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Anesthesia and cerebrospinal microcirculation: assessment using cranial- and spinal-window techniques

Hiroki Iida · Mami Iida · Motoyasu Takenaka

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H. Iida

A good understanding of the characteristics of cerebrospinal-vessel reactivity is advantageous if an appropriate circulation is to be maintained within the central nervous system (CNS) during surgery. In addition, it is useful to know that ischemia–reperfusion, disruption of the blood–brain (spinal cord)-barrier (BBB), and hypothermia could all potentially modulate the effects on cerebrospinal circulation and cerebrospinal-vessel reactivity induced by any vasoactive drugs administered during anesthesia. We therefore focused on, and present here, the significance of changes in cerebrospinal microcirculation that occur in relation to the perioperative period. Our studies entailed an assessment of the relevant parameters by means of the cranial- and spinal-window techniques in animals in vivo. It is generally agreed that such techniques facilitate in vivo observations of pial vessels. We originated the spinal-window technique presented here, although it is closely based on the cranial-window technique (Fig. 1). Measurement of pial-vessel diameter provides direct information about the effects of test drugs and physiological changes on cranial and spinal vessels. However, such information is obtainable only from the superficial vessels and does not provide a direct measurement of cerebral or spinal cord blood flow (SCBF), unlike the use of microspheres, hydrogen clearance, or laser Doppler flowmetry.

H. Iida (✉) · M. Iida · M. Takenaka
Department of Anesthesiology and Pain Medicine,
Gifu University Graduate School of Medicine,
1-1 Yanagido, Gifu, Gifu 501-1194, Japan
e-mail: iida@gifu-u.ac.jp

Response characteristics of spinal vessels

As far as we knew, there was little information as to the differences between the responses of cerebral and spinal vessels. We therefore investigated such differences in responses to arterial carbon dioxide (CO_2) tension [partial pressure of carbon dioxide in arterial blood ($PaCO_2$)] and adrenergic agonists using cranial- and spinal-window techniques [1]. Although previous studies indicated a lower sensitivity to changes in $PaCO_2$ for SCBF than for cerebral blood flow (CBF) [2, 3], our study demonstrated similar responses between cerebral and spinal vessels to such changes (Fig. 2). In addition, spinal arterioles seemed to be more sensitive to alpha-1-adrenergic stimulation than to alpha-2-adrenergic stimulation, whereas for cerebral arterioles, the reverse was true (i.e., more sensitive to alpha-2-adrenergic stimulation than to alpha-1-adrenergic stimulation) [4].

When studying the effects of local anesthetics on the spinal microcirculation, we noted that changes in SCBF or spinal vessels induced by local anesthetics could influence the duration of action of spinally administered agents [5]. Earlier, we established that ropivacaine constricts whereas bupivacaine dilates spinal pial vessels, each in a

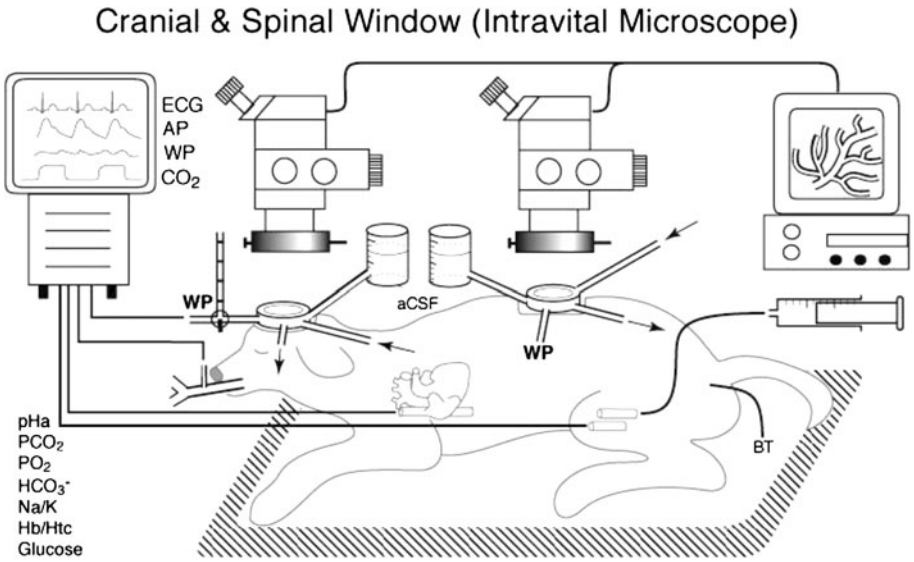

Fig. 1 Cranial- and spinal-window techniques

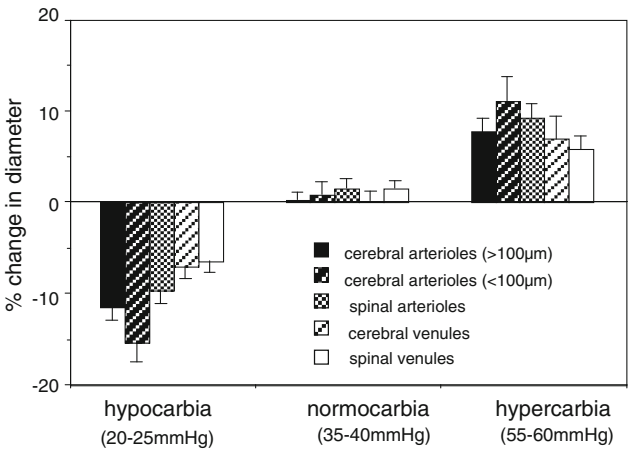

Fig. 2 Responses of cerebral and spinal vessels to changes in arterial carbon dioxide (CO_2) tension (mean ± standard error of mean) (modified from [1], with the publisher's permission)

concentration-dependent manner [6]. In addition, although theoretically any additional spinal vasoconstriction induced by hypocapnia might be hazardous under spinal ropivacaine, we demonstrated that hypocapnia does not induce an additional constriction in spinal arterioles under such conditions [7].

Effects on cerebrospinal fluid pressure induced by vasodilators

Cross-clamping of the aorta induces a decrease in distal aortic pressure and an increase in cerebrospinal fluid (CSF) pressure, leading to a decreased spinal cord perfusion (SCP) pressure. Thus, controlling proximal hypertension during aortic cross-clamping by administering a vasodilator agent could influence SCP. In previous studies, sodium nitroprusside (SNP) or nitroglycerin (NTG) was found to worsen the neurological outcome more than isoflurane or trimethaphan due to more potent elevations in CSF pressure (leading to decreased SCP pressure) [8–10]. In other studies, we observed: (a) that sevoflurane and isoflurane have weaker dilator effects on cerebral venules than on cerebral arterioles [11], and (b) that the same is true for topical prostaglandin E1 (PGE1) and nicardipine (i.e., weaker dilator effects on cerebral venules than on arterioles) [12]. We therefore suggested that sevoflurane, PGE1, or nicardipine could be used safely as regards effects on CSF pressure—like isoflurane and trimethaphan, as suggested before—because these agents have less influence over the venous compartment and that compartment has more effect on intracranial pressure.

Changes in reactivity of cerebrospinal vessels in pathological conditions

Ischemia–reperfusion

In general, following ischemia–reperfusion injury, the vasoconstrictor response to hypocapnia is maintained, whereas the vasodilator response to hypercapnia is attenuated, in cerebrospinal vessels [13]. Moreover, in that condition, endothelium-independent vasodilation but not endothelium-dependent vasodilation is maintained if the ischemia is short term, whereas long-term ischemia reduces both endothelium-independent and -dependent vasodilations in the CNS [14]. In such a situation, we evaluated whether responses to arginine vasopressin (AVP), which is used clinically during cardiopulmonary resuscitation

(CPR), are altered after transient ischemia, such as cardiac arrest. Our study demonstrated that the vasoconstrictor effect of AVP could be reduced after transient cerebral ischemia, and we pointed out that such an alteration in the response to AVP after transient ischemia could be favorable for maintaining CBF when AVP is used during CPR [15].

Disruption of BBB

It is well known that BBB disruption can modify the effects on the cerebrospinal circulation induced by drugs that do not pass through the BBB under physiological conditions. For example, the high molecular weight and water solubility of alpha-human atrial natriuretic peptide (HANP) suggest that it will not pass through the BBB under physiological conditions. However, we reported that when the BBB had been pharmacologically disrupted, intravenously administered HANP caused a significant pial arteriolar dilation without venular dilation (although it does not have this effect when the BBB is intact) [16]. Consequently, care should be taken if such a drug is used in critically ill patients in whom the BBB may be dysfunctional.

Hypothermia

In general, hypothermia itself reduces both CBF and metabolic rate [17]. Although the reactivity of CBF to changes in $PaCO_2$ is preserved during hypothermia, hypothermia can alter certain responses of blood vessels in the CNS [18]. For example, hypothermia can enhance sodium nitroprusside (SNP)-induced vasodilation [19] but attenuate NTG-induced vasodilation in cerebral vessels [20]. We indicated that in rabbits, mild to moderate hypothermia can attenuate dilator responses to dexmedetomidine in cerebral arterioles [21].

Aortic clamp and declamp

In addition to the abrupt hemodynamic changes that occur during and after aortic cross-clamping and unclamping, many factors—including CO_2, pH, potassium (K^+), prostaglandins, cytokines, endothelins, anaphylatoxin, and neutrophils—are known to affect cerebral microcirculation. In our 2003 study, aortic cross-clamping did not affect cerebral pial vessel diameter, but releasing a 20-min aortic cross-clamp caused cerebral pial arterioles first to dilate and then to constrict [22]. Because such unclamping-induced cerebral vasoconstriction could be attenuated by administering seratrodast, edaravone, or valsartan, it is likely to be partially mediated via thromboxane A2, free radicals, and angiotensin II produced in the ischemic region during the clamp itself and after cross-clamp release.

Conclusion

In conclusion, on the basis of the above evidence, we believe it to be important for anesthesiologists to possess as full an understanding as possible of the effects on the cerebrospinal microcirculation exerted by those anesthetics and anesthesia-related agents that have vasoactive properties. Only in that way can they avoid damaging, or exacerbating existing damage to, the patient's CNS.

References

1. Iida H, Watanabe Y, Ishiyama T, Iida M, Dohi S: The differences of the cerebral and spinal vessels in sensitivity to $PaCO_2$ and vasoconstrictors. Masui (Jpn J Anesthesiol) 1997;46:2–9 (in Japanese with English abstract).
2. Sandler AN, Tator CH. Review of the measurement of normal spinal cord blood flow. Brain Res. 1976;118:181–98.
3. Severinghaus JW, Lassen N. Step hypocapnia to separate arterial from tissue PCO_2 in the regulation of cerebral blood flow. Circ Res. 1967;20:272–8.
4. Iida H, Ohata H, Iida M, Watanabe Y, Dohi S. Direct effects of alpha1- and alpha2-adrenergic agonists on spinal and cerebral pial vessels in dogs. Anesthesiology. 1999;91:479–85.
5. Iida H, Iida M. Effects of spinal analgesics on spinal circulation: the safety standpoint. J Neurosurg Anesthesiol. 2008;20:180–7.
6. Iida H, Watanabe Y, Dohi S, Ishiyama T. Direct effects of ropivacaine and bupivacaine on spinal pial vessels in canine. Assessment with closed spinal window technique. Anesthesiology. 1997;87:75–81.
7. Iida H, Ohata H, Iida M, Watanabe Y, Nagase K, Dohi S. Attenuated additional hypocapnic constriction, but not hypercapnic dilation, of spinal pial arterioles during spinal ropivacaine. Anesth Analg. 1999;89:1510–3.
8. Simpson JI, Eide TR, Schiff GA, Clagnaz JF, Zisbrod Z, Newman SB, Hossain I. Isoflurane versus sodium nitroprusside for the control of proximal hypertension during thoracic aortic cross-clamping: effects on spinal cord ischemia. J Cardiothorac Vasc Anesth. 1995;9:491–6.
9. Simpson JI, Eide TR, Newman SB, Schiff GA, Levine D, Bermudez R, D'Ambra T, Lebowitz P. Trimethaphan versus sodium nitroprusside for the control of proximal hypertension during thoracic aortic cross-clamping: the effects on spinal cord ischemia. Anesth Analg. 1996;82:68–74.
10. Simpson JI, Eide TR, Schiff GA, Newman SB, Clagnaz JF, Hossain I, Schulman SB, Gropper JE. Effect of nitroglycerin on spinal cord ischemia after thoracic aortic cross-clamping. Ann Thorac Surg. 1996;61:113–7.
11. Iida H, Ohata H, Iida M, Watanabe Y, Dohi S. Isoflurane and sevoflurane induce vasodilation of cerebral vessels via ATP-sensitive K+ channel activation. Anesthesiology. 1998;89:954–60.
12. Takenaka M, Iida H, Iida M, Uchida M, Dohi S: The comparative effects of prostaglandin E1 and nicardipine on cerebral microcirculation in rabbits. Anesth Analg. 2003;96:1139–44 (table of contents).
13. Mirro R, Lowery-Smith L, Armstead WM, Shibata M, Zuckerman SL, Leffler CW. Cerebral vasoconstriction in response to hypocapnia is maintained after ischemia/reperfusion injury in newborn pigs. Stroke. 1992;23:1613–6.

14. Mayhan WG, Amundsen SM, Faraci FM, Heistad DD. Responses of cerebral arteries after ischemia and reperfusion in cats. Am J Physiol. 1988;255:H879–84.
15. Kumazawa M, Iida H, Uchida M, Iida M, Takenaka M, Fukuoka N, Michino T, Dohi S: The effects of transient cerebral ischemia on vasopressin-induced vasoconstriction in rabbit cerebral vessels. Anesth Analg. 2008;106:910–5 (table of contents).
16. Iida H, Iida M, Takenaka M, Oda A, Uchida M, Fujiwara H, Dohi S. The effects of alpha-human atrial natriuretic peptide and milrinone on pial vessels during blood-brain barrier disruption in rabbits. Anesth Analg. 2001;93:177–82.
17. Michenfelder JD, Milde JH. The relationship among canine brain temperature, metabolism, and function during hypothermia. Anesthesiology. 1991;75:130–6.
18. Kern FH, Ungerleider RM, Quill TJ, Baldwin B, White WD, Reves JG, Greeley WJ. Cerebral blood flow response to changes in arterial carbon dioxide tension during hypothermic cardiopulmonary bypass in children. J Thorac Cardiovasc Surg. 1991;101:618–22.
19. Speziali G, Russo P, Davis DA, Wagerle LC. Hypothermia enhances contractility in cerebral arteries of newborn lambs. J Surg Res. 1994;57:80–4.
20. Kawaguchi M, Ishimura N, Kurehara K, Sakamoto T, Kitaguchi K, Furuya H. Mild hypothermia can attenuate nitroglycerin-induced vasodilation of pial arterioles in the cat. Anesth Analg. 1998;86:546–51.
21. Iida H, Iida M, Ohata H, Nagase K, Dohi S: Hypothermia attenuates the vasodilator effects of dexmedetomidine on pial vessels in rabbits in vivo. Anesth Analg. 2004;98:477–82 (table of contents).
22. Uchida M, Iida H, Iida M, Dohi S: Changes in cerebral microcirculation during and after abdominal aortic cross-clamping in rabbits: the role of thromboxane A2 receptor. Anesth Analg. 2003;96:651–6 (table of contents).