Laboratory Investigations

Haemodynamic and cerebral blood flow alterations after reduction of increased cerebrospinal fluid pressure in dogs

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To clarify some of the mechanisms for the hypotension that may occur after cranial decompression, the authors examined alterations in cerebral blood flow (CBF) and systemic and pulmonary haemodynamic variables when cerebrospinal fluid (CSF) pressure was increased and then suddenly reduced in eight anaesthetized dogs. After CSF pressure was elevated to 50–85 mmHg for two hours, CBF decreased from 46.3 ± 4.4 to 31.6 ± 8.5 ml · 100 g⁻¹ · min⁻¹ (mean ± SD, $P < 0.01$). Mean systemic arterial pressure (MAP), mean pulmonary artery pressure (MPAP), pulmonary artery wedge pressure (PAWP), and systemic vascular resistance index (SVRI) increased by 20 ± 11 mmHg, 3.9 ± 2.5 mmHg, 5.2 ± 3.3 mmHg, and 1448 ± 1377 dynes · sec · cm⁻⁵ · m² from baseline values, respectively ($P < 0.01$). Rapid reduction of increased CSF pressure caused

CBF to increase to 61.5 ± 19.1 ml · 100 g⁻¹ · min⁻¹, whereas MAP, MPAP, PAWP, and SVRI decreased by 22 ± 11 mmHg, 2.4 ± 0.9 mmHg, 2.3 ± 2.0 mmHg, and 1289 ± 1237 dynes · sec · cm⁻⁵ · m² from previous values ($P < 0.01$) at 30 min following the decompression. However, cardiac index and pulmonary vascular resistance index remained unchanged during the study period. The present animal data indicate that the decrease in MAP after decompression is mainly a result of a reduction in systemic vascular resistance.

Key words

BLOOD PRESSURE: peripheral vascular resistance;

BRAIN: blood flow;

CEREBROSPINAL FLUID: pressure;

HEART: cardiac output.

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Afin d'éclaircir certains des mécanismes de l'hypotension pouvant survenir après décompression cérébrale, les auteurs ont examiné les altérations du flot sanguin cérébral (CBF) et les variables hémodynamiques pulmonaire et systémique quand la pression du liquide céphalo-rachidien (CSF) fut augmentée et soudainement réduite chez huit chiens anesthésiés. Après l'élévation de la pression CSF à 50–85 mmHg pour deux heures, le CBF a diminué de $46,3 \pm 4,4$ à $31,6 \pm 8,5$ ml · 100 g⁻¹ · min⁻¹ (moyenne ± SD, $P < 0.01$). La pression artérielle systémique moyenne (MAP), la pression moyenne de l'artère pulmonaire (MPAP), la pression de l'artère pulmonaire occluse (PAWP), et la résistance systémique vasculaire indexée (SVRI) ont augmenté de 20 ± 11 mmHg, $3,9 \pm 2,5$ mmHg, $5,2 \pm 3,3$ mmHg, et 1448 ± 1377 dynes · sec · cm⁻⁵ · m² à partir des valeurs de contrôle, respectivement ($P < 0.01$). La diminution rapide de cette augmentation de la pression du CSF a amené une augmentation du CBF à $61,5 \pm 19,1$ ml · 100 g⁻¹ · min⁻¹, alors que la MAP, MPAP, PAWP, et SVRI ont diminué à 22 ± 11 mmHg, $2,4 \pm 0,9$ mmHg, $2,3 \pm 2,0$ mmHg, et 1289 ± 1237 dynes · sec · cm⁻⁵ · m² des valeurs préalables ($P < 0.01$) à 30 min. après la décompression. Cependant, l'index cardiaque et la résistance vasculaire pulmonaire indexée sont demeurés inchangés durant la période d'étude. Ces données expérimentales

indiquent que la diminution de la MAP après décompression est principalement en résultat de la diminution de la résistance vasculaire systémique.

A rapid reduction of intracranial pressure (ICP) in patients with intracranial hypertension has been reported to cause systemic hypotension and cardiac arrest.¹ This circulatory collapse has been attributed to redistribution of circulating blood volume to the cerebral vascular bed,² and/or to preexisting hypovolaemia.¹ However, there is little information about the changes in cerebral blood flow (CBF) and systemic and pulmonary haemodynamic variables that could occur when an increased ICP is suddenly reduced.

Thus, cerebral and cardiopulmonary haemodynamic variables were investigated in anaesthetized dogs with sustained, elevated cerebrospinal fluid (CSF) pressure. Subsequently, the changes associated with a sudden reduction of the increased CSF pressure were observed to elucidate some of the mechanisms for the decompression phenomenon.

Methods

Experiments were performed in eight adult mongrel dogs of either sex, weighing from 6–14 kg. The protocol was approved by the institutional Animal Investigation Committee. After all animals were anaesthetized with iv thiamylal 15–20 mg·kg⁻¹, the lungs were mechanically ventilated through a cuffed endotracheal tube, using a volume-cycled animal ventilator (model R-60, Aika, Tokyo, Japan), to maintain normocapnia (PaCO₂ 35–42 mmHg) by measuring end-tidal CO₂ concentration with a CO₂ analyzer (NEC San-ei Instruments Ltd., Tokyo). Anaesthesia was maintained with halothane, 0.7–1.0% inspired, in oxygen (1 L·min⁻¹) and air. Succinylcholine 20 mg, iv, was given initially, and continued at 50 mg·hr⁻¹ to produce immobilization. During the experiments, temperature was measured through the thermistor probe of the pulmonary arterial catheter and was maintained between 36.5 and 38.5° C with an electric heating pad. Sodium bicarbonate was given as needed, before baseline measurements, to maintain normal buffer base.

An iv cannula was placed in a limb vein for the administration of lactated Ringer's solution at a rate of 5 ml·kg⁻¹·hr⁻¹. Lead II of the ECG (model 2236 A, NEC San-ei Instruments Co., Ltd.) was monitored, and heart rate (HR) was measured by a cardi tachometer (model 1321, NEC San-ei Instruments Co. Ltd.) triggered by lead II of the ECG. Arterial blood pressure (AP) measurements and blood gas samples were obtained from a femoral arterial catheter. A balloon-tipped, flow-directed pulmonary artery catheter (model 93-132-5F, Baxter Edwards

Laboratories, Irvine, California, USA) was inserted via the femoral vein for measurements of pulmonary artery pressure (PAP), pulmonary artery wedge pressure (PAWP), right atrial pressure (RAP), and for thermodilution cardiac output (CO) determination. The CO was measured in triplicate using injection of 3 ml, 5% dextrose at 0° C and a computer (Gould, Cleveland, Ohio, USA).

A small parietal craniectomy was performed, one bipolar platinum hydrogen electrode (model BE-ND 400–30, Biomedical Science Co., Ltd., Kanazawa, Japan) was inserted into the cerebral cortex through a small hole in the dura mater. The electrode was advanced to a depth of approximately 3–5 mm from the surface of the brain and was connected to an electrolytic flowmeter (model RBF-2, Biomedical Science Co., Ltd.) and an electronic recorder (model R-02, Rikadenki Kogyo Co., Ltd., Tokyo, Japan). This bipolar electrode was designed to generate hydrogen gas and to detect hydrogen gas by a polarographical method.³ A silver/silver chloride electrode (disk type, Biomedical Science Co., Ltd.) placed subcutaneously, was used as a reference electrode. The CBF was measured using the hydrogen clearance method.⁴ After cessation of hydrogen gas production, the "washout" curve of hydrogen was recorded. This curve was transposed on to semilogarithmic paper and the half time (t_{1/2}) was measured. When the clearance was monoexponential, CBF was calculated from the formula:

$$\text{Flow} = \lambda \frac{0.693}{t_{1/2}} \text{ ml} \cdot \text{g}^{-1} \cdot \text{min}^{-1}$$

λ (tissue/blood partition coefficient) was taken to be 1. When the clearance curve was biexponential, flows in the fast and slow flow compartments were calculated separately from the slope of each monoexponential clearance curve using the formula above. Thereafter, the total flow was calculated from the formula:

$$\text{Total flow} = \frac{I_f + I_s}{I_f/F_f + I_s/F_s}$$

Where I_f and I_s are the zero time Y-axis intercepts of the fast and slow compartments, respectively, which give the "weight" of each compartment, and F_f and F_s are the flows in the fast and slow compartments, respectively. A 16-G needle was also placed in the cisterna magna for continuous measurement of CSF pressure. Calibrated Statham P23ID transducers (Gould) were used for all pressure measurements. The dogs were placed supine, and the zero reference was leveled at midchest.

Following a stable period of 30 min after surgical preparation, baseline measurements were made. Then, CSF pressure was elevated to 50–85 mmHg by the injection of autologous blood, 5–6 ml over 30 sec, followed

TABLE Mean values ($\pm$ SD, $n = 8$) of cerebral and cardiopulmonary haemodynamic variables during increased cerebrospinal fluid (CSF) pressure and following decompression

Variables	Baseline	Increased CSF pressure				Decompression	
		30 min	60 min	90 min	120 min	5 min	30 min
CSFP (mmHg)	5.5 $\pm$ 2.1	62.8 $\pm$ 11.5*	63.7 $\pm$ 7.9*	62.1 $\pm$ 8.0*	61.2 $\pm$ 9.8*	8.1 $\pm$ 5.2†	8.3 $\pm$ 4.8†
CPP (mmHg)	116 $\pm$ 16	67 $\pm$ 10*	71 $\pm$ 9*	78 $\pm$ 10*	81 $\pm$ 11*	123 $\pm$ 13†	113 $\pm$ 13†
CBF (ml $\cdot$ 100 g ⁻¹ $\cdot$ min ⁻¹)	46.3 $\pm$ 4.4	30.9 $\pm$ 4.3*	29.8 $\pm$ 6.8*	29.8 $\pm$ 8.3*	31.6 $\pm$ 8.5*	45.6 $\pm$ 8.6†	61.5 $\pm$ 19.1†
MAP (mmHg)	122 $\pm$ 17	131 $\pm$ 13*	135 $\pm$ 11*	140 $\pm$ 14*	143 $\pm$ 15*	131 $\pm$ 12†	120 $\pm$ 13†
HR (beat $\cdot$ min ⁻¹)	121 $\pm$ 30	113 $\pm$ 23	107 $\pm$ 20	107 $\pm$ 23	105 $\pm$ 23	102 $\pm$ 18	112 $\pm$ 22
MPAP (mmHg)	13.3 $\pm$ 4.6	15.3 $\pm$ 4.6*	16.3 $\pm$ 4.3*	17.1 $\pm$ 3.6*	17.2 $\pm$ 3.6*	16.6 $\pm$ 3.6	14.8 $\pm$ 4.8†
PAWP (mmHg)	5.6 $\pm$ 5.1	8.2 $\pm$ 5.5*	9.0 $\pm$ 5.0*	10.1 $\pm$ 5.4*	10.8 $\pm$ 5.8*	9.3 $\pm$ 4.8	8.0 $\pm$ 6.2†
RAP (mmHg)	3.2 $\pm$ 3.1	4.5 $\pm$ 3.5	4.1 $\pm$ 3.1	4.1 $\pm$ 3.1	4.2 $\pm$ 3.0	3.6 $\pm$ 3.1	2.6 $\pm$ 2.8†
CI (L $\cdot$ min ⁻¹ $\cdot$ m ⁻²)	3.42 $\pm$ 1.26	2.90 $\pm$ 1.09	2.80 $\pm$ 1.15	2.90 $\pm$ 1.40	3.02 $\pm$ 1.77	3.15 $\pm$ 1.58	3.44 $\pm$ 1.62
SVRI (dynes $\cdot$ sec $\cdot$ cm ⁻⁵ $\cdot$ m ²)	3212 $\pm$ 1416	4010 $\pm$ 1623*	4330 $\pm$ 1802*	4481 $\pm$ 2105*	4660 $\pm$ 2453*	3815 $\pm$ 1575†	3391 $\pm$ 1932†
PVRI (dynes $\cdot$ sec $\cdot$ cm ⁻⁵ $\cdot$ m ²)	189 $\pm$ 55	186 $\pm$ 53	215 $\pm$ 45	191 $\pm$ 59	178 $\pm$ 54	216 $\pm$ 78	154 $\pm$ 58

Abbreviations: CSFP, cerebrospinal fluid pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow; MAP, mean arterial pressure; HR, heart rate; MPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; RAP, right atrial pressure; CI, cardiac index; SVRI, systemic vascular resistance index; PVRI, pulmonary vascular resistance index.

* $P < 0.01$ vs baseline.

† $P < 0.01$ vs value at 120 min after increased CSF pressure.

by the continuous infusion of 0.9% NaCl solution at a rate of 50–70 ml $\cdot$ hr⁻¹ through the needle placed in the cisterna magna. The infusion bottle of 0.9% NaCl solution was fixed to the ceiling and was hung above the level of the animal's head so that a fluid column was maintained more than 68 cm in order to obtain steady CSF pressure of more than 50 mmHg. Measurements of CBF, CSF pressure, and haemodynamic variables (HR, AP, PAP, PAWP, RAP, CO) were repeated at intervals of 30 min, while the increased CSF pressure was maintained for two hours. Thereafter, the elevated CSF pressure was reduced suddenly to normal by leaking infused blood and normal saline. The measurements of CBF, CSF pressure, and haemodynamic variables were repeated at 5 and 30 min after decompression. Arterial blood gas tensions and haemoglobin concentrations were measured before, 30, 60, 90, and 120 min following increased CSF pressure, and 30 min after decompression, using Acid-Base Laboratory (model ABL 300, Radiometer, Copenhagen, Denmark).

Mean arterial pressure (MAP) and mean pulmonary artery pressure (MPAP) were calculated as the diastolic pressure plus one-third of pulse pressure. Cardiac index (CI, L $\cdot$ min⁻¹ $\cdot$ m⁻²) was calculated as CO $\cdot$ body surface area (BSA, m²)⁻¹ where BSA was calculated using the formula:⁵ $0.112 \times \text{weight (kg)}^{2/3}$. Systemic vascular resistance index (SVRI, dynes $\cdot$ sec $\cdot$ cm⁻⁵ $\cdot$ m²) was calculated as (MAP-RAP) $\cdot$ CI⁻¹ $\times$ 80, and pulmonary vascular resistance index (PVRI, dynes $\cdot$ sec $\cdot$ cm⁻⁵ $\cdot$ m²) as (MPAP-PAWP) $\cdot$ CI⁻¹ $\times$ 80. Cerebral perfusion pressure (CPP) was calculated as MAP minus CSF pressure.

All data are reported as mean $\pm$ SD. Results were analyzed by analysis of variance with repeated measures and Student's *t* test. A *P* value < 0.05 was considered to be statistically significant.

Results

During the two hours of increased CSF pressure, CBF decreased by a mean of approximately 15 ml $\cdot$ 100 g⁻¹ $\cdot$ min⁻¹ and remained at the same decreased value ($P < 0.01$), although CPP initially decreased to 67 mmHg, then gradually increased to 81 mmHg ($P < 0.01$, Table). On the other hand, MAP, MPAP, PAWP, and SVRI showed progressive increases. Neither HR, RAP, CI nor PVRI showed significant changes, and no changes in pH, PaO₂, PaCO₂, and haemoglobin concentrations were found.

Following rapid decompression, MAP, MPAP, PAWP, RAP, and SVRI decreased ($P < 0.01$). The CBF increased to baseline values ($P < 0.01$, Table). However, CI, HR, and PVRI did not change significantly.

Discussion

The present animal experiments indicated that rapid normalization of increased CSF pressure caused a decrease in MAP which was associated with decreases in MPAP, PAWP, and RAP compared with those obtained during increased CSF pressure. This phenomenon is mainly due to peripheral vasodilatation, since there was a decrease in SVRI but no change in CI.

Intracranial hypertension is characterized by decreased CBF and elevated plasma catecholamine concentrations associated with increased AP and PAP. Several investiga-

tors have demonstrated that CBF decreases during intracranial hypertension;⁶⁻¹¹ graded increases in ICP produce graded reductions in CBF. Meanwhile, a sudden reduction of increased ICP is almost invariably followed by reactive hyperaemia if ICP is markedly increased, and CPP is reduced to the extreme low level of approximately 10–50 mmHg.^{8,11} These CBF responses to alterations in ICP were observed in our experiment. However, the reduction in CBF during the time of increased CSF pressure seems to have remained greater than that in other reports.^{7,8} It has been demonstrated, in rabbits, that CBF decreased by 33% when CPP was reduced to approximately 50 mmHg.⁸ Furthermore, CBF has been reported to show no change when CPP was above 60 mmHg in sheep.⁷ Therefore, the greater CBF reduction during increased CSF pressure, despite the modest decreases in CPP, was probably due to constriction of cerebral vessels by intracisternally infused autologous blood.¹² This mechanism could also explain why the increase in CBF following decompression was less pronounced, and why CBF increased significantly from the previous value but not above the baseline (Table).

According to a previous clinical report,¹¹ hypotension (20% or more decrease in systolic blood pressure) occurred in 41% of the children during evacuation of subdural haematomas. It was suggested that hypovolaemia was caused, in part, by the blood loss into the subdural haematoma, and was responsible for the hypotension.¹ In addition, some neurosurgical patients receiving diuretics (furosemide, mannitol, etc.) tend to be dehydrated, and thus seem likely to develop hypotension after decompression. In the current experiment the amount of administered fluids (lactated Ringer's solution iv at a rate of 5 ml·kg⁻¹·hr⁻¹ plus intracisternal infusion of 0.9% NaCl solution at a rate of 50–70 ml·hr⁻¹ seems to have been larger than that would be appropriate in neurosurgical patients. This may have reduced the haemodynamic changes which occurred after decompression of increased CSF pressure in the present experiment.

The endocrine and haemodynamic alterations associated with intracranial hypertension include elevated plasma catecholamines,¹³ increased systemic and pulmonary arterial pressures,¹⁴ and a shift of blood to the low-resistance system of the pulmonary circulation due to peripheral vasoconstriction.¹⁵ These cardiovascular responses to increased ICP are often complicated by pulmonary oedema^{15,16} or cardiomyopathy.¹³ Of all these changes, vasoconstriction is the primary factor in response to intracranial hypertension.^{14,15,17-19} In the present experiment, CPP showed slow recovery (Table) which was considered to be due to a gradual increase in MAP secondary to increased SVRI (systemic vasocon-

striction). These circulatory changes have been presumed to be caused by sympathetic overactivity, since sympathetic blockade abolished the haemodynamic phenomena during intracranial hypertension.^{15,17,18} However, CO changes during increased CSF pressure in the present experiment were inconsistent with those reported by Koehler *et al.*⁷ who observed increases in CO during intracranial hypertension. This difference in CO response to increased ICP or CSF pressure could be attributed to differences in methods used to increase supratentorial or infratentorial pressure, species, or the anaesthetics used in the experiment. Halothane was used as the underlying anaesthetic in the current experiment. It is a potent cardiodepressant²⁰ and may blunt the autonomic responses associated with increased CSF pressure.

Following decompression of the increased CSF pressure, we observed systemic vasodilatation in all animals. Thus, it is likely that systemic vasodilatation is primarily responsible for the decompression phenomenon, and that this hypotension is secondary to a rapid withdrawal of sympathetic overactivity.

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