The Hemodynamic Effects of Changes in Blood Volume during Intermittent Positive-pressure Ventilation

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The hemodynamic effects of changes in blood volume during intermittent positive-pressure ventilation (IPPV) were studied in lightly anesthetized dogs following recovery from implantation of pulsed ultrasonic flow transducers on vena cava and aorta. Alveolar ventilation was maintained in excess of normal, and arterial carbon dioxide tension (\(P_{\text{aco}}\)) was varied by alteration of concentration of inspired \(CO_2\). Blood volume was altered by the bleeding of 20 per cent of estimated blood volume, following this, by reinfusion of the shed blood plus an equal amount of dextran. During each of these periods low (peak airway pressure 10 cm \(H_2O\), inspiratory-to-expiratory ratio 1:2) and high (peak airway pressure 30 cm \(H_2O\), inspiratory-to-expiratory ratio 2:1) levels of ventilation were employed. The three variables, blood volume, \(P_{\text{aco}}\) and intrathoracic pressure, exerted separate effects on stroke volume (S.V.) and cardiac output (C.O.): C.O. and S.V. increased with increasing blood volume and with rising \(P_{\text{aco}}\) but decreased with increasing intrathoracic pressure. These findings suggest that the deleterious effects of high levels of intrathoracic pressure on cardiac output may be compensated by expanding blood volume.

The increase in extracardiac pressure produced by intermittent positive-pressure ventilation (IPPV) has been shown to decrease the distending pressure of the right ventricle and impede systemic venous return, resulting in lowered cardiac output.\(^1\) Infusion of blood has been shown to cause an increase in the mean circulatory pressure, resulting in a moderate rise in cardiac output.\(^2\) However, there have been no systematic attempts to compensate for the circulatory effects of intermittent positive-pressure ventilation by expansion of blood volume. The purpose of the present study was to investigate the effects of alterations in blood volume on venous return and cardiac output of animals subjected to IPPV with known levels of \(P_{\text{aco}}\).

Materials and Methods

Pulsed ultrasonic flow transducers\(^3\),\(^4\) were implanted under aseptic conditions on the superior and/or inferior vena cava and on the descending thoracic aorta in mongrel dogs of both sexes. Following a minimum of seven days’ recovery, the animals were lightly anesthetized with morphine, 1.5 to 2 mg/kg intramuscularly, and pentobarbital (Nembutal\(^5\)), 10 to 12 mg/kg intravenously. A supplementary dose of 30 to 60 mg of pentobarbital was administered as required to maintain a stable anesthetic level throughout the four-to-five-hour experiment; however, no additional doses of anesthetic were given between determinations when results were compared. Tracheal intubation was accomplished and 100 per cent oxygen administered via a nonbreathing system for 15 minutes for denitrogenation. End-tidal \(CO_2\) concentration was monitored continuously from an 18-gauge needle in the endotracheal tube, using a Beckman LS-1 infrared carbon dioxide analyzer, sampling at a rate of 500 ml/min. A Bird 9X respirator with a recording ventilator was used to generate the patterns of IPPV.

Aortic and vena caval blood flows were recorded from the implanted transducers. Intrathoracic pressure was measured by means of a
<table>
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<th>Blood Volume</th>
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<th>Pacot</th>
<th>Mean Stroke Volume (Percent Control) 9 Experiments</th>
<th>Mean Cardiac Output (Percent Control) 9 Experiments</th>
<th>Arterial Blood Pressure**</th>
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SD = standard deviation; SE = standard error.
* Assumed control.
** In torr; mean value for nine experiments.
*** Values for high-level ventilation not given because of wide pressure swings during the respiratory cycle.

20 × 25 mm flat silastic balloon (containing sufficient saline solution to allow coupling), which had been placed in the pleural space at the time of surgery. Airway pressure was monitored via an 18-gauge needle in the endotracheal tube, while arterial and venous pressures were measured by cannulation of femoral vessels, the venous catheter being placed in the abdominal vena cava. Arterial blood samples were obtained for determination of PaO₂, PaCO₂ and pH, using modified Clark, Severinghaus and Radiometer electrodes, respectively, and correction of gas tensions and pH for temperature was performed using the blood gas calculator of Severinghaus. Two-ml samples were collected at ten-minute intervals to confirm PaCO₂ as calculated from end-tidal CO₂ and to assure adequate oxygenation and absence of metabolic acidosis; less than 40 ml of blood were removed from the animals for sampling, and this volume was replaced with saline solution.

Nine separate studies were performed on five dogs in the supine position. Observations were made during two levels of ventilation, low (peak inspiratory pressure 10 cm H₂O, inspiratory-to-expiratory ratio 1:2) and high (peak inspiratory pressure 30 cm H₂O, inspiratory-to-expiratory ratio 2:1).

Each respiratory pattern was employed for ten-minute periods at PaCO₂ values of 20, 40 and 60 torr, with randomization of the sequence of levels of ventilation and PaCO₂ values at each blood volume. PaCO₂ was changed by altering the CO₂ concentration of inspired gas. Each respiratory pattern at each PaCO₂ value was applied with the animal in the normovolemic state. Following this, each animal was bled 20 per cent of his blood volume (18 to 20 ml/kg) and the experiment repeated, following a stabilization period of 30 minutes. For the final portion of the study, the blood which had been removed aseptically was infused, and in addition, an equal amount
of dextran was administered to make the animal hypervolemic. A stabilization period of 30 minutes was allowed before data were recorded. Flow in the descending aorta was considered to be representative of cardiac output, since only relative changes were of interest. Zero flow was obtained by acetylcholine cardiac arrest. Stroke volume was obtained by electronic integration of aortic flow and by planimetry, and averaged over several respiratory cycles. Cardiac output was obtained by multiplying the stroke volume times the heart rate. Changes in stroke volume and cardiac output were plotted as percentages of those values obtained at normal blood volume, \( P_{aCO_2} \) 40 torr, low level of ventilation (peak pressure 10 cm \( H_2O \), inspiratory-to-expiratory ratio 1:2). Comparison of data between groups was made using Student's \( t \) test.

**Results**

Three separate effects on stroke volume (S.V.) and cardiac output (C.O.) were observed (table 1, figs. 1 and 2), the effects of increasing mean intrathoracic pressure (fig. 3), changes in \( P_{aCO_2} \) (fig. 4), and alteration in blood volume (fig. 5). Maximum values for S.V. and C.O. were recorded in the hypervolemic state, while minimum values were observed with the animal hypovolemic. At each blood volume, high levels of ventilation (peak pressure 30 cm \( H_2O \), inspiratory-to-expiratory ratio 2:1) decreased the S.V. and C.O., compared with values obtained at low levels of ventilation (peak pressure 10 cm \( H_2O \), inspiratory-to-expiratory ratio 1:2). At each blood volume and at each level of ventilation, changes in \( P_{aCO_2} \) also altered S.V. and C.O. with reference to control levels, with both variables increasing directly with increasing \( P_{aCO_2} \) (figs. 1 and 2).

In the hypovolemic animals, low levels of ventilation were associated with reduction in C.O. to 46 per cent (\( P_{aCO_2} \) 20 torr), 51 per cent (\( P_{aCO_2} \) 40 torr), and 60 per cent of controls (\( P_{aCO_2} \) 60 torr); at high levels of ventilation the values for cardiac output at 20, 40 and 60 torr \( P_{aCO_2} \) were, respectively, 32 per cent.
Fig. 3. Typical example of the effect of increasing intrathoracic pressure on aortic flow and arterial pressure. A (left) shows effect of low-level ventilation (peak airway pressure 10 cm H₂O, inspiratory-expiratory ratio 1:2); B (right) shows effect of high-level ventilation (peak airway pressure 30 cm H₂O, inspiratory-expiratory ratio 2:1). Femoral arterial pressure in torr; airway, intrapleural pressure in cm H₂O.
FIG. 4. Typical example of hemodynamic effect of increasing $P_{acO_2}$ by rapidly increasing CO$_2$ concentration in inspired gas. Femoral arterial pressure in torr; airway, intrapleural pressures in cm H$_2$O. $P_{acO_2} = 20$ torr at beginning of record, $P_{acO_2} = 60$ torr at end of record.
cent, 41 per cent and 51 per cent of controls (table 1, fig. 2). In the normovolemic animal, at low levels of ventilation, a PaCO₂ of 20 torr was associated with a cardiac output of 92 per cent, compared with the 100 per cent value obtained under conditions defined as control (low level of ventilation, PaCO₂ 40 torr); at PaCO₂ 60 torr the cardiac output was 154 per cent of control. During high levels of ventilation with normovolemia, the per cent cardiac output obtained at PaCO₂ values of 20, 40 and 60 torr, respectively, were 77 per cent, 81 per cent and 103 per cent. In the hypervolemic animal, cardiac output, at low levels of ventilation, was 114 per cent at PaCO₂ 20 torr, 133 per cent at PaCO₂ 40 torr, and 171 per cent at PaCO₂ 60 torr; the values at high levels of ventilation for 20, 40 and 60 torr, respectively, were 106 per cent, 118 per cent and 154 per cent. Comparable values were obtained for stroke volume (table 1, fig. 1).

Superior and/or inferior vena caval blood flow changes paralleled the changes in cardiac output. Venal caval blood flow was decreased by increasing mean intrathoracic pressure, decreasing blood volume, and decreasing PaCO₂.

Changes in S.V. and C.O. at each PaCO₂ and to each condition of blood volume were compared at low vs. high levels of ventilation (table 2). The most significant differences were those secondary to changes in blood volume.

Changes in heart rate were more variable. Hypovolemia uniformly produced tachycardia of some degree; hypervolemia had a more variable effect on heart rate, a decrease in heart rate occurring in some animals in the hypovolemic state, while in others, heart rate increased. High levels of ventilation increased heart rates in all animals, as compared with low levels in both normovolemic and hypovolemic states. The hypervolemic state was more variable in this regard, the heart rate frequently being unchanged at high as compared with low levels of ventilation. It was of interest that the cardioacceleration of sinus arrhythmia occurred during expiration as intrathoracic pressure fell toward normal.

Arterial blood pressures were decreased by hemorrhage in all animals. Frequently, however, C.O. decreased by 50 per cent or more before any appreciable change in blood pressure was observed. Hypervolemia caused the arterial blood pressures to return to values which usually slightly exceeded those recorded during the normovolemic state. The average increase with hypervolemia in nine experiments in which systolic and diastolic arterial blood pressures were determined was approximately 15 torr.

Mean venous pressure (abdominal vena cava, average of nine experiments) at a low level of ventilation was 2.8 cm H₂O during hypovolemia, 3.6 cm H₂O in normovolemic animals, and 5.0 cm H₂O during hypervolemia.

Discussion

Hemodynamic consequences of induced changes in blood volume in dogs have been reviewed recently by Conway, who demonstrated an initial increase in C.O. and blood pressure, with increased blood volume; C.O. returned to normal levels after one to one and a half hours, with persistence of elevation of blood pressure. This experiment also demonstrated initial decreases in cardiac output and peripheral resistance after bleeding, with return to former levels after three hours, but did not, however, evaluate the effects of IPPV on the variables studied. In our experiments, hypervolemia produced significant increases in cardiac output at any levels of ventilation and PaCO₂.

The mechanisms by which infusion of whole blood affects stroke volume and cardiac output have been detailed by Guyton et al., who showed that the infusion caused an increase in the mean circulatory pressure. The interaction between mean circulatory pressure, right atrial pressure, and venous return and cardiac output curves is somewhat complex, but a careful consideration of these relationships permits at least qualitative predictions of the effects of varying degrees of IPPV and blood volume changes. Specifically, Guyton demonstrated that the increase in intrathoracic pressure produced by IPPV decreased the distending pressure of the right ventricle (intracardiac pressure minus intrathoracic pressure) and elevated right atrial pressure, causing a decrease in venous return and decreased cardiac output. Ordinarily, compensatory
Fig. 5. Typical example of hemodynamic effect of decreasing blood volume 20 per cent (15 kg dog bled 300 ml). Femoral arterial pressure in torr; airway, intrapleural pressures in cm H2O. Time interval between A and B is three minutes.
The effect of IPPV, from Guyton’s curves, would be exaggerated by hypovolemia, although this combination was not actually reported by his laboratory. Carr and Essex showed a close relationship between blood volume, venous pressure and survival during positive-pressure ventilation. They measured arterial and venous pressure in dogs subjected to positive-pressure ventilation and demonstrated that hemorrhage decreased the animal’s tolerance to increased intrathoracic pressure, which was improved by partial retransfusion. Our study confirms these findings and extends the earlier study by demonstrating that graded increases in blood volume increase cardiac output and stroke volume during comparable levels of IPPV.

It is worth noting that the dog is better equipped to withstand IPPV or hemorrhage than man. The dog’s spleen is highly contractile and is capable of autotransfusion of as much as 19 per cent of the total blood volume; it delivers blood of high hematocrit in response to a wide variety of stressful stimuli. The human spleen has relatively little reservoir function, which presumably would exaggerate the effects on cardiac output of IPPV and hemorrhage, as compared with our results in dogs. In addition, our animals were lightly anesthetized with reflexes intact, whereas deep surgical anesthesia in man may inhibit or abolish compensatory reflex mechanisms.
Thus, the anesthetized, hypovolemic human patient may be particularly sensitive to the deleterious cardiovascular effects of IPPV.

Previously, we demonstrated progressive decreases in S.V. and C.O. with increasing mean intrathoracic pressure during varying levels of IPPV at constant $P_aCO_2$. We subsequently showed a separate effect of increasing S.V. and C.O. with increasing $P_aCO_2$ at comparable levels of IPPV, and comparable changes in cardiac output with alterations in $P_aCO_2$ in anesthetized man have been shown recently. The present study adds a third factor influencing S.V. and C.O. during IPPV, the blood volume.

From a clinical point of view, it is clear that hypovolemic patients represent a group with increased risk when surgical anesthesia with IPPV is required. In addition to the obvious measures of blood or plasma volume expanders, simple postural maneuvers are helpful. Berner et al. demonstrated that the head-down or Trendelenburg position restored cardiac output in patients during IPPV by restoring the central blood volume. We have shown that simple elevation of the legs, with the trunk level, accomplished a comparable restoration without the disadvantages of the Trendelenburg position. Vasoconstrictor therapy also has been demonstrated as an effective method of increasing the central blood volume and cardiac output, although this method is less physiologic except in situations in which reflexes have been abnormally abolished or inhibited.

In summary, IPPV, particularly with high pressures and prolonged inflation cycle, is a hazard to normal cardiac function, and its effects, which will be exaggerated by respiratory alkalosis, may be disastrous to a patient with hypovolemia.

References