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Regional Organ Blood Flow during High-frequency Positive-pressure Ventilation (HFPPV) and Intermittent Positive-pressure Ventilation (IPPV)

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The effect of high-frequency ventilation (HFV) on cerebral blood flow (CBF) at normal and elevated intracranial pressure (ICP) was compared with flows measured under the same conditions during intermittent positive pressure ventilation (IPPV). Renal, lung (bronchial artery supply), and cardiac blood flows also were measured during HFV and compared with flows observed during IPPV. Measurements were made in canines with stable hemodynamic variables and arterial CO_2 and O_2 tensions in the normal range. CBF during HFV was comparable to the CBF during IPPV. Following an increase in ICP to a mean of 44 ± 18 mmHg (SD), mean CBF decreased to 22.5 ± 11 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ (SD) during IPPV and 21.7 ± 13.2 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ (SD) during HFV. No statistical differences could be noted in regional or global flow as a function of ventilatory mode. Renal, lung (bronchial artery supply), and cardiac blood flows also showed no statistical variation between HFV and IPPV. Ventilator-synchronous fluctuations in ICP observed during IPPV were reduced during HFV at normal ICP and eliminated by HFV at elevated ICP. Key words: Brain: blood flow; intracranial pressure. Hemodynamics: regional blood flow. Ventilation: high frequency positive pressure ventilation (HFPPV); high frequency ventilation (HFV); intermittent positive-pressure ventilation (IPPV).

SINCE the introduction of high-frequency ventilation (HFV), substantial emphasis has been placed on determining its effects on circulatory hemodynamics and pulmonary function.[1] The elimination of ventilator-synchronous pressure fluctuations has been described in both the systemic and pulmonary arterial vasculature.[1,2] Recently, the attenuation of ventilator–synchronous pressure fluctuations in intracranial pressure (ICP) also was demonstrated during ventilation with HFV techniques.[3,4] While HFV is being considered more often for primary ventilatory support of patients,[5–13] little is still known of its effects on organ blood flow. This information may be particularly important for the brain where cerebral blood flow (CBF) may be influenced disproportionately by small changes in either compliance or ICP. Because of the lack of information regarding organ blood flow, the purpose of this article is to describe studies on CBF during high-frequency positive-pressure ventilation (HFPPV) at normocarbia under normal and elevated ICP. Similarly, renal, lung (bronchial artery supply), and cardiac blood flows were compared with flows observed during intermittent positive-pressure ventilation (IPPV).

Materials and Methods

Six mongrel dogs were anesthetized with an intravenous injection of thiopental 25 mg/kg. Animals were intubated and maintained at a light level of anesthesia on 2% thiopental 2.5–5.0 $mg \cdot kg^{-1} \cdot h^{-1}$ and paralyzed with pancuronium bromide 0.02 $mg \cdot kg^{-1} \cdot h^{-1}$.[14] Fluid maintenance was achieved with an intravenous infusion of a balanced salt solution containing 5% dextrose at a rate of 3 $ml \cdot kg^{-1} \cdot h^{-1}$. Both a femoral artery and vein were catheterized and a Swan-Ganz® catheter was inserted through an external jugular vein. The dogs then were moved to the prone position and fixed into a stereotactic frame so as to provide free clearance for chest wall movement. A catheter also was placed into the cisterna magna for ICP measurements and connected to a fluid-filled transducer positioned at the level of the cisterna magna. After a scalp incision, a small burr hole was trephined into the skull over the right temporal lobe, through which an 18 French Foley catheter was inserted for the purpose of increasing the ICP. Arterial, venous, pulmonary artery, and capillary wedge pressures were monitored continuously. Cardiac output measurements, using thermodilution, were made by injecting 5 ml 5% dextrose in water at 0° C into the venous port of the Swan–Ganz® catheter at end expiration. Four injections were made, and the average of the three closest values was taken as the cardiac output. Outputs were determined after blood gas stabilization (30 min of ventilation after ventilator setting changes) and prior to blood flow measurements. Each animal was ventilated

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TABLE 1. Physiological Responses to IPPV and HFPPV under Normal and Elevated ICP
(Data Represented as Mean Values ± Standard Deviation)

	Normal ICP		Elevated ICP	
	IPPV	HFPPV	IPPV	HFPPV
pH	7.36 ± 0.03	7.36 ± 0.02	7.36 ± 0.05	7.33 ± 0.01
Pa_{CO_2} (mmHg)	40 ± 2	41 ± 2	40 ± 2	40 ± 3
Pa_{O_2} (mmHg)	100 ± 10	87 ± 9	91 ± 20	91 ± 7
MAP (mmHg)	181 ± 43	172 ± 44	119 ± 41	111 ± 25
CVP (mmHg)	9 ± 3	7 ± 2	8 ± 2	9 ± 1
PAP (mmHg)	31 ± 7	33 ± 4	29 ± 9	31 ± 5
Paw (mmHg)	3.4 ± 1.0	4.1 ± 1.3	4.8 ± 1.1	4.8 ± 3.0
SVI ($ml \cdot beat^{-1} \cdot m^{-2}$)	21.0 ± 6.1	18.5 ± 2.2	18.6 ± 6.8	26.5 ± 22.1
ICP (mmHg)	7.4 ± 2.8	6.8 ± 3.5	44 ± 18	44 ± 21
ΔICP (mmHg)	1.8 ± 1.6	0.2 ± 0.3*	1.1 ± 1.0	0.0 ± 0.0*
Temp (°C)	37.7 ± 0.7	37.4 ± 0.6	37.8 ± 0.6	37.3 ± 0.8

* Statistically significant as compared with IPPV, $P < 0.025$.

by either a Siemens® Servo-ventilator 900C at 20 breaths/min or a low-compressive volume-controlled system (system H) previously described,[7] utilizing the Bronchovent® Special at a rate of 100 pulses/min. The initial tidal volume for IPPV was set at 15 ml/kg. For HFPPV, the initial tidal volume was taken from previously published nomograms.[6] Both ventilators were set to have an inspiratory time of 22% of the ventilatory cycle. Airway pressure was monitored using a saline-filled catheter placed just above the carina and connected to a standard strain gauge transducer. Conditioned gas (95–98% relative humidity at 37° C using the wet/dry bulb technique) was provided during both ventilatory modes. The initial ventilatory mode was selected randomly to be either HFPPV or IPPV.

Radioactive microspheres of mean diameter 15 ± 5 μm labeled with four separate gamma-emitting isotopes (^{57}CO, ^{113}Sn, ^{103}Ru, ^{46}Sc) were used for blood flow measurements according to the method of Heymann *et al.*[15] This allowed for serial measurements of blood flow. A homogenous mixture of 75,000 to 100,000 microspheres in 1.5 ml of isotonic saline were injected rapidly into the left ventricle via a catheter inserted from the femoral artery and followed by an immediate saline flush of 5 ml. Rapid injection into the left ventricle assured adequate mixing of the spheres with blood, resulting in a distribution of microspheres to organs in direct proportion to their blood flow. Reference arterial blood samples were withdrawn simultaneously from a catheter positioned in the aorta at a rate of 10 ml/min for 2 min. Reference blood was collected for 15 s in each of eight counting vials. Isotope injection order for serial measurements in each experiment were randomized.

Brains were sectioned into 68 pieces measuring 1 cm^2 and 0.5 cm thick. Representative sections from the cortex, medulla, and papilla of both kidneys, as well as sections from the apical, cardiac, and diaphragmatic lobes of both lungs were used in determining mean organ blood flow. Mean cardiac blood flows also were estimated from representative sections taken from various areas of the cardiac muscle. Radioactivity of the tissue and reference blood samples was measured by counting for 1 min on a Packard® multichannel AutoGamma Scintillation Spectrometer Model 5360. Isotope activity was corrected for cross-talk by computer solution of a set of four simultaneous linear equations defining radiation spill-over of each isotope into adjacent isotope analysis channels. Regional flows were calculated by multiplying a nuclid reference factor (reference blood withdrawal rate divided by total radioactivity in the reference blood, $ml \cdot min^{-1} \cdot CPM^{-1}$) by the total radioactivity of each tissue section then normalizing for tissue weight. Blood flow was measured at normocarbia and normoxia with normal ICP during IPPV and HFPPV. ICP then was elevated to approximately 40 mmHg by infusing 6–12 ml saline into the balloon of the Foley catheter and maintained for 2 h. Measurements of pressures and organ blood flows were repeated for both modes of ventilation following blood gas stabilization. A two-way analysis of variance for repeated measures with equal cell size was performed on each variable. Group differences were determined by means of a Student–Newman–Keuls test ($P < 0.05$ was considered significant). Data are represented as mean values ± standard deviation.

Results

Mean Pa_{CO_2} during both ventilatory modes at normal and elevated ICP was 40 ± 3 mmHg. pH_a and Pa_{O_2} also were within normal limits (table 1). Mean values for arterial, central venous, pulmonary artery, and capillary wedge pressures for both modes of ventilation at normal and elevated ICP also remained within normal limits (table 1). Stroke volume index (SVI) and airway pressures (P_{aw}) showed no statistical variation between ventilatory modes at normal and elevated ICP (table 1). Also, no immediate changes in cardiovascular or cerebral hemo-

TABLE 2. Mean Organ Blood Flow (ml · 100 g^{-1} · min^{-1}) ± SD

	Normal ICP		Elevated ICP	
	IPPV	HFPPV	IPPV	HFPPV
ICP mmHg	7.4 ± 2.8	6.8 ± 3.5	44 ± 18	44 ± 21
Organ				
Lung	60 ± 30	62 ± 58	50 ± 20	51 ± 26
Kidney	241 ± 107	258 ± 123	292 ± 152	319 ± 120
Heart	106 ± 41	82 ± 41	60 ± 28	54 ± 14

dynamics were observed following switches from IPPV to HFPPV and *vice versa* during the course of the experiment. Ventilator-synchronous fluctuation in ICP observed during IPPV was reduced ($P < 0.025$) during HFPPV at normal ICP. At elevated ICP, ventilator-synchronous fluctuation in ICP (ΔICP) totally was eliminated ($P < 0.025$) during HFPPV (table 1). No significant alterations in lung (pertaining to bronchial arterial supply), renal, and cardiac blood flow were observed for either mode of ventilation at normal and elevated ICP (table 2). CBF during HFPPV was comparable to the CBF during IPPV (table 3, fig. 1). Following an increase in ICP to a mean of 44 ± 18 mmHg, mean CBF decreased to 22.5 ± 11 ml · 100 g^{-1} · min^{-1} during IPPV and 21.7 ± 13.2 ml · 100 g^{-1} · min^{-1} during HFPPV (table 3). These flows, however, showed no statistical variation regionally or globally as a function of ventilatory mode.

Discussion

The clinical use of HFV largely has been confined to HFPPV, as in this experiment, or to high frequency jet ventilation (HFJV).[1,2,5-10] In general, high-frequency ventilators have low internal compliance and deliver a small volume of gas at a high initial flow. This results in lower peak, and often decreased, mean airway pressures.[1,2,5,9,10] However, the effects of HFV on distal airway pressure is still unknown and ultimately may have an adverse effect on circulation, not only through the lung, but also through other major organ systems as well. Blood flow to the lung via the bronchial arteries that supply peribronchial connective tissue, bronchial mucous membranes, and tracheobronchial lymph nodes appears to be similar with HFPPV and IPPV. Furthermore, blood flow through major organs (heart and kidneys) during HFV also appears to remain comparable to flow during conventional ventilation. These findings

TABLE 3. Mean Cerebral Blood Flow (ml · 100 g^{-1} · min^{-1}) ± SD

	IPPV		HFPPV	
	P_{aCO_2} mmHg	CBF	P_{aCO_2} mmHg	CBF
Normal ICP	40 ± 2	49.8 ± 18.5	41 ± 2	52.1 ± 16.3
Elevated ICP	40 ± 2	22.6 ± 11.0	40 ± 2	21.7 ± 13.2

are further supported by observations made by Gioia and co-workers[16] in a study using an HFV system operating at 600 cycles/min. Blood flow through the skin, muscle, liver, adrenal gland, pancreas, jejunum, and kidney showed no significant variation from flow during conventional low-frequency large-volume ventilation. At an increased ICP, our observations indicate no significant differences in blood flow to the heart, lung, and kidney using either mode of ventilation.

During IPPV, ventilator–synchronous fluctuations in intrathoracic pressure are believed to cause momentary venous congestion and may be responsible for the ventilator–synchronous pressure fluctuations in hemodynamic and other physiological pressures.[17,18] In the closed cranium, where volume, hemodynamic factors, and tissue compliance affect ICP, ventilator-synchronous pressure fluctuations induced during IPPV may be substantial, particularly in those therapies where high airway pressure must be applied to provide adequate oxygenation. Rapid fluctuations in ICP may result from momentary variations in brain volume and may be associated with decreased blood flow.[19,20] Using HFPPV, Babinski *et al.* showed that ventilator-synchronous fluctuations in ICP are decreased dramatically at normal ICP.[3] However, our observations indicate that CBF is not affected by their reduction. There is, on the other hand, some evidence to suggest that CBF decreases slightly with increased airway pressure.[16] The decrease in CBF amounts to 9–20% and is not statistically significant up to mean airway pressures of 13 cmH_2O. However, ventilatory therapies that generate mean airway pressures in excess of 13 cmH_2O may produce marked changes in CBF.

The observation that CBF during HFV at normal ICP does not change has been confirmed by Gioia *et al.* using a similar microsphere technique.[16] More recently, Toutant *et al.* provided further confirmation using ^{133}Xe wash-out techniques that CBF at normal ICP during HFV is unchanged.[21]

While a decrease in CBF at an increased ICP was observed, a further decrease from ventilator-synchronous fluctuations in ICP during IPPV did not occur. The decrease and/or elimination of ventilator-synchronous fluctuations at both normal and increased ICP by HFPPV does not appear to improve CBF. While these findings may accurately describe the CBF at the ICP levels studied in this experiment, at higher ICPs, or in brains where compliance capability is reduced severely, responses may be different in terms of CBF with the application of HFV.

During craniotomy, ventilator-induced brain pulsation often is observed in mechanically ventilated neurosurgical patients.[4,22] These excursions in the brain surface, when magnified by a microscope, may render the application of microsurgical techniques difficult, if not at times impossible. Our observations at normal and elevated

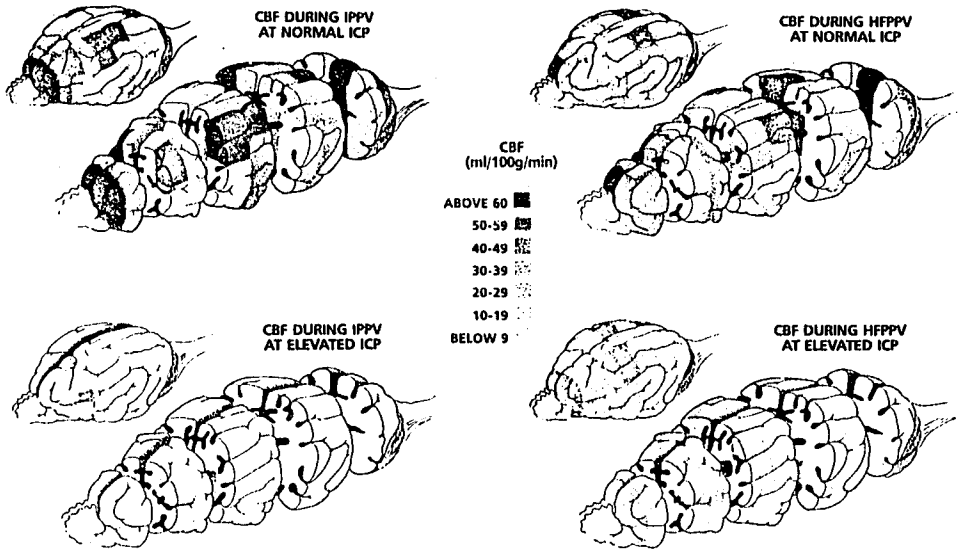

FIG. 1. Cortical and regional blood flow during IPPV and HFPPV at normal and elevated ICP using radiolabeled microspheres.

ICP, as well as those of Babinski *et al.*[3] and Todd *et al.*,[4] have shown that HFV dramatically can decrease this ventilator-synchronous brain movement. Not only is the brain placed into a quiescent state, but in other organs, such as the heart and lungs,[7] much less movement due to ventilation occurs. Since blood flow through the organs examined in this and other studies during HFV appears to be within the range found during IPPV,[16,18] it appears possible that satisfactory operating conditions may be established for a wide variety of organ systems during normal and pathologic states with low-compressive HFV systems.

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