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Treatment of Cardiac and Renal Effects of PEEP with Dopamine in Patients with Acute Respiratory Failure

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The hemodynamic and renal effects of mechanical ventilation with positive end-expiratory pressure (PEEP) were studied with and without continuous dopamine administration in ten patients who had acute pulmonary failure. The application of 20 cm H_2O PEEP during mechanical ventilation resulted in improvements in arterial blood oxygen tension, from 63 ± 6 to 81 ± 12 torr (mean ± SE), and intrapulmonary shunt fraction, from 29 ± 3 to 21 ± 3 per cent, whereas cardiac output, systemic oxygen transport and renal function were impaired by 20, 19 and 47 per cent, respectively. Dopamine infusion at a rate of 5 ± 0.05 μg/kg/min reversed the deleterious effects of PEEP on cardiovascular and renal function: cardiac output increased from 4.5 ± 0.3 to 6.0 ± 0.5 l, urinary output from 1.0 ± 0.3 to 1.7 ± 0.4 ml/min, sodium excretion and creatinine clearance by 50 per cent. Systemic oxygen transport was improved from 680 ± 44 to 925 ± 78 ml, arterial oxygen tension from 81 ± 12 to 102 ± 14 torr, and total deadspace to tidal volume ratio from 0.49 ± 0.02 to 0.44 ± 0.03 with dopamine. The authors conclude that the depression of cardiovascular and renal functions that may occur in patients who need high levels of PEEP for the treatment of acute pulmonary failure can be treated successfully with dopamine infusion. This represents a valuable alternative to expansion of blood volume for the improvement of systemic oxygen transport and arterial blood oxygen tension in critically ill patients. (Key words: Heart: cardiac output; dopamine; failure; inotropism; vascular pressures. Kidney: blood flow; function. Sympathetic nervous system: dopamine. Ventilation: deadspace; continuous positive-pressure breathing; mechanical, intermittent positive-pressure breathing; positive end-expiratory pressure; shunting.)

CONTINUOUS POSITIVE-PRESSURE VENTILATION is widely used for the treatment of acute respiratory failure.[1–3] The aim of this therapy is to improve pulmonary gas exchange and systemic oxygen transport. Oxygen transport is the product of blood oxygen content times cardiac output, and thus depends on both pulmonary and cardiovascular effects of CPPV. High levels of PEEP are generally associated with diminution of venous return and central blood volume, and this can decrease ventricular filling pressures and cardiac output.[2,4,5] An additional depression of atrial or ventricular function, probably of primary or reflex origin, has been reported recently.[6] These hemodynamic effects can decrease oxygen transport in spite of an increase in Pa_{O_2} and a decrease in intrapulmonary shunt.[7–9] PEEP also alters renal function, including decreasing urinary output and sodium excretion, probably as a result of a decrease in total renal perfusion, modifications in the distribution of intrarenal blood flow, and increases in antidiuretic hormone secretion.[10–12]

Dopamine in small doses is known to increase cardiac contractility[13,14] and, in particular, to increase right ventricular filling pressures by increasing venous return through a venoconstrictor mechanism.[15,16] In addition, dopamine increases total renal blood flow by a specific renal vasodilatation[13,17] and induces an augmentation of urinary output and sodium excretion.[14,18] The purpose of this study was to examine whether small doses of dopamine could correct the impairment of cardiac and renal function produced by PEEP in patients needing ventilation with high levels of PEEP.

Methods

We studied ten patients, seven men and three women, ranging in age from 19 to 65 years (mean age 44 years). They were being treated for various conditions, including trauma to the chest and severe pul-

ABBREVIATIONS

AP	= arterial blood pressure
BSA	= body surface area
Ca_{O_2}	= arterial blood oxygen content
$C\bar{v}_{O_2}$	= mixed venous blood oxygen content
CPPV	= continuous positive-pressure ventilation
C_{cr}	= creatinine clearance
HR	= heart rate
IPPV	= intermittent positive-pressure ventilation
LVSWI	= left ventricular stroke work index
MAP	= mean arterial pressure
MPAP	= mean pulmonary arterial pressure
Pa_{O_2}	= partial pressure of oxygen in arterial blood
Pa_{CO_2}	= partial pressure of carbon dioxide in arterial blood
PCWP	= pulmonary capillary wedge pressure
PEEP	= positive end-expiratory pressure
PVR	= pulmonary vascular resistance
$\dot{Q}_T$	= cardiac output
$\dot{Q}_S/\dot{Q}_T$	= intrapulmonary shunt fraction
RAP	= right atrial pressure
RVSWI	= right ventricular stroke work index
SI	= stroke index
SV	= stroke volume
SVR	= systemic vascular resistance
V_D/V_T	= deadspace to tidal volume ratio
V/Q	= ventilation/perfusion ratio
T_{O_2}	= systemic oxygen transport

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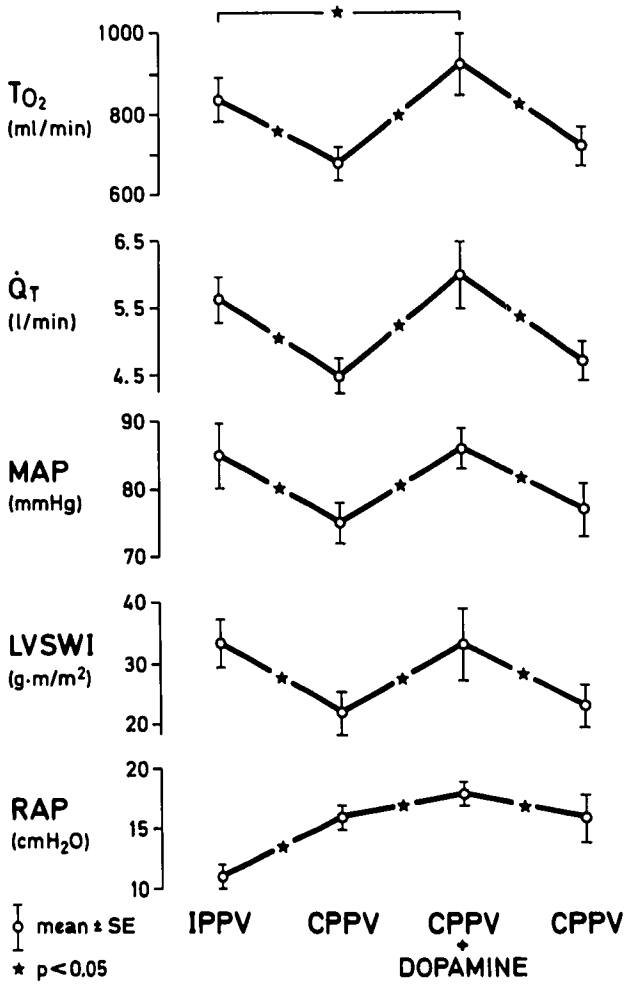

FIG. 1. Mean values for systemic oxygen transport (T_{O_2} = cardiac output × arterial oxygen content), cardiac output ($\dot{Q}_t$), mean arterial pressure (MAP), left ventricular stroke work index (LVSWI), and right atrial pressure (RAP) during the following ventilatory conditions: intermittent positive-pressure ventilation (IPPV), continuous positive-pressure ventilation with 20 cm H_2O PEEP (CPPV), CPPV and a continuous perfusion of dopamine (5 ± 0.5 μg/kg/min), and a control period of CPPV.

monary infection, and needed mechanical ventilation because of acute respiratory failure. The patients were judged to have normal blood volumes on the basis of central venous pressures of 9–14 cm H_2O and pulmonary capillary wedge pressures of 10–15 torr, during IPPV. Prior to the performance of the study, they had received PEEP, 5–10 cm H_2O. None was in septic shock at the time of the study. Volume-controlled ventilators were used, delivering a constant tidal volume of 15 ml/kg. Catheters were placed into the right atrium, pulmonary (Swan-Ganz 7F) and radial arteries, and the bladder. Inspired oxygen concentrations varied between 60 and 80 per cent in the patient group and were held constant for each patient during the study periods. The investigations were done under the following ventilatory conditions: 1) intermittent positive-pressure ventilation with zero end-expiratory pressure; 2) continuous positive-pressure ventilation with a positive end-expiratory pressure of 20 cm H_2O; 3) CPPV with PEEP 20 cm H_2O associated with administration of dopamine, 5.0 ± 0.5 μg/kg/min (mean ± SE), by continuous intravenous infusion. This dose of dopamine was selected by adjusting the infusion rate until systemic arterial pressure was the same as that during condition 1; 4) CPPV with PEEP 20 cm H_2O (control period). Each ventilatory period was maintained for 60 min to obtain a steady state, before the hemodynamic and blood-gas measurements were performed. The sequence 1–2–3–4 was carried out in studying all patients. A constant intravenous infusion of dextrose, 10 per cent, at a rate of 100 ml/hour was maintained during the study.

Systolic, diastolic and mean arterial blood pressures, mean pulmonary arterial pressure, pulmonary capillary wedge pressure, and right atrial pressure were obtained with standard pressure transducers and monitoring equipment. Cardiac output ($\dot{Q}_t$) was determined by thermodilution (Edwards 91500 thermodilution computer). Arterial blood oxygen and carbon dioxide tensions and *p*H, mixed venous blood gas values ($P\bar{v}_{O_2}$, $P\bar{v}_{CO_2}$) and *p*H, and mixed expired P_{CO_2} ($P_{\bar{E}CO_2}$) were measured with standard electrode techniques. Oxygen saturation was determined with a CO-Oximeter, Instrumentation Laboratories, Lexington, Massachusetts 02173.

The following data (see abbreviations) were derived:

$$\text{Stroke volume} = \frac{\dot{Q}_t}{HR} \text{ (ml/systole)}$$

TABLE 1. Cardiovascular Variables and Pulmonary Gas Exchange (Mean Values ± SE)

	IPPV	CPPV	CPPV + Dopamine	CPPV
HR (min^{-1})	97 ± 7	100 ± 8	101 ± 9	101 ± 9
AP, systolic (torr)	132 ± 12	115 ± 19	133 ± 20	112 ± 19
HR × AP systolic (torr · $min^{-1} \cdot 10^3$)	12.8 ± 1.2	11.5 ± 1.0	13.4 ± 1.3	11.3 ± 1.1
MPAP (torr)	23 ± 1	29 ± 2	31 ± 3	29 ± 2
PCWP (torr)	12 ± 1	15 ± 1	16 ± 1	15 ± 1
SV (ml)	61 ± 9	47 ± 7	63 ± 11	49 ± 8
SVR (units)	13.1 ± 1.1	13.2 ± 1.4	11.3 ± 1.5	12.9 ± 1.6
PVR (units)	2.0 ± 0.4	3.1 ± 0.6	2.5 ± 0.4	3.0 ± 0.5
LVSWI (g·m/m²)	33.8 ± 4.2	22.0 ± 3.6	33.3 ± 5.9	23.6 ± 3.5
RVSWI (g·m/m²)	6.9 ± 0.7	6.3 ± 1.0	8.4 ± 1.3	6.5 ± 1.0
Pa_{O_2} (torr)	63 ± 6	81 ± 12	102 ± 14	83 ± 14
Pa_{CO_2} (torr)	36 ± 2	35 ± 1	35 ± 1	36 ± 1
*p*H	7.44 ± 0.02	7.43 ± 0.02	7.43 ± 0.02	7.43 ± 0.02

$$\text{Stroke index} = \frac{SV}{BSA}\ (\text{ml/systole/m}^2)$$

$$\text{Systemic vascular resistance} = \frac{MAP - RAP}{\dot{Q}_t}\ (\text{units})$$

Left ventricular stroke work index was estimated with the equation:

$$LVSWI = [(MAP - PCWP) \times 0.0136] \times SI$$

and right ventricular stroke work index from

$$RVSWI = [(MPAP - RAP) \times 0.0136] \times SI$$

Arterial and mixed venous blood oxygen contents, intrapulmonary shunt, oxygen transport ($T_{O_2} = \dot{Q}_t \times Ca_{O_2}$), and dead space-to-tidal volume ratio were calculated using standard formulas. Myocardial oxygen consumption was estimated from the product of heart rate times systolic arterial pressure.[19]

During the last 30 min of each ventilatory period, we measured urinary output, urinary electrolytes, osmolality, urea nitrogen and creatinine by standard laboratory techniques. Creatinine clearance, free water and osmolal clearance were calculated. Statistical analysis was performed using the Student *t* test for paired data.[20]

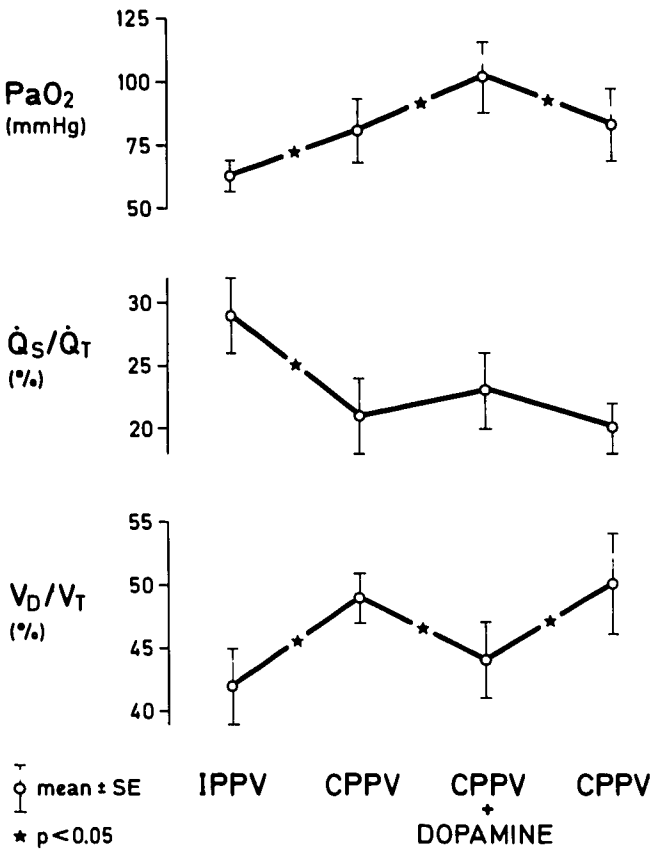

FIG. 2. Effects of CPPV and dopamine on pulmonary gas exchange. Indicated are arterial blood oxygen tension (Pa_{O_2}), intrapulmonary shunt fraction ($\dot{Q}_s/\dot{Q}_t$) and physiologic dead space (V_D/V_T).

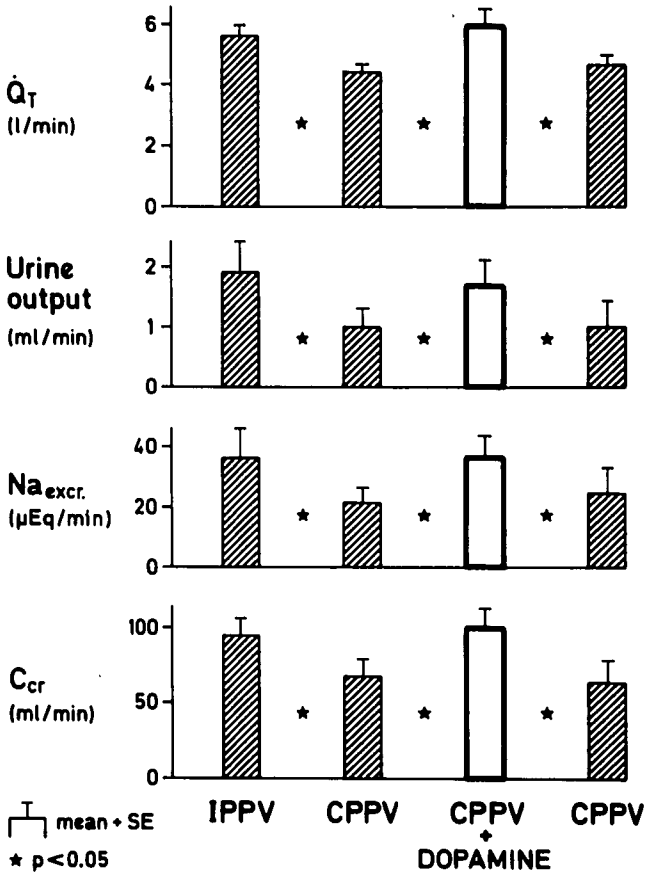

FIG. 3. Changes in cardiac output ($\dot{Q}_t$) and renal function during the four ventilatory conditions. Na_{excr} = urinary excretion of sodium; C_{cr} = creatinine clearance.

Results

A decrease in MAP was observed when 20 cm H_2O PEEP was instituted, and an increase to the initial value was obtained with dopamine (fig. 1; table 1). The changes in MPAP and PCWP were not significant. A small but significant increase in RAP was observed when dopamine was given during CPPV. $\dot{Q}_t$ and SV decreased by 20 per cent with the application of PEEP, and increased markedly with dopamine without a significant change in heart rate. Systemic and pulmonary vascular resistance were the same with CPPV alone and CPPV with dopamine (table 1). Administration of dopamine during CPPV increased LVSWI to a value similar to that seen during IPPV. The increase of RVSWI during dopamine infusion was not significant. The rate–pressure product, reflecting myocardial oxygen consumption,[19] increased when dopamine was administered during CPPV, but

there was no significant difference between values found during CPPV plus dopamine and during IPPV. A decrease in systemic oxygen transport parallel to the decrease in $\dot{Q}_t$ was observed during the CPPV period, but marked improvement was noticed when dopamine was administered (fig. 1).

Pa_{O_2} values were higher during CPPV than during IPPV, and a further improvement was seen with dopamine (fig. 2; table 1). V_D/V_T increased with the addition of PEEP and decreased during dopamine administration. No significant change in Pa_{CO_2} or pH was observed during the four periods.

Urinary output decreased when PEEP was instituted; a marked increase was observed when dopamine was administered during PEEP, and a subsequent decrease was noticed during a control period of ventilation with PEEP (fig. 3). These changes in urinary flow were associated with parallel but smaller variations in cardiac output. The changes in creatinine clearance paralleled the variations in urinary output. Urinary sodium excretion diminished with application of PEEP; an important augmentation was observed when dopamine was administered. The increase in sodium excretion was due to an augmented urinary flow and to an increase in urinary sodium concentration. Free-water clearance did not change significantly with dopamine, whereas osmolal clearance increased by 10 per cent.

Discussion

The principal finding of this study was the improvment of cardiac output, systemic oxygen transport, and renal function by dopamine in normovolemic patients ventilated with 20 cm H_2O PEEP. Cardiac output and oxygen delivery may decrease at high levels of PEEP in patients who need mechanical ventilation with PEEP for the treatment of severe pulmonary failure. This decrease in cardiac output is the result of an impedance on venous return by the increased intrathoracic pressure, a subsequent decrease in central blood volume and ventricular filling pressures,[2–5] and direct myocardial depression.[6] In the dog, the deterioration of cardiac function is more important in the hypovolemic than in the normovolemic or hypervolemic animal,[21] and a transfusion of a substantial amount of blood reverses this.[5] Intravascular volume expansion is frequently used to minimize the adverse cardiovascular effects of high PEEP levels in patients with acute respiratory failure.[22] However, in some of these patients expanding blood volume may be dangerous, especially in the presence of cardiac failure.[23] PEEP additionally increases the secretion of antidiuretic hormone[12] and water retention,[24] and favors the accumulation of liquid in the extravascular space of the lung.[25,26]

Intermittent mandatory ventilation with high PEEP levels may have less deleterious effects on cardiac output and renal function, but the effects of this therapy have not yet been documented.

Cardiac filling pressures can be difficult to interpret in the presence of high PEEP levels and pulmonary parenchymal disease, and true transmural pressure cannot be obtained in these patients. At constant levels of PEEP and identical ventilatory conditions, however, changes in these variables can be regarded as secondary to other therapeutic interventions. In the patients studied, infusion of dopamine corrected the decrease in cardiac output caused by 20 cm H_2O PEEP and increased oxygen transport significantly. The increase of right atrial pressure with dopamine could result from venous vasoconstriction by alpha-adrenergic stimulation.[15,16] The increase in cardiac filling pressure may in part be responsible for the observed augmentation of cardiac output. In addition, myocardial performance and ventricular stroke work were probably improved by the positive inotropic effect of dopamine.[13]

An increase in intrapulmonary shunt with dopamine during mechanical ventilation has been reported to occur in critically ill patients[27] and in the experimental animal.[28] We observed no change in intrapulmonary shunt during dopamine infusion. These contradictory results may have been due to the different doses of dopamine administered, other ventilatory conditions, or differences in the underlying pulmonary diseases. The physiologic dead space-to-tidal volume ratio can be increased by PEEP as a result of the decrease in cardiac output or alveolar overdistention[9] and production of areas with high ventilation/perfusion ratios. Dopamine decreased the increased V_D/V_T, possibly by improving cardiac output and perfusion to the low V/Q areas.

An additional beneficial effect of dopamine infusion during CPPV consisted of a marked sustained increase in urinary output, sodium excretion, and creatinine clearance. This observation suggests that the increased fractional reabsorption of sodium, as well as the decreased creatinine clearance, caused by a diminution of total renal blood flow and a redistribution of intrarenal perfusion during CPPV[10] can be treated effectively by dopamine. The specific actions of this drug, including vasodilation of the renal vasculature,[13,17] augmentation of glomerular filtration rate,[18] and diminution of tubular reabsorption of sodium secondary to a redistribution of renal blood flow,[29] are probably in part responsible for these results, in addition to the important improvement in cardiac output measured.

In conclusion, dopamine application during mechan-

ical ventilation with 20 cm H_2O PEEP increased cardiac output and oxygen transport and decreased V_D/V_T in the patients studied. This therapy also reversed the depression of renal function occurring during CPPV. The administration of small doses of dopamine during mechanical ventilation with PEEP presents an interesting alternative to expansion of intravascular volume for the treatment of the cardiovascular and renal impairment produced by PEEP.

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