Anesthesiology
66:49–54, 1987

Pulmonary Hemodynamic Response to Dopamine and Dobutamine in Hyperoxic and in Hypoxic Dogs

Philippe Lejeune, M.D., Marc Leeman, M.D.,† Thierry Deloof, M.D.,‡ Robert Naeije, M.D., Ph.D.§*

The pulmonary hemodynamic response to dopamine and to dobutamine was investigated in dogs ventilated with hyperoxia (fraction of inspired O_2 concentration [$F_{I_{O_2}}$], 0.4 balance nitrogen) and challenged with short periods of inspiratory hypoxia ($F_{I_{O_2}}$ 0.125 or 0.1 for 10 min). Dopamine at doses of 5, 10, and 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7 dogs) increased cardiac index (CI) and pulmonary artery pressure (PAP) without change in indexed pulmonary vascular resistance (PVRI) at both $F_{I_{O_2}}$ 0.4 and 0.125. Hypoxia-induced increases in PVRI were unaffected by dopamine. Dobutamine at doses of 5, 10, and 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7 dogs) increased CI, with an increase in PAP without change in PVRI at $F_{I_{O_2}}$ 0.4, and at $F_{I_{O_2}}$ 0.125 there was no change in PAP and a decrease in PVRI. Hypoxia-induced increases in PVRI were inhibited by dobutamine, partially at 5 and 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and completely at 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$. In two additional groups of seven dogs the effects of reducing $F_{I_{O_2}}$ from 0.4 to 0.1 without and with dopamine or dobutamine either at 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7) or at 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7) were studied at an unchanged CI obtained by stepwise inflations of a balloon placed in the inferior vena cava. At constant flow both amines increased PVRI at $F_{I_{O_2}}$ 0.4 and did not significantly affect hypoxia-induced increases in PVRI. It is concluded that at doses up to 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$, dopamine and dobutamine have similar effects on the pulmonary circulation of intact animals. Neither amine seems directly to inhibit hypoxic pulmonary vasoconstriction. (Key words: Lung: hypoxic pulmonary vasoconstriction. Pharmacology: dobutamine; dopamine. Sympathetic nervous system: dopamine.)

DOPAMINE, AN ENDOGENOUS catecholamine, and dobutamine, a synthetic derivative of norepinephrine, are currently used as inotropic agents in patients with circulatory failure. Good agreement exists about their effects on systemic circulation and cardiac function,[1,2] but their effects on the pulmonary circulation remain controversial. Both dopamine and dobutamine have been reported either not to affect,[3–9] to increase,[10,11] or to decrease[12–15] normoxic pulmonary vascular tone. Hypoxic pulmonary vasoconstriction (HPV) has been found to be either unchanged,[16,17] enhanced,[18] or inhibited[19] after dopamine, and inhibited[16,17] after dobutamine. Whereas arterial blood gases are known to deteriorate with both amines,[20] it remains uncertain as to whether this is due to a direct impairment of hypoxic regulation of the pulmonary circulation.

We therefore investigated the pulmonary hemodynamic response to dopamine and dobutamine infused at clinically relevant dosages (*i.e.*, up to 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$)[21] in intact dogs ventilated with high concentrations of oxygen and challenged with short periods of inspiratory hypoxia.

Materials and Methods

Twenty-eight healthy mongrel dogs (mean weight 27 kg, range 21–50) were anesthetized with iv sodium pentobarbital (25 $mg \cdot kg^{-1}$), placed supine in a V-shaped trough, and ventilated (Elema 900 B® Servo-ventilator, Siemens Elema, Solna, Sweden) *via* a cuffed endotracheal tube. The fraction of inspired O_2 ($F_{I_{O_2}}$) was 0.4, the respiratory rate 12 $\cdot min^{-1}$, and the tidal volume 15–20 $ml \cdot kg^{-1}$, adjusted to achieve an end-tidal P_{CO_2} of 30–35 mmHg. A thermistor-tipped Swan-Ganz catheter (model 93A-131-7F, Edwards Laboratories, Santa Ana, CA) was inserted *via* the right external jugular vein and positioned by means of pressure monitoring in a branch of the pulmonary artery for measurements of pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) and mixed venous blood sampling. A polyethylene catheter was placed in the abdominal aorta *via* the right femoral artery for systemic blood pressure (BP) measurements and arterial blood sampling. Throughout the experiment, normal saline was infused 4 $ml \cdot kg^{-1} \cdot h^{-1}$ in a femoral vein. Temperature was monitored through the thermistor probe of the Swan-Ganz catheter and was maintained at 37–38° C with an electric heating pad. All the animals were maintained paralyzed with pancuronium 0.2 $mg \cdot kg^{-1} \cdot h^{-1}$ and anesthetized with pentobarbital 2 $mg \cdot kg^{-1}$ in 60 s once hourly. In 14 dogs, a balloon catheter (Peri-Cor®, 45, Datascope, Paramus, NJ) was placed into the inferior vena cava through a right femoral venotomy. Inflation of this balloon produced a titratable decrease in cardiac output by reducing venous return. Thrombus formation along the catheter was prevented by sodium heparin 100 $U \cdot kg^{-1}$ iv just before insertion and 50 $U \cdot kg^{-1}$ iv repeated every 2 h thereafter.

Pulmonary and systemic vascular pressures were measured using Bentley transducers and the Heres® Computer system (ACEC, Charleroi, Belgium). Pressure curves were

* Research Fellow, Resident in training, Intensive Care Medicine.
† Attending Physician, Intensive Care Medicine.
‡ Staff Anesthesiologist, Associate Professor.
§ Staff Intensivist, Associate Professor.

Received from the Respiratory Research Unit, Departments of Intensive Care and Anesthesiology, Erasme University Hospital, Brussels, Belgium. Accepted for publication August 26, 1986. Presented at the Annual Meeting of the American Thoracic Society, May 11–14, 1986, Kansas City, Missouri.

Dr. Lejeune is a fellow of the Erasme Foundation and a recipient of the Therabel Foundation Fellowship.

Address reprint requests to Dr. Lejeune: Department of Intensive Care, Erasme University Hospital, 808, route de Lennik, B-1070 Brussels, Belgium.

recorded on a four-channel Gould® 2400 S recorder (Gould, Inc., Instruments Division, Cleveland, OH) and read at end-expiration. The zero reference was leveled at midchest. Heart rate (HR) was determined from a continuously monitored electrocardiographic lead. Cardiac output was measured in triplicate by thermodilution using injections of 5 ml of 5% dextrose at 0° C and the 9520-A computer of Edwards Laboratories. Arterial and mixed venous *p*H, P_{CO_2}, and P_{O_2} were measured by an automated analyzer (IL 613, Instrumentation Laboratories, Lexington, MA) and corrected for temperature. End-tidal P_{CO_2} was measured with an HP 47217 infrared capnometer (Hewlett Packard, Palo Alto, CA). Hemoglobin levels were determined using the IL 282 Co-oxymeter® (Instrumentation Laboratories). O_2 saturations were calculated from the nomogram of Rossing and Cain.[22] Body surface area was calculated as $0.112 \times \text{weight (kg)}^{2/3}$, m^2. Systemic vascular resistance index (SVRI) was calculated as (mean BP − right atrial pressure [RAP]) × cardiac index $(CI)^{-1} \times 80$, dyne · s · cm^{-5} · m^2 and pulmonary vascular resistance index (PVRI) as (mean PAP [MPAP] − PCWP) × $CI^{-1} \times 80$, dyne · s · cm^{-5} · m^2.

In the first 14 dogs, after ensuring steady-state conditions (stable BP, PAP, HR, and end-tidal P_{CO_2}) for 20 min at $F_{I_{O_2}}$ 0.4, hemodynamic and blood gas determinations were performed first before an then at the 10th min of an acute hypoxic challenge ($F_{I_{O_2}}$ 0.125). This sequence was repeated six times alternatively without and with a drug regimen consisting of either dopamine (n = 7) or dobutamine (n = 7) at 5, 10, and 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ given in a random order. Thus, a total of 12 series of determinations were performed in each animal, six at $F_{I_{O_2}}$ 0.4 (three of these with a dopamine or a dobutamine infusion) and six at $F_{I_{O_2}}$ 0.125 (three of these with a dopamine or a dobutamine infusion). Drugs were given intravenously using a calibrated pump (Braun Melsungen AG, Melsungen, Germany), and measurements were performed after 15 min of drug infusion at the selected dosage. When drug infusion was stopped, the next sequence of measurements without drug was started after 20 min of equilibration at $F_{I_{O_2}}$ 0.4.

In the next 14 dogs, a sequence of hemodynamic and blood gas measurements successively after 20 min at $F_{I_{O_2}}$ 0.4 and after 10 min at $F_{I_{CO_2}}$ 0.1 was repeated three times: first without drug, then, successively in random order, with dopamine and dobutamine at 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7) or at 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7). In each dog, cardiac output was maintained at the same value as the first $F_{I_{O_2}}$ 0.4 measurement by stepwise inflations of the balloon placed in the inferior vena cava. Each drug was infused for 15 min before any measurement, and a 30-min interval elapsed between two different drug administrations.

Statistical analysis was performed using analysis of variance for repeated measurements in each study group. Modified *t* tests with the Bonferroni adjustment for multiple comparisons were calculated if the F ratio of the analysis of variance reached a $P < 0.05$.[23]

Results

Uncontrolled Flow (tables 1 and 2)

There was no significant difference between the first series of measurements and the two control series at $F_{I_{O_2}}$ 0.4 and $F_{I_{O_2}}$ 0.125. Therefore, only the first measurements at both $F_{I_{O_2}}$ are shown in tables 1 and 2. For the purpose of clarity also, only the measurements at the highest doses of dopamine and dobutamine at both $F_{I_{O_2}}$ are shown in these tables. The effects of intermediate doses of 5 and 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ on PVRI are presented in figure 1.

Individual increases in PVRI induced by acute inspiratory hypoxia ($F_{I_{O_2}}$ 0.125) ranged from 10 to 310%.

Dopamine (table 1) at $F_{I_{O_2}}$ 0.4 increased CI, PCWP, and PAP, but PVRI remained unaffected. Similar changes occurred at $F_{I_{O_2}}$ 0.125, except for no change in PCWP.

Dobutamine (table 2) at $F_{I_{O_2}}$ 0.4 increased CI and PAP, while PCWP and PVRI did not change. Similar effects occurred at $F_{I_{O_2}}$ 0.125, except for no change in PAP and a decrease in PVRI.

As shown in figure 1, hypoxia-induced increases in PVRI were unaffected by dopamine and were inhibited by dobutamine, partially at 5 and 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and completely at 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Controlled Flow (tables 3 and 4)

In these series of dogs more severe hypoxic challenges were applied ($F_{I_{O_2}}$ 0.1 instead of 0.125). This resulted in more profound hypoxemia, a still variable (+12 to +197%) but as an average more important increase in PVRI, and otherwise similar systemic hemodynamic effects.

Dopamine and dobutamine 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (table 3) increased PVRI at $F_{I_{O_2}}$ 0.4 but not at $F_{I_{O_2}}$ 0.1.

Dopamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (table 4) increased PVRI at $F_{I_{O_2}}$ 0.4 and at $F_{I_{O_2}}$ 0.1.

Dobutamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (table 4) increased PVRI at $F_{I_{O_2}}$ 0.4 but not at $F_{I_{O_2}}$ 0.1.

Neither dopamine nor dobutamine significantly depressed hypoxia-induced increases in PVRI (fig. 2) when CI was controlled.

Discussion

In this study pulmonary hemodynamic determinations were performed before and after dopamine and dobu-

TABLE 1. Blood Gases and Hemodynamics in Seven Dogs Given Dopamine in Hyperoxic and Hypoxic Conditions

Variable	$F_{I_{O_2}}$ 0.4		$F_{I_{O_2}}$ 0.125	
	Baseline	Dopamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Baseline	Dopamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$
pH_a	7.33 ± 0.02	7.28 ± 0.02*	7.36 ± 0.02*	7.30 ± 0.01†
Pa_{O_2} (mmHg)	187 ± 19	177 ± 17	48 ± 4‡	37 ± 3‡
Pa_{CO_2} (mmHg)	36 ± 1	40 ± 2†	33 ± 1*	39 ± 1‡
$P\bar{v}_{O_2}$ (mmHg)	57 ± 4	64 ± 3*	37 ± 4‡	31 ± 2*
CI ($l \cdot min^{-1} \cdot m^2$)	4.75 ± 0.58	7.68 ± 0.67‡	5.13 ± 0.58	8.12 ± 0.89‡
HR (beats/min)	148 ± 13	158 ± 19	163 ± 12	219 ± 19†
BP (mmHg)	118 ± 4	194 ± 12‡	133 ± 7*	153 ± 12
SVRI ($dyne \cdot s \cdot cm^{-5} \cdot m^2$)	2003 ± 216	2012 ± 212	2080 ± 189	1553 ± 244*
PCWP (mmHg)	8 ± 1	12 ± 2*	9 ± 2	10 ± 1
RAP (mmHg)	8 ± 1	9 ± 1	8 ± 1	8 ± 1
MPAP (mmHg)	17 ± 2	24 ± 3‡	23 ± 4†	27 ± 4†
PVRI ($dyne \cdot s \cdot cm^{-5} \cdot m^2$)	151 ± 33	135 ± 25	215 ± 43†	193 ± 45

See text for abbreviations.
"Baseline" indicates the first series of determinations at $F_{I_{O_2}}$ 0.4 and at $F_{I_{O_2}}$ 0.125, respectively. Values are expressed as mean ± SEM. Second and third columns are compared with the first. Fourth column is compared with the third. Significance of differences: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$.

tamine administration while cardiac output was both changed and kept constant. The aim of this approach was to differentiate direct effects of the drugs on pulmonary vessels from indirect effects due to increased pulmonary blood flow and possibly associated changes in mixed venous oxygenation. In addition, the use of calculated PVR for the evaluation of pulmonary vascular tone at variable cardiac output may be misleading.[24] The pressure–flow relationship within the pulmonary circulation is rectilinear over a wide range of flows but is curvilinear when flow is low. The extrapolation of the linear part of the curve has a positive intercept at zero flow, *i.e.*, the mean "critical closing pressure" of the pulmonary vessels.[11,24] If cardiac output increases without change in critical closing pressure, PVR may decrease when pulmonary vascular tone, in fact, does not change.[24] In an isolated canine lung lobe preparation, both dopamine and dobutamine have been reported to increase the slope of the pressure–flow relationship without change in critical closing pressure.[11] This effect was alpha-mediated because it could be blocked by phentolamine.[11] In our intact dogs with uncontrolled cardiac output, unchanged PVRI in the presence of increased flow probably reflected an increase in pulmonary vascular tone, but reduced PVRI as, for example, after dobutamine in hypoxic conditions is more difficult to interpret. At constant flow, a tendency for pulmonary artery pressure

TABLE 2. Blood Gases and Hemodynamics in Seven Dogs Given Dobutamine in Hyperoxic and Hypoxic Conditions

Variable	$F_{I_{O_2}}$ 0.4		$F_{I_{O_2}}$ 0.125	
	Baseline	Dobutamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Baseline	Dobutamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$
pH_a	7.36 ± 0.02	7.29 ± 0.02‡	7.39 ± 0.02*	7.31 ± 0.02‡
Pa_{O_2} (mmHg)	201 ± 10	175 ± 15*	46 ± 1‡	38 ± 2*
Pa_{CO_2} (mmHg)	35 ± 1	38 ± 1*	33 ± 1	36 ± 1†
$P\bar{v}_{O_2}$ (mmHg)	54 ± 2	65 ± 4†	35 ± 1‡	31 ± 1*
CI ($l \cdot min^{-1} \cdot m^2$)	4.71 ± 0.47	9.37 ± 1.15‡	5.08 ± 0.54	9.13 ± 1‡
HR ($beats/min^{-1}$)	143 ± 9	213 ± 10‡	165 ± 9	204 ± 16‡
BP (mmHg)	124 ± 8	129 ± 8	130 ± 7	129 ± 7
SVRI ($dyne \cdot s \cdot cm^{-5} \cdot m^2$)	2125 ± 277	1093 ± 98‡	2075 ± 256	1129 ± 130‡
PCWP (mmHg)	8 ± 1	8 ± 1	8 ± 1	9 ± 1
RAP (mmHg)	7 ± 1	7 ± 1	7 ± 1	7 ± 1
MPAP (mmHg)	15 ± 1	23 ± 2‡	23 ± 4‡	23 ± 2
PVRI ($dyne \cdot s \cdot cm^{-5} \cdot m^2$)	134 ± 12	130 ± 13	255 ± 74†	133 ± 11*

See text for abbreviations.
"Baseline" indicates the first series of determinations at $F_{I_{O_2}}$ 0.4 and $F_{I_{O_2}}$ 0.125, respectively. Values are expressed as mean ± SEM. Second and third columns are compared with the first. Fourth column is compared with the third. Significance of differences: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$.

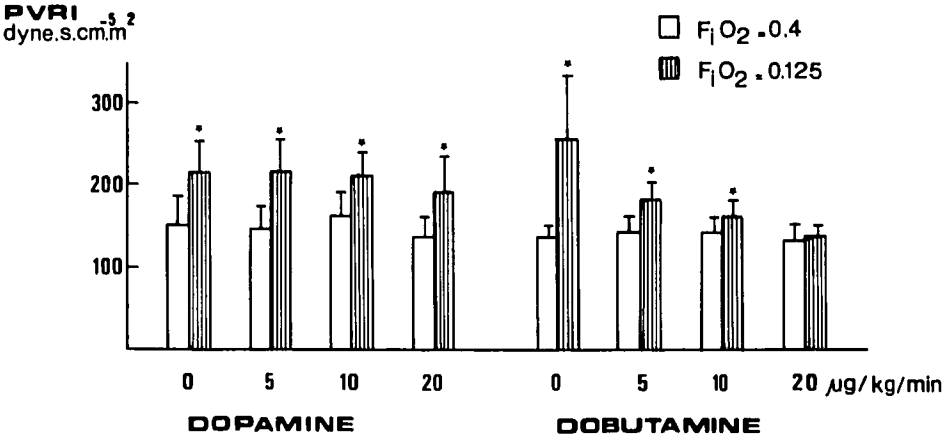

FIG. 1. Pulmonary vascular resistance index (mean ± SEM) responses to hypoxia without and with dopamine (n = 7) and dobutamine (n = 7) at dosages of 5, 10, and 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in ventilated dogs with uncontrolled cardiac output. Asterisks indicate significant difference between hyperoxic and hypoxic conditions at each dose (*$P < 0.05$).

to increase and increased PVRI at FI_{O_2} 0.4 probably represent an increased pulmonary vascular tone, in agreement with above mentioned work on isolated lung lobes.[11]

Repeated hypoxia has been reported previously either to enhance[25,26] or not to affect[27,28] HPV. In our intact dog preparation, repeatedly decreasing FI_{O_2} 0.4 to 0.125 did not affect the magnitude of the hypoxic pressor response. These results are in agreement with recent studies on dogs in similar experimental conditions.[27]

Our dogs were anesthetized with pentobarbital. This agent does not affect HPV.[29]

HPV has been observed to be variably affected by dopamine[16-19] and inhibited by dobutamine.[16,17] These discrepancies between studies and the present data may be accounted for by the misleading use of PVR calculations and also by differences in dosages and methodology. In this study, at doses up to 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$, which are clinically relevant, neither dopamine nor dobutamine affected the magnitude of the hypoxic pulmonary pressor response when flow was kept constant. In uncontrolled flow conditions, dobutamine at the highest dose inhibited hypoxia-induced increases in PVRI, which can be explained, at least in part, by the effects of increased cardiac output on PVR calculations. Inhibitory effects of higher mixed venous blood oxygen ($P\bar{v}_{O_2}$)[30] and/or higher pulmonary vascular pressures [31] did not seem to be implicated. It cannot be excluded that dobutamine at 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ had some direct pulmonary vasodilating effect that was not significant at constant flow because of the small number of animals. An FI_{O_2} of 0.1 instead of 0.125 was imposed during the controlled cardiac output set of experiments, which resulted in more severe hypox-

TABLE 3. Blood Gases and Hemodynamics in Seven Dogs Given, Alternatively, Dopamine and Dobutamine in Hyperoxic and Hypoxic Conditions at Constant Flow

	FI_{O_2} 0.4			FI_{O_2} 0.1		
Variable	Baseline	Dopamine 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Dobutamine 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Baseline	Dopamine 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Dobutamine 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$
pH_a	7.32 ± 0.02	7.27 ± 0.02	7.30 ± 0.02	7.35 ± 0.02*	7.26 ± 0.02*	7.30 ± 0.02
Pa_{O_2} (mmHg)	175 ± 15	165 ± 14	169 ± 19	29 ± 2‡	25 ± 1	27 ± 1
Pa_{CO_2} (mmHg)	36 ± 1	39 ± 2	39 ± 1	34 ± 2	40 ± 2†	39 ± 1*
$P\bar{v}_{O_2}$ (mmHg)	51 ± 4	58 ± 4*	59 ± 3†	20 ± 2‡	13 ± 2*	16 ± 1
CI ($l \cdot min^{-1} \cdot m^2$)	4.21 ± 0.52	4.25 ± 0.49	4.35 ± 0.54	4.45 ± 0.56	4.35 ± 0.51	4.15 ± 0.53
HR (beats/min)	166 ± 12	166 ± 13	172 ± 7	169 ± 9	207 ± 9†	185 ± 10
BP (mmHg)	118 ± 8	120 ± 9	109 ± 9	120 ± 9	98 ± 8†	109 ± 8
SVRI ($dyne \cdot s \cdot cm^{-5} \cdot m^2$)	2407 ± 330	2362 ± 260	2187 ± 332	2331 ± 346	1888 ± 234*	2216 ± 236
PCWP (mmHg)	5 ± 1	4 ± 1*	3 ± 1*	4 ± 1	4 ± 1	3 ± 1
RAP (mmHg)	3 ± 1	2 ± 1	2 ± 1	3 ± 1	3 ± 1	2 ± 1
MPAP (mmHg)	11 ± 1	12 ± 1*	12 ± 1†	21 ± 2‡	20 ± 1	18 ± 2
PVRI ($dyne \cdot s \cdot cm^{-5} \cdot m^2$)	134 ± 23	172 ± 26†	181 ± 26‡	346 ± 71‡	339 ± 64	333 ± 62

See text for abbreviations.

"Baseline" indicates the first series of determinations at FI_{O_2} 0.4 and FI_{O_2} 0.1, respectively. Values are expressed as mean ± SEM. Second, third, and fourth columns are compared with the first. Fifth and sixth columns are compared with the fourth. Significance of changes: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$.

TABLE 4. Blood Gases and Hemodynamics in Seven Dogs Given, Alternatively, Dopamine and Dobutamine in Hyperoxic and Hypoxic Conditions at Constant Flow

Variable	$F_{I_{O_2}}$ 0.4			$F_{I_{O_2}}$ 0.1		
	Baseline	Dopamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Dobutamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Baseline	Dopamine 20 $\mu g \cdot kg^{-1} min^{-1}$	Dobutamine 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$
pH_a	7.32 ± 0.01	7.29 ± 0.02	7.29 ± 0.02	7.36 ± 0.01*	7.27 ± 0.01‡	7.29 ± 0.02†
Pa_{O_2} (mmHg)	180 ± 17	161 ± 18*	165 ± 18*	30 ± 2‡	25 ± 1*	27 ± 1
Pa_{CO_2} (mmHg)	36 ± 1	45 ± 2‡	44 ± 2‡	34 ± 2	42 ± 2†	41 ± 2†
$P\bar{v}_{O_2}$ (mmHg)	49 ± 2	55 ± 3*	55 ± 3*	21 ± 2‡	16 ± 2*	15 ± 2*
CI ($l \cdot min^{-1} \cdot m^2$)	3.68 ± 0.5	3.70 ± 0.44	3.66 ± 0.47	3.72 ± 0.44	3.67 ± 0.45	3.81 ± 0.47
HR (beats/min)	140 ± 11	186 ± 10†	209 ± 10†	164 ± 16*	246 ± 8‡	198 ± 10†
BP (mmHg)	119 ± 3	144 ± 15	101 ± 7	124 ± 4	123 ± 16	112 ± 12
SVRI (dyne · s · $cm^{-5} \cdot m^2$)	2894 ± 447	3476 ± 638*	2264 ± 152	2845 ± 362	2764 ± 326	2325 ± 162
PCWP (mmHg)	4 ± 1	2 ± 1	3 ± 1	4 ± 1	3 ± 1	3 ± 1
RAP (mmHg)	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1
MPAP (mmHg)	13 ± 1	14 ± 2	15 ± 1	20 ± 2‡	23 ± 2*	20 ± 2
PVRI (dyne · s · $cm^{-5} \cdot m^2$)	221 ± 54	286 ± 56*	291 ± 54*	385 ± 67‡	467 ± 69*	404 ± 77

See text for abbreviations.

"Baseline" indicates the first series of determinations at $F_{I_{O_2}}$ 0.4 and $F_{I_{O_2}}$ 0.1. Values are expressed as mean ± SEM. Second, third, and fourth columns are compared with the first. Fifth and sixth columns are compared with the fourth. Significance of changes: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$.

emia and, more important, average increases in PVRI, but no other additional hemodynamic effect. It is unlikely that absence of significant inhibition of HPV by dobutamine would be related to this slightly more severe O_2 deprivation.

The systemic hemodynamic changes in our hyperoxic dogs after dopamine and dobutamine were in keeping with previous work.[1,2] At constant flow, alpha-mediated vasoconstriction after dopamine was seen only at the highest dosage and in hyperoxic conditions, while dobutamine was vasodilatory as expected. In hypoxic conditions, systemic vascular tone as assessed by SVRI calculations was unaffected by both amines at the highest doses. No explanation for such $F_{I_{O_2}}$-dependent changes in vasoconstricting and vasodilating activities of dopamine and dobutamine is available.

Both dopamine and dobutamine constrict capacitance vessels and so enhance venous return in experimental animal preparations[32,33] and in patients during cardiopulmonary bypass.[34] As in our dogs without flow control, dopamine has been shown to increase left ventricular filling pressures in clinical circumstances.[35,36] Absence of this effect at identical dosages of dobutamine may be due to concomitant reduction in left ventricular afterload.

The main mechanisms that have been invoked to explain the hypoxemic effects of dopamine and dobutamine

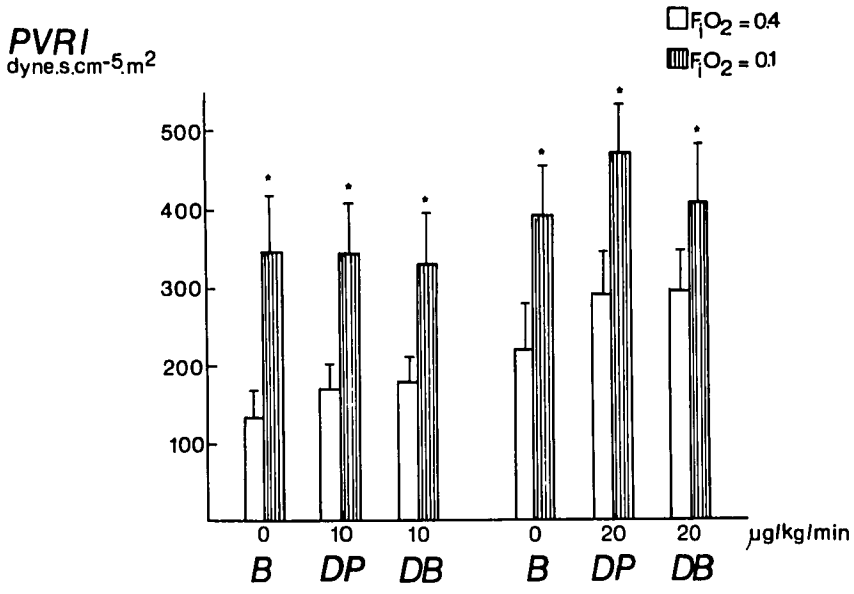

FIG. 2. Pulmonary vascular resistance index (mean ± SEM) responses to hypoxia without drug (B), with dopamine (DP), and with dobutamine (DB) at doses of 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7) and 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7) in ventilated dogs with cardiac output kept constant. Asterisks indicate significant difference between hyperoxic and hypoxic conditions at each dose (*$P < 0.05$).

are[20]: 1) an increase in venous admixture due to augmented pulmonary blood flow; 2) an inhibition of HPV; and 3) an increased O_2 consumption. In our dogs at constant cardiac output, decreases in arterial oxygenation were observed after both dopamine and dobutamine at the highest doses. A decrease in Pa_{O_2} in the presence of an increased $P\bar{v}_{O_2}$ at FI_{O_2} 0.4 (table 4) suggests an increased venous admixture. Oxygen consumption and CO_2 production were not measured, so the contribution of a vasoactive amine-induced increase in metabolism could not be evaluated. We therefore conclude that changes in cardiac output (in part) and ventilation/perfusion mismatch, but not a direct impairment of hypoxic vasoconstriction, may account for the deterioration in arterial blood gases associated with the administration of dopamine and dobutamine.

References

1. Goldberg LI: Cardiovascular and renal actions of dopamine: Potential clinical applications. Pharmacol Rev 24:1–29, 1972
2. Leier CV, Unverferth DV: Dobutamine. Ann Intern Med 99: 490–496, 1983
3. Harrison DC, Pirages S, Robison SC, Wintroub BU: The pulmonary and systemic circulatory response to dopamine infusion. Br J Pharmacol 37:618–626, 1969
4. Holloway EL, Polumbo RA, Harrison DC: Acute circulatory effects of dopamine in patients with pulmonary hypertension. Br Heart J 37:482–485, 1975
5. Beregovich J, Branchi C, Rubler S, Lomnitz E, Cagin N, Levitt B: Dose related hemodynamic and renal effects of dopamine in congestive heart failure. Am Heart J 87:550–557, 1974
6. Tyden H, Nyström SO: Dopamine *versus* dobutamine after open-heart surgery. Acta Anaesthesiol Scand 27:193–198, 1983
7. Orchard CH, Chakrabarti MK, Sykes MK: Cardiorespiratory responses to an iv infusion of dobutamine in the intact anesthetized dog. Br J Anaesth 54:673–679, 1982
8. Jewitt D, Brikhead J, Mitchell A, Dollery C: Clinical cardiovascular pharmacology of dobutamine, a selective inotropic catecholamine. Lancet 2:363–367, 1974
9. Morishita H, Furukawa T: Possible modes of action of dobutamine in dog femoral and pulmonary arteries. Cardiovasc Res 14: 103–107, 1980
10. Waaler BA: Effect of dopamine on the isolated perfused lung lobes of the dog. Br J Pharmacol 16:195–202, 1961
11. Graham R, Skoog C, Macedo W, Carter J, Oppenheimer L, Rabson J, Goldberg HS: Dopamine, dobutamine, and phentolamine effects on pulmonary vascular mechanics. J Appl Physiol 54: 1277–1283, 1983
12. Regnier B, Rapin M, Gory G, Lemaire F, Teisseire B, Harari A: Haemodynamic effects of dopamine in septic shock. Intensive Care Med 3:47–53, 1977
13. Jardin F, Gurdjian F, Desfonds P, Margairaz A: Effect of dopamine on intrapulmonary shunt fraction and oxygen transport in severe sepsis with circulatory and respiratory failure. Crit Care Med 7:273–277, 1979
14. Jardin F, Sportiche M, Bazin M, Bourokba A, Margairaz A: Dobutamine: A hemodynamic evaluation in human septic shock. Crit Care Med 9:329–332, 1981
15. Akhtar N, Mikulic E, Cohn JN, Chaudhry MH: Hemodynamic effect of dobutamine in patients with severe heart failure. Am J Cardiol 36:202–205, 1975
16. Furman WR, Summer WR, Kennedy TP, Sylvester JT: Comparison of the effects of dobutamine, dopamine and isoproterenol on hypoxic pulmonary vasoconstriction in the pig. Crit Care Med 10:371–374, 1982
17. Mc Farlane PA, Mortimer AJ, Ryder WA, Madgwick RG, Gardaz JP, Harrison BJ, Sykes MK: Effects of dopamine and dobutamine on the distribution of pulmonary blood flow during lobar ventilation hypoxia and lobar collapse in dogs. Eur J Clin Invest 15:53–59, 1985
18. Mentzer RM, Alegre CA, Nolan SP: The effects of dopamine and isoproterenol on the pulmonary circulation. J Thorac Cardiovasc Surg 71:807–814, 1976
19. Marin JLB, Orchard C, Chakrabarti MK, Sykes MK: Depression of hypoxic pulmonary vasoconstriction in the dog by dopamine and isoprenaline. Br J Anaesth 51:303–312, 1979
20. Lemaire F: Effects of catecholamines on pulmonary right-to-left shunl. Int Anesthesiol Clin 21:43–58, 1983
21. Chernow B, Rainey TG, Lake CR: Endogenous and exogenous catecholamines in critical care medicine. Crit Care Med 10: 409–416, 1982
22. Rossing RG, Cain SM: A nomogram relating P_{O_2}, *p*H, temperature, and hemoglobin saturation in the dog. J Appl Physiol 21:195–201, 1966
23. Wallenstein S, Zucker CL, Fleiss JL: Some statistical methods useful in circulation research. Circ Res 47:1–9, 1980
24. Mc Gregor M, Sniderman A: On pulmonary vascular resistance: The need for more precise definition. Am J Cardiol 55:217–221, 1985
25. Unger M, Atkins M, Briscoe WA, King TKC: Potentiation of pulmonary vasoconstrictor response with repeated intermittent hypoxia. J Appl Physiol 43:662–667, 1977
26. Pirlo AF, Benumof JL, Trousdale FR: Potentiation of lobar hypoxic pulmonary vasoconstriction by intermittent hypoxia in dogs. ANESTHESIOLOGY 55:226–230, 1981
27. Bishop MJ, Kennard S, Artman LD, Cheney FW: Hydralazine does not inhibit canine hypoxic pulmonary vasoconstriction. Am Rev Respir Dis 128:998–1001, 1983
28. Miller MA, Hales CA: Stability of alveolar hypoxic vasoconstriction with intermittent hypoxia. J Appl Physiol 49:846–850, 1980
29. Benumof JL: One lung ventilation and hypoxic pulmonary vasoconstriction: Implications for anesthetic management. Anesth Analg 64:821–833, 1985
30. Domino KB, Wetstein L, Glasser SA, Lindgren L, Marshall C, Harken A, Marshall BE: Influence of mixed venous oxygen tension ($P\bar{v}_{O_2}$) on blood flow to atelectatic lung. ANESTHESIOLOGY 59:428–434, 1983
31. Benumof JL, Wahrenbrock EA: Blunted hypoxic pulmonary vasoconstriction by increased lung vascular pressures. J Appl Physiol 38:846–850, 1975
32. Fuchs RM, Rutlen DL, Powell W: Effect of dobutamine on systemic capacity in the dog. Circ Res 46:133–138, 1980
33. Mark AL, Iizuka T, Wendling MG, Eckstein JW: Responses of saphenous and mesenteric veins to administration of dopamine. J Clin Invest 49:259–266, 1970
34. Marino RJ, Romagnoli A, Keats AS: Selective vasoconstriction by dopamine in comparison with isoproterenol and phenylephrine. ANESTHESIOLOGY 43:570–572, 1975
35. Richard C, Ricome JL, Rimailho A, Bottineau G, Auzepy P: Combined hemodynamic effects of dopamine and dobutamine in cardiogenic shock. Circulation 67:620–626, 1983
36. Molloy WD, Dobson K, Girling L, Greenberg ID, Prewitt RM: Effects of dopamine on cardiopulmonary function and left ventricular volumes in patients with acute respiratory failure. Am Rev Respir Dis 130:396–399, 1984