

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

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The pulmonary hemodynamic response to dopamine and to dobutamine was investigated in dogs ventilated with hyperoxia (fraction of inspired O₂ concentration [F_IO₂], 0.4 balance nitrogen) and challenged with short periods of inspiratory hypoxia (F_IO₂ 0.125 or 0.1 for 10 min). Dopamine at doses of 5, 10, and 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (n = 7 dogs) increased cardiac index (CI) and pulmonary artery pressure (PAP) without change in indexed pulmonary vascular resistance (PVRI) at both F_IO₂ 0.4 and 0.125. Hypoxia-induced increases in PVRI were unaffected by dopamine. Dobutamine at doses of 5, 10, and 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (n = 7 dogs) increased CI, with an increase in PAP without change in PVRI at F_IO₂ 0.4, and at F_IO₂ 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 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, and completely at 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. In two additional groups of seven dogs the effects of reducing F_IO₂ from 0.4 to 0.1 without and with dopamine or dobutamine either at 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (n = 7) or at 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (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_IO₂ 0.4 and did not significantly affect hypoxia-induced increases in PVRI. It is concluded that at doses up to 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, 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 decrease¹²⁻¹⁵ normoxic pulmonary vascular tone. Hypoxic pulmonary vasoconstriction (HPV) has been found to be either unchanged,^{16,17} enhanced,¹⁸ or inhibited¹⁹ 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 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)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 $\text{mg} \cdot \text{kg}^{-1}$), 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 O₂ (F_IO₂) was 0.4, the respiratory rate 12 $\cdot \text{min}^{-1}$, and the tidal volume 15-20 $\text{ml} \cdot \text{kg}^{-1}$, adjusted to achieve an end-tidal P_{CO₂} 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 $\text{ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 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 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ and anesthetized with pentobarbital 2 $\text{mg} \cdot \text{kg}^{-1}$ 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 $\cdot \text{kg}^{-1}$ iv just before insertion and 50 U $\cdot \text{kg}^{-1}$ 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

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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.

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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 pH, P_{CO₂}, and P_{O₂} were measured by an automated analyzer (IL 613, Instrumentation Laboratories, Lexington, MA) and corrected for temperature. End-tidal P_{CO₂} 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). O₂ saturations were calculated from the nomogram of Rossing and Cain.²² Body surface area was calculated as $0.112 \times \text{weight (kg)}^{2/3}$, m². Systemic vascular resistance index (SVRI) was calculated as $(\text{mean BP} - \text{right atrial pressure [RAP]}) \times \text{cardiac index (CI)}^{-1} \times 80$, dyne · s · cm⁻⁵ · m² and pulmonary vascular resistance index (PVRI) as $(\text{mean PAP [MPAP]} - \text{PCWP}) \times \text{CI}^{-1} \times 80$, dyne · s · cm⁻⁵ · m².

In the first 14 dogs, after ensuring steady-state conditions (stable BP, PAP, HR, and end-tidal P_{CO₂}) for 20 min at FI_{O₂} 0.4, hemodynamic and blood gas determinations were performed first before and then at the 10th min of an acute hypoxic challenge (FI_{O₂} 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 μg · kg⁻¹ · min⁻¹ given in a random order. Thus, a total of 12 series of determinations were performed in each animal, six at FI_{O₂} 0.4 (three of these with a dopamine or a dobutamine infusion) and six at FI_{O₂} 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 FI_{O₂} 0.4.

In the next 14 dogs, a sequence of hemodynamic and blood gas measurements successively after 20 min at FI_{O₂} 0.4 and after 10 min at FI_{CO₂} 0.1 was repeated three times: first without drug, then, successively in random order, with dopamine and dobutamine at 10 μg · kg⁻¹ · min⁻¹ (n = 7) or at 20 μg · kg⁻¹ · min⁻¹ (n = 7). In each dog, cardiac output was maintained at the same value as the first FI_{O₂} 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 FI_{O₂} 0.4 and FI_{O₂} 0.125. Therefore, only the first measurements at both FI_{O₂} 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 FI_{O₂} are shown in these tables. The effects of intermediate doses of 5 and 10 μg · kg⁻¹ · min⁻¹ on PVRI are presented in figure 1.

Individual increases in PVRI induced by acute inspiratory hypoxia (FI_{O₂} 0.125) ranged from 10 to 310%.

Dopamine (table 1) at FI_{O₂} 0.4 increased CI, PCWP, and PAP, but PVRI remained unaffected. Similar changes occurred at FI_{O₂} 0.125, except for no change in PCWP.

Dobutamine (table 2) at FI_{O₂} 0.4 increased CI and PAP, while PCWP and PVRI did not change. Similar effects occurred at FI_{O₂} 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 μg · kg⁻¹ · min⁻¹ and completely at 20 μg · kg⁻¹ · min⁻¹.

CONTROLLED FLOW (TABLES 3 AND 4)

In these series of dogs more severe hypoxic challenges were applied (FI_{O₂} 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 μg · kg⁻¹ · min⁻¹ (table 3) increased PVRI at FI_{O₂} 0.4 but not at FI_{O₂} 0.1.

Dopamine 20 μg · kg⁻¹ · min⁻¹ (table 4) increased PVRI at FI_{O₂} 0.4 and at FI_{O₂} 0.1.

Dobutamine 20 μg · kg⁻¹ · min⁻¹ (table 4) increased PVRI at FI_{O₂} 0.4 but not at FI_{O₂} 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	FiO ₂ 0.4		FiO ₂ 0.125	
	Baseline	Dopamine 20 μg · kg ⁻¹ · min ⁻¹	Baseline	Dopamine 20 μg · kg ⁻¹ · min ⁻¹
pH _a	7.33 ± 0.02	7.28 ± 0.02*	7.36 ± 0.02*	7.30 ± 0.01†
PaO ₂ (mmHg)	187 ± 19	177 ± 17	48 ± 4‡	37 ± 3‡
PaCO ₂ (mmHg)	36 ± 1	40 ± 2†	33 ± 1*	39 ± 1‡
PvO ₂ (mmHg)	57 ± 4	64 ± 3*	37 ± 4‡	31 ± 2*
CI (l · min ⁻¹ · 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 · s · cm ⁻⁵ · 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 · s · cm ⁻⁵ · m ²)	151 ± 33	135 ± 25	215 ± 43†	193 ± 45

See text for abbreviations.
"Baseline" indicates the first series of determinations at FiO₂ 0.4 and at FiO₂ 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	FiO ₂ 0.4		FiO ₂ 0.125	
	Baseline	Dobutamine 20 μg · kg ⁻¹ · min ⁻¹	Baseline	Dobutamine 20 μg · kg ⁻¹ · min ⁻¹
pH _a	7.36 ± 0.02	7.29 ± 0.02‡	7.39 ± 0.02*	7.31 ± 0.02‡
PaO ₂ (mmHg)	201 ± 10	175 ± 15*	46 ± 1‡	38 ± 2*
PaCO ₂ (mmHg)	35 ± 1	38 ± 1*	33 ± 1	36 ± 1†
PvO ₂ (mmHg)	54 ± 2	65 ± 4†	35 ± 1‡	31 ± 1*
CI (l · min ⁻¹ · 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 · s · cm ⁻⁵ · 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 · s · cm ⁻⁵ · m ²)	134 ± 12	130 ± 13	255 ± 74†	133 ± 11*

See text for abbreviations.
"Baseline" indicates the first series of determinations at FiO₂ 0.4 and FiO₂ 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.

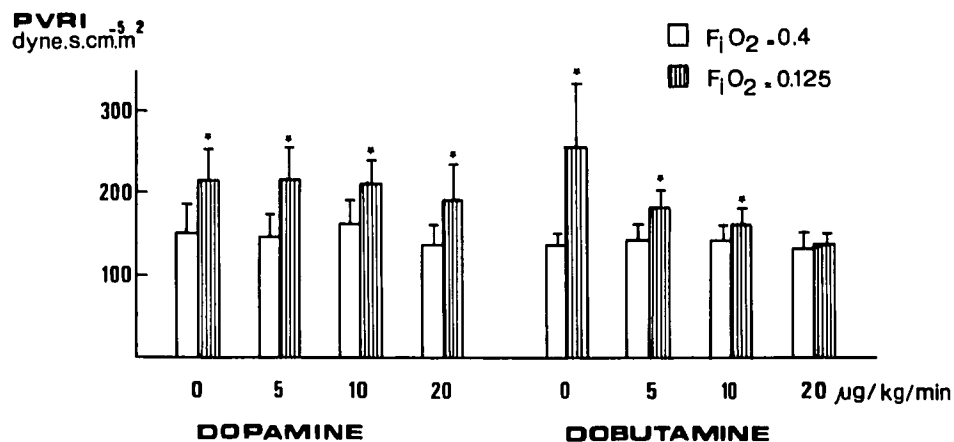


FIG. 1. Pulmonary vascular resistance index (mean \pm SEM) responses to hypoxia without and with dopamine ($n = 7$) and dobutamine ($n = 7$) at dosages of 5, 10, and 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in ventilated dogs with uncontrolled cardiac output. Asterisks indicate significant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

to increase and increased PVRI at F_{iO_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 F_{iO_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 dopamine¹⁶⁻¹⁹ 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 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, 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 pressures³¹ did not seem to be implicated. It cannot be excluded that dobutamine at 20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ had some direct pulmonary vasodilating effect that was not significant at constant flow because of the small number of animals. An F_{iO_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

Variable	F_{iO_2} 0.4			F_{iO_2} 0.1		
	Baseline	Dopamine 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$	Dobutamine 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$	Baseline	Dopamine 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$	Dobutamine 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$
pH_a	7.32 \pm 0.02	7.27 \pm 0.02	7.30 \pm 0.02	7.35 \pm 0.02*	7.26 \pm 0.02*	7.30 \pm 0.02
Pa_{O_2} (mmHg)	175 \pm 15	165 \pm 14	169 \pm 19	29 \pm 2‡	25 \pm 1	27 \pm 1
Pa_{CO_2} (mmHg)	36 \pm 1	39 \pm 2	39 \pm 1	34 \pm 2	40 \pm 2‡	39 \pm 1*
$P\bar{v}O_2$ (mmHg)	51 \pm 4	58 \pm 4*	59 \pm 3‡	20 \pm 2‡	13 \pm 2*	16 \pm 1
CI ($l \cdot \text{min}^{-1} \cdot \text{m}^2$)	4.21 \pm 0.52	4.25 \pm 0.49	4.35 \pm 0.54	4.45 \pm 0.56	4.35 \pm 0.51	4.15 \pm 0.53
HR (beats/min)	166 \pm 12	166 \pm 13	172 \pm 7	169 \pm 9	207 \pm 9‡	185 \pm 10
BP (mmHg)	118 \pm 8	120 \pm 9	109 \pm 9	120 \pm 9	98 \pm 8‡	109 \pm 8
SVRI ($\text{dyne} \cdot \text{s} \cdot \text{cm}^{-5} \cdot \text{m}^2$)	2407 \pm 330	2362 \pm 260	2187 \pm 332	2331 \pm 346	1888 \pm 234*	2216 \pm 236
PCWP (mmHg)	5 \pm 1	4 \pm 1*	3 \pm 1*	4 \pm 1	4 \pm 1	3 \pm 1
RAP (mmHg)	3 \pm 1	2 \pm 1	2 \pm 1	3 \pm 1	3 \pm 1	2 \pm 1
MPAP (mmHg)	11 \pm 1	12 \pm 1*	12 \pm 1‡	21 \pm 2‡	20 \pm 1	18 \pm 2
PVRI ($\text{dyne} \cdot \text{s} \cdot \text{cm}^{-5} \cdot \text{m}^2$)	134 \pm 23	172 \pm 26‡	181 \pm 26‡	346 \pm 71‡	339 \pm 64	333 \pm 62

See text for abbreviations.

"Baseline" indicates the first series of determinations at F_{iO_2} 0.4 and F_{iO_2} 0.1, respectively. Values are expressed as mean \pm SEM. Sec-

ond, 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 μg · kg ⁻¹ · min ⁻¹	Dobutamine 20 μg · kg ⁻¹ · min ⁻¹	Baseline	Dopamine 20 μg · kg ⁻¹ · min ⁻¹	Dobutamine 20 μg · kg ⁻¹ · 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‡
PaO ₂ (mmHg)	180 ± 17	161 ± 18*	165 ± 18*	30 ± 2‡	25 ± 1*	27 ± 1
PaCO 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 · min ⁻¹ · 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 · 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 · 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_IO₂ 0.4 and F_IO₂ 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 O₂ 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_IO₂-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

PVRI
dyne.s.cm⁻⁵.m²

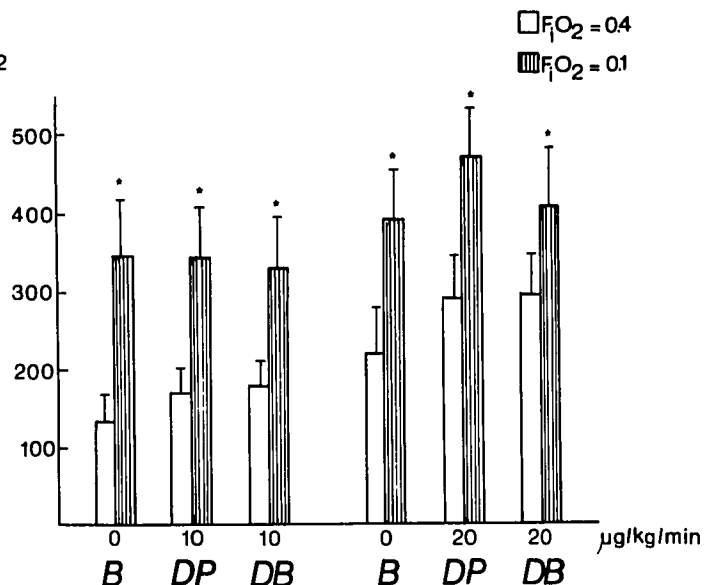


FIG. 2. Pulmonary vascular resistance index (mean ± SEM) responses to hypoxia without drug (B), with dopamine (DP), and with dobutamine (DB) at doses of 10 μg · kg⁻¹ · min⁻¹ (n = 7) and 20 μg · kg⁻¹ · min⁻¹ (n = 7) in ventilated dogs with cardiac output kept constant. Asterisks indicate significant difference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

are²⁰: 1) an increase in venous admixture due to augmented pulmonary blood flow; 2) an inhibition of HPV; and 3) an increased O₂ 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 PaO₂ in the presence of an increased P \bar{v} O₂ at FI_{O₂} 0.4 (table 4) suggests an increased venous admixture. Oxygen consumption and CO₂ 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.

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