

Plasma Antidiuretic Hormone and Urinary Output during Continuous Positive-pressure Breathing in Dogs

Robert A. Baratz, Ph.D., M.D.,* Daniel M. Philbin, M.D.,†
Richard W. Patterson, M.D.‡

Continuous positive-pressure breathing (CPPB) with an end-expiratory pressure of 10 cm H₂O decreased cardiac output and urinary output, with an increase in plasma antidiuretic hormone (ADH). Similar results were obtained after bilateral cervical vagotomy. Oliguria during CPPB was caused neither by ADH release controlled by an intrathoracic volume receptor mechanism nor by changes in PaCO₂, but was apparently related to the decrease in cardiac output. Arterial oxygenation did not change during the periods of CPPB, but was increased upon release of the end-expiratory pressure. These changes in blood gases can be explained by the measured decrease in cardiac output or by an increase in pulmonary vascular shunting. (Key words: Antidiuretic hormone; Urinary output; Continuous positive-pressure breathing.)

THE MAINTENANCE of a positive end-expiratory pressure (PEEP) is used extensively during respiratory intensive care in an effort to increase oxygenation of arterial blood.¹⁻³ It was determined in a previous study that intermittent positive-pressure breathing (IPPB) increased urinary output and decreased plasma antidiuretic hormone (ADH).⁴ It is proposed that an airway pressure of zero during the expiratory phase of the respiratory cycle is important in this response, and that a positive end-expiratory pressure such as that used during CPPB will alter these results.

* Assistant Professor of Anesthesiology.

† Present address: Assistant Professor of Anesthesiology, Medical College of Wisconsin, Milwaukee, Wisconsin.

‡ Associate Professor of Anesthesiology.

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Sustained elevation of airway pressure has been reported to increase PaCO₂,⁵ impede venous return, and decrease cardiac output.⁶ Henry *et al.* postulated that these changes activate the volume receptor mechanism in the left atrium, leading to release of ADH from the neurohypophyseal tract and antidiuresis.⁷ The afferent neural pathway from the stretch receptors to the hypophysis is the vagus nerve.⁸ If this pathway were interrupted by vagotomy, this volume receptor mechanism would no longer be active.

The present study was designed to determine whether CPPB and a positive end-expiratory pressure would alter urinary output and, if so, whether the mechanism involved was through changes in carbon dioxide tension, cardiac output, or the volume receptors in the left atrium.

Methods

Six female mongrel dogs weighing 14–26 kg were anesthetized with sodium pentobarbital, 50 mg/kg, injected intravenously. The trachea of each dog was intubated with a wide-bore endotracheal tube and the cuff inflated to a gas-tight fit. Halothane, 0.4–0.5 per cent as measured by an Analytical Systems Model 10 ultraviolet analyzer, was administered via a Copper Kettle, with air as the carrier.

The tip of a cardiac catheter was introduced through the jugular vein into the right ventricle or pulmonary artery (as indicated by the pulse-pressure contour). The femoral artery was catheterized and all pressures were measured with appropriate transducers and recorders. Standard laboratory techniques were used to determine arterial blood gases. Cardiac output was measured using the dye-dilution technique with indocyanine green and a

TABLE 1. Cardiorespiratory and Renal Data

	1 IPPB	2 CPPB	3 IPPB	BILATERAL VAGOTOMY	4 IPPB	5 CPPB	6 IPPB
Urinary flow (ml/min)	7.5 ± 0.9	3.9 ± 0.4*	6.1 ± 0.8		8.5 ± 1.1	3.5 ± 0.5†	5.0 ± 0.9
Plasma ADH (μ U/ml)	10 ± 4	16 ± 4*	8 ± 4		10 ± 3	21 ± 4‡	15 ± 5
Cardiac index (l/min/m ²)	3.90 ± 0.54	2.79 ± 0.24*	3.49 ± 0.40		3.69 ± 0.48	2.69 ± 0.41†	3.40 ± 0.36
PaCO ₂ (mm Hg)	19.6 ± 1.9	23.1 ± 3.9	19.9 ± 1.8		20.7 ± 3.0	24.4 ± 3.9	19.1 ± 1.8
PaO ₂ (mm Hg)	101 ± 8	100 ± 7	109 ± 5		100 ± 5	111 ± 4	123 ± 6
Sodium excretion (mEq/min)	0.87 ± 0.14	0.55 ± 0.15*	0.75 ± 0.21		1.01 ± 0.19	0.49 ± 0.12†	0.67 ± 0.12

* $P < 0.05$ (column 1 vs. column 2).† $P < 0.01$ (column 4 vs. column 5).‡ $P < 0.001$ (column 4 vs. column 5).

Beckman recording densitometer. Sodium concentrations in serum and urine were measured with a flame photometer.

Plasma antidiuretic hormone was measured by concentration of the plasma sample on an ion-exchange resin, followed by bioassay of the concentrated sample in a water-loaded, alcohol-anesthetized rat, as described by Yoshido *et al.*⁹ A four-point assay was used for each sample.

The dogs were hydrated intravenously with 25 ml/kg/hour of Ringer's lactate solution until a urinary flow of at least 2 ml/min was obtained, after which the infusion was continued at the rate of 15 ml/kg/hour. Urine was collected continuously from an indwelling bladder catheter. At the end of each period of urine collection, the bladder was evacuated by aspiration and washed with 10 ml of air.

Immediately after placement of the endotracheal tube, ventilation of the dog with an Ohio volume-controlled respirator, using a non-rebreathing circuit, was begun. Tidal volume and frequency were adjusted so that end-expired CO₂ values were between 2 and 3 per cent, as measured by an infrared CO₂ analyzer (Beckman Model LB-4). Neither volume nor frequency of the respirator was changed for the rest of the study. End-expiratory pressure was zero.

After a stable urinary flow had been achieved, the experiment was divided into six periods of 30 minutes each, with measurements made during the second 15 minutes of each period. During the first period, intermittent positive-

pressure breathing (IPPB) with an end-expiratory pressure of zero was used. In the second, CPPB with an end-expiratory pressure of 10 cm H₂O was applied with a spring-loaded valve in the expiratory line. The conditions of the first period were reinstated during the third period. Bilateral cervical vagotomy was then performed, and the sequence of IPPB, CPPB, and IPPB repeated. All results were analyzed statistically by Student's *t* test for paired data.

Results

The means and standard errors of the means of all measurements are presented in table 1 and figure 1. Using IPPB values as controls, the institution of CPPB with an end-expiratory pressure of 10 cm H₂O significantly decreased urinary output and increased plasma ADH. This was seen with the vagus nerve intact, as well as following vagotomy. Bilateral cervical vagotomy resulted in a 25 per cent increase in heart rate. The magnitudes of changes in urinary output and plasma ADH were approximately equal before and after vagotomy.

Cardiac index decreased significantly, from an average of 3.90 l/min/m² during IPPB to 2.79 l/min/m² during CPPB. The same effect was observed after vagotomy. Likewise, sodium excretion decreased during CPPB.

The maintenance of an end-expiratory pressure during CPPB did not increase PaO₂. Release of the end-expiratory pressure and reinstatement of IPPB caused increases in PaO₂ of 9 and 12 mm Hg before and after vagotomy,

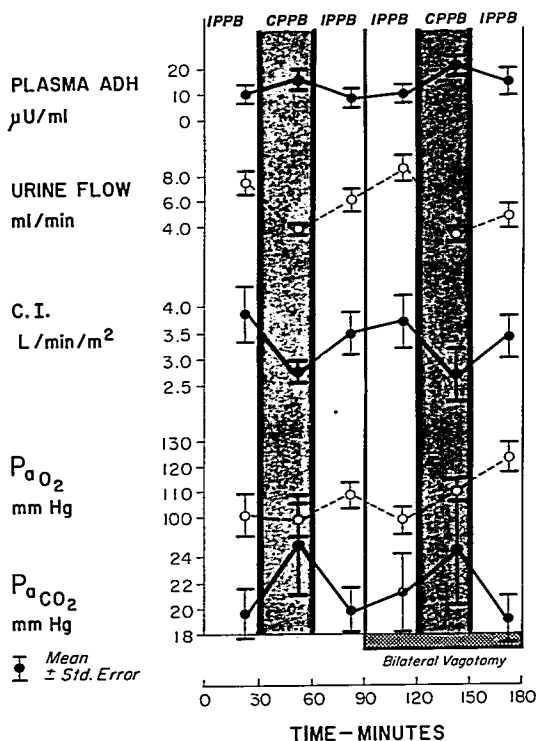


FIG. 1. Effects of IPPB and CPPB on measured values.

respectively. P_{aCO_2} was elevated 3.7 to 5.5 mm Hg during periods of continuous positive-pressure breathing.

Discussion

It has been reported that changes in renal hemodynamics, urine output, and plasma ADH during IPPB are related to elevations of P_{aCO_2} greater than 50 mm Hg.^{10, 11} However, this cannot explain the present results, because the small increases in P_{aCO_2} were insufficient to account for the increases in plasma ADH and antidiuresis.

As changes in urinary flow and plasma ADH during CPPB were approximately the same be-

fore and after vagotomy, it is apparent that the left atrial volume receptor mechanism is not involved in the reduction in urinary output with continuous elevation of the end-expiratory pressure. The increase in plasma ADH even after vagotomy can possibly be explained by volume receptors other than those in the left atrium, non-vagal afferent pathways, or a mechanism activated by the 25 per cent decrease in cardiac output during CPPB.

It has been well documented that glomerular filtration rate and renal plasma flow decrease during CPPB.¹² The significant decrease in sodium excretion found during continuous positive-pressure breathing in the present experi-

ments is further evidence of the diminished renal blood flow. It is concluded that the decrease in urinary output during CPPB is a direct effect of the decrease in cardiac output.

Pa_{O_2} consistently increased when expiratory resistance was removed, rather than during CPPB, while Pa_{CO_2} increased during CPPB. Although an improvement in arterial oxygenation with continuous positive-pressure breathing has been reported,¹⁻³ Cheney *et al.* found no change in Pa_{O_2} in anesthetized patients subjected to a positive end-expiratory pressure.⁵ While increased expiratory resistance prevented atelectasis, the elevated airway pressure caused an increase in pulmonary vascular resistance, resulting in shunting of blood away from ventilated alveoli, and Pa_{O_2} improved only when the expiratory resistance was released. Cheney believed that elevated expiratory resistance was responsible for the decrease in cardiac output, which when combined with constant oxygen consumption would contribute to a decrease in Pa_{O_2} . Philbin *et al.*¹³ demonstrated that Pa_{O_2} was directly related to cardiac output, and thus the increase in cardiac output following the release of CPPB may account for the increase in Pa_{O_2} found after the re-establishment of IPPB.

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Drugs

PHENOBARBITAL AND DIPHENYLHYDANTOIN The half-life of phenobarbital in the sera of children treated for epilepsy with phenobarbital and diphenylhydantoin was determined. The serum half-life in children was shorter than that reported for adults. Phenobarbital may also depress the diphenylhydantoin levels, indicating microsomal enzyme induction. (Garrettson, L. K., and Dayton, P. G.: *Disappearance of Phenobarbital and Diphenylhydantoin from Serum of Children, Clin. Pharmacol. Ther.* 11: 674 (Sept.) 1970.)