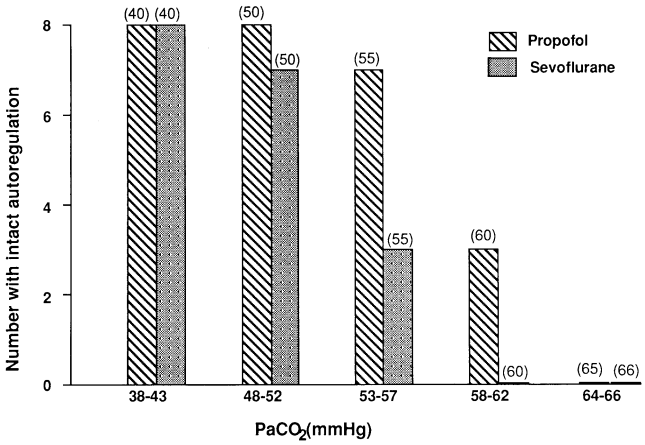

Fig. 1. The number of subjects with intact autoregulation at each arterial carbon dioxide partial pressure ($Paco_2$) range. Shown in brackets is the mean $Paco_2$ for each column.

degree of cerebral vasodilation.[12] When tested in a similar manner to this study, autoregulation is preserved with 1.2 MAC[11] and 1.5 MAC[6] sevoflurane in normal humans with normal $Paco_2$. In normocapnic humans, 1.5 MAC sevoflurane marginally affects dynamic autoregulation in response to rapid deflation of thigh cuffs,[13] but the transient hyperemic response to carotid artery compression is preserved.[14] In rats, 2.0 MAC sevoflurane abolished the autoregulatory response to hypotension.[15] The interaction seen in this study between hypercapnia and choice of anesthetic agent could indicate an underlying vasodilatory effect that is not normally apparent with 0.5 MAC sevoflurane.

The doses of sevoflurane and propofol used in this study were chosen to provide a reasonable certainty of ensuring unconsciousness during surgery. The doses of the two agents may not have been equipotent in terms of their hypnotic effect. Propofol was administered at a constant infusion rate, and plasma levels were not measured. The minimum time from commencing infusion to commencing autoregulation testing was 30 min, although in some subjects the time was more than 60 min. Plasma propofol concentration could still have been increasing significantly during the study. If this factor was significant, then the later tests with propofol (generally those at higher $Paco_2$) would have been performed at a higher plasma propofol concentration. A changing concentration of propofol would not invalidate the finding of better preservation of autoregulation compared with sevoflurane. Remifentanil would not be expected to have any direct effect on cerebral blood flow at the doses used in this study. Remifentanil has been reported to leave Vmca unchanged at 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ but to reduce Vmca at 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$.[16]

The carbon dioxide reactivity values reported here are higher than those in previously published reports. For example, calculating carbon dioxide reactivity from data reported during sevoflurane[11] or propofol–nitrous oxide anesthesia[17] yields mean values of 4–5%. At normocapnia, Vmca does not alter significantly with an increase in MAP from 80 to 100 mmHg but with hypercapnia autoregulation fails and Vmca increases in parallel with the MAP. This causes the calculated carbon dioxide reactivity to change depending on the blood pressure at which measurements are made. A possible explanation for the difference between our results and previous reports is that previous studies were conducted at a lower blood pressure[17] or that blood pressure was not specifically controlled during testing. It is well known that hypotension may decrease carbon dioxide reactivity,[18] but it has not previously been shown that MAP influences reactivity even if, as in the present study, blood pressure remains within the normal range.

Carbon dioxide reactivity testing is gaining popularity in the clinical evaluation of cerebrovascular disease.[19] Typically, such testing involves adding carbon dioxide to inspired gas to induce hypercapnia while simultaneously monitoring changes in cerebral blood flow by TCD. In patients with known cerebrovascular disease, it has been shown that changes in MAP confound the results of carbon dioxide reactivity tests.[20] The results of this study demonstrate that, even if blood pressure remains constant during the test, the absolute level of MAP alters carbon dioxide reactivity when $Paco_2$ increases enough to impair autoregulation. We found mean carbon dioxide reactivity to be approximately 30% higher when calculated from measurements taken at a MAP of 100 mmHg compared with a MAP of 80 mmHg. Changes in blood pressure from day to day could therefore contribute to variability in carbon dioxide reactivity measurements within an individual patient.

Using Vmca as a surrogate measure of changes in cerebral blood flow is problematic because any change in the diameter of the insonated vessel would alter the relation between flow velocity and actual blood flow. The validity of TCD as an index of changes in cerebral blood flow is supported by a good correlation between

Table 2. CO_2 Reactivity

Measurements	Sevoflurane		Propofol	
MAP (mmHg)	80 ± 1	100 ± 2	80 ± 1	101 ± 2
CO_2 reactivity (%/mmHg)	8 ± 3 (4–12)	10 ± 3* (6–12)	7 ± 2 (4–10)	9 ± 3* (5–11)

Values are mean ± SD (range).

*P = 0.02 compared with a mean arterial pressure (MAP) of 80 mmHg.

CO_2 = carbon dioxide.

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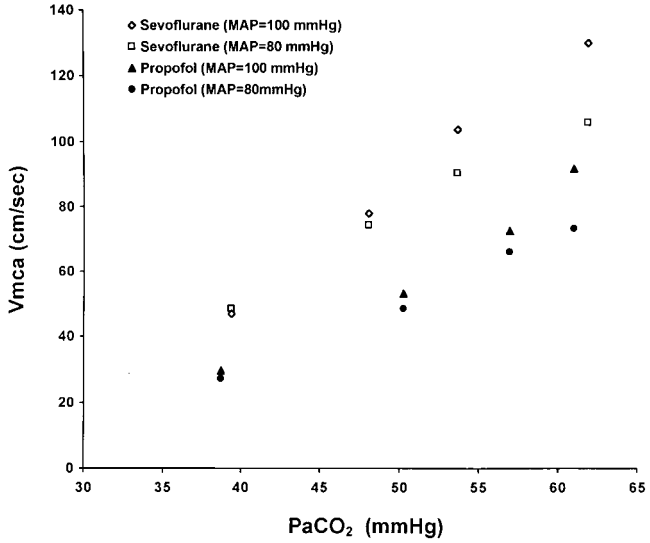

Fig. 2. Middle cerebral artery flow velocity measurements in a single subject (subject No. 5). Influence of arterial blood pressure on carbon dioxide reactivity is evident. MAP = mean arterial pressure; Vmca = middle cerebral artery blood flow velocity; $Paco_2$ = arterial carbon dioxide partial pressure.

TCD and ^{133}Xe-clearance determinations of carbon dioxide reactivity.[21] Intraoperative changes in $Paco_2$ and MAP have not been found to significantly alter direct measurements of proximal middle cerebral artery diameter,[22] although indirect evidence suggests that middle cerebral artery diameter may increase with hypercapnia.[23] If middle cerebral artery diameter did increase with hypercapnia in this study, then the true carbon dioxide reactivity would be even higher than indicated by our data. There is little published evidence regarding possible effects of general anesthetic agents on middle cerebral artery diameter. Presumably, any effect of anesthetic drugs would be constant if drug concentration remains constant; therefore, it is unlikely that any such effect would change over the 2–5 min of the autoregulation test.

In conclusion, even mild hypercapnia should be avoided if attempting to preserve cerebral autoregulation. Propofol may have advantages over volatile agents such as sevoflurane if hypercapnia cannot be prevented when attempting to preserve cerebral autoregulation. It is important to control for any changes in arterial blood pressure when measuring carbon dioxide reactivity with hypercapnia.

References

1. Haggendal E, Johansson B: Effects of arterial carbon dioxide tension and oxygen saturation on cerebral blood flow autoregulation in dogs. Acta Physiol Scand Suppl 1965; 258:27–53

2. Harper AM: Autoregulation of cerebral blood flow: Influence of the arterial blood pressure on the blood flow through the cerebral cortex. J Neurol Neurosurg Psychiatry 1966; 29:398–403

3. Raichle ME, Stone HL: Cerebral blood flow autoregulation and graded hypercapnia. Eur Neurol 1971; 6:1–5

4. Aaslid R, Lindegaard KF, Sorteberg W, Nornes H: Cerebral autoregulation dynamics in humans. Stroke 1989; 20:45–52

5. Strebel S, Lam AM, Matta B, Mayberg TS, Aaslid R, Newell DW: Dynamic and static cerebral autoregulation during isoflurane, desflurane, and propofol anesthesia. ANESTHESIOLOGY 1995; 83:66–76

6. Gupta S, Heath K, Matta BF: Effect of incremental doses of sevoflurane on cerebral pressure autoregulation in humans. Br J Anaesth 1997; 79:469–72

7. Matta BF, Lam AM, Strebel S, Mayberg TS: Cerebral pressure autoregulation and carbon dioxide reactivity during propofol-induced EEG suppression. Br J Anaesth 1995; 74:159–63

8. Lam AM: Intraoperative transcranial Doppler monitoring. ANESTHESIOLOGY 1995; 82:1536–7

9. Ursino M, Lodi CA: Interaction among autoregulation, CO_2 reactivity, and intracranial pressure: A mathematical model. Am J Physiol 1998; 274:H1715–28

10. Matta BF, Mayberg TS, Lam AM: Direct cerebrovasodilatory effects of halothane, isoflurane, and desflurane during propofol-induced isoelectric electroencephalogram in humans. ANESTHESIOLOGY 1995; 83:980–5

11. Cho S, Fujigaki T, Uchiyama Y, Fukusaki M, Shibata O, Sumikawa K: Effects of sevoflurane with and without nitrous oxide on human cerebral circulation: Transcranial Doppler study. ANESTHESIOLOGY 1996; 85:755–60

12. Bundgaard H, von Oettingen G, Larsen KM, Landsfeldt U, Jensen KA, Nielsen E, Cold GE: Effects of sevoflurane on intracranial pressure, cerebral blood flow and cerebral metabolism: A dose-response study in patients subjected to craniotomy for cerebral tumours. Acta Anaesthesiol Scand 1998; 42:621–7

13. Summors AC, Gupta AK, Matta BF: Dynamic cerebral autoregulation during sevoflurane anesthesia: A comparison with isoflurane. Anesth Analg 1999; 88:341–5

14. Bedforth NM, Girling KJ, Harrison JM, Mahajan RP: The effects of sevoflurane and nitrous oxide on middle cerebral artery blood flow velocity and transient hyperemic response. Anesth Analg 1999; 89:170–4

15. Lu H, Werner C, Engelhard K, Scholz M, Kochs E: The effects of sevoflurane on cerebral blood flow autoregulation in rats. Anesth Analg 1998; 87:854–8

16. Paris A, Scholz J, von Knobelsdorff G, Tonner PH, Schulte am Esch J: The effect of remifentanil on cerebral blood flow velocity. Anesth Analg 1998; 87:569–73

17. Fox J, Gelb AW, Enns J, Murkin JM, Farrar JK, Manninen PH: The responsiveness of cerebral blood flow to changes in arterial carbon dioxide is maintained during propofol-nitrous oxide anesthesia in humans. ANESTHESIOLOGY 1992; 77:453–6

18. Matta BF, Lam AM, Mayberg TS, Eng CC, Strebel S: Cerebrovascular response to carbon dioxide during sodium nitroprusside- and isoflurane-induced hypotension. Br J Anaesth 1995; 74:296–300

19. Gur AY, Bova I, Bornstein NM: Is impaired cerebral vasomotor reactivity a predictive factor of stroke in asymptomatic patients? Stroke 1996; 27:2188–90

20. Dumville J, Panerai RB, Lennard NS, Naylor AR, Evans DH: Can cerebrovascular reactivity be assessed without measuring blood pressure in patients with carotid artery disease? Stroke 1998; 29:968–74

21. Bishop CC, Powell S, Rutt D, Browse NL: Transcranial Doppler measurement of middle cerebral artery blood flow velocity: A validation study. Stroke 1986; 17:913–5

22. Giller CA, Bowman G, Dyer H, Mootz L, Krippner W: Cerebral arterial diameters during changes in blood pressure and carbon dioxide during craniotomy. Neurosurgery 1993; 32:737–41

23. Valdueza JM, Draganski B, Hoffmann O, Dirnagl U, Einhaupl KM: Analysis of CO_2 vasomotor reactivity and vessel diameter changes by simultaneous venous and arterial Doppler recordings. Stroke 1999; 30:81–6

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