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 hypoxia (fraction of inspired O₂ concentration [FIO₂] 0.4 balance nitrogen) and challenged with short periods of inspiratory hypoxia (FIO₂ 0.125 or 0.1 for 10 min). Dopamine at doses of 5, 10, and 20 μg·kg⁻¹·min⁻¹ (n = 7 dogs) increased cardiac index (CI) and pulmonary artery pressure (PAP) without change in indexed pulmonary vascular resistance (PVRI) at both FIO₂ 0.4 and 0.125. Hypoxia-induced increases in PVRI were unaffected by dopamine. Dobutamine at doses of 5, 10, and 20 μg·kg⁻¹·min⁻¹ (n = 7 dogs) increased CI, with an increase in PAP without change in PVRI at FIO₂ 0.4, and at FIO₂ 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 μg·kg⁻¹·min⁻¹, and completely at 20 μg·kg⁻¹·min⁻¹. In two additional groups of seven dogs the effects of reducing FIO₂ from 0.4 to 0.1 without and with dopamine or dobutamine either at 10 μg·kg⁻¹·min⁻¹ (n = 7) or at 20 μg·kg⁻¹·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 FIO₂ 0.4 and did not significantly affect hypoxia-induced increases in PVRI. It is concluded that at doses up to 20 μg·kg⁻¹·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: 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, but their effects on the pulmonary circulation remain controversial. Both dopamine and dobutamine have been reported either not to affect, or to increase, or to decrease normoxic pulmonary vascular tone. Hypoxic pulmonary vasoconstriction (HPV) has been found to be either unchanged, enhanced, or inhibited after dopamine, and inhibited after dobutamine. Whereas arterial blood gases are known to deteriorate with both amines, 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 μg·kg⁻¹·min⁻¹) 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 sodium pentobarbital (25 mg·kg⁻¹), placed supine in a V-shaped trough, and ventilated (Elema 900 B³ Servo-ventilator, Siemens Elema, Solna, Sweden) via a cuffed endotracheal tube. The fraction of inspired O₂ (FIO₂) was 0.4, the respiratory rate 12·min⁻¹, and the tidal volume 15–20 ml·kg⁻¹, adjusted to achieve an end-tidal PCO₂ of 30–35 mmHg. A thermostor-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·kg⁻¹·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·kg⁻¹·h⁻¹ and anesthetized with pentobarbital 2 mg·kg⁻¹ in 60 s once hourly. In 14 dogs, a balloon catheter (Peri-Cor®, 45, Datascop, 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·kg⁻¹ iv just before insertion and 50 U·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
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, PCO₂, and PO₂ were measured by an automated
analyzer (IL 613, Instrumentation Laboratories, Lexing-
ton, MA) and corrected for temperature. End-tidal
PCO₂ was measured with an HP 47217 infrared capno-
meter (Hewlett Packard, Palo Alto, CA). Hemoglobin
levels were determined using the IL 282 Co-oxymeter®
(Instrumentation Laboratories). O₂ saturations were cal-
culated from the nomogram of Rossing and Cain.²² Body
surface area was calculated as 0.112 × weight (kg)²/3, m².
Systemic vascular resistance index (SVRI) was calculated as
(mean BP − right atrial pressure [RAP]) × cardiac index
(CI) × 80, dyne ⋅ s ⋅ cm⁻⁵ ⋅ m² and pulmonary vas-
cular resistance index (PVRI) as (mean PAP [MPAP]
− PCWP) × CI⁻¹ × 80, dyne ⋅ s ⋅ cm⁻⁵ ⋅ m².

In the first 14 dogs, after ensuring steady-state condi-
tions (stable BP, PAP, HR, and end-tidal PCO₂) for 20 min
at FiO₂ 0.4, hemodynamic and blood gas determinations
were performed first before an then at the 10th min of
an acute hypoxic challenge (FiO₂ 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 deter-
nations were performed in each animal, six at FiO₂ 0.4
(three of these with a dopamine or a dobutamine infusion)
and six at FiO₂ 0.125 (three of these with a dopamine or
a dobutamine infusion). Drugs were given intravenously
using a calibrated pump (Braun Melsungen AG, Melsun-
gen, Germany), and measurements were performed after
15 min of drug infusion at the selected dosage. When
drug infusion was stopped, the next sequence of mea-
surements without drug was started after 20 min of equil-
ibration at FiO₂ 0.4.

In the next 14 dogs, a sequence of hemodynamic and
blood gas measurements successively after 20 min at
FiO₂ 0.4 and after 10 min at FiO₂ 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 FiO₂ 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 ad-
ministrations.

Statistical analysis was performed using analysis of vari-
ce for repeated measurements in each study group.
Modified t tests with the Bonferroni adjustment for mul-
tiple 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
FiO₂ 0.4 and FiO₂ 0.125. Therefore, only the first mea-
surements at both FiO₂ 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 FiO₂
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 inspira-
atory hypoxia (FiO₂ 0.125) ranged from 10 to 510%.
Dopamine (table 1) at FiO₂ 0.4 increased CI, PCWP,
and PAP, but PVRI remained unaffected. Similar changes
occurred at FiO₂ 0.125, except for no change in PCWP.
Dobutamine (table 2) at FiO₂ 0.4 increased CI and PAP,
while PCWP and PVRI did not change. Similar effects
occurred at FiO₂ 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 (FiO₂ 0.1 instead of 0.125). This resulted in
more profound hypoxia, a still variable (+12 to
+197%) but as an average more important increase in
PVRI, and otherwise similar systemic hemodynamic ef-
facts.

Dopamine and dobutamine 10 µg ⋅ kg⁻¹ ⋅ min⁻¹ (table
3) increased PVRI at FiO₂ 0.4 but not at FiO₂ 0.1.
Dopamine 20 µg ⋅ kg⁻¹ ⋅ min⁻¹ (table 4) increased PVRI
at FiO₂ 0.4 and at FiO₂ 0.1.
Dobutamine 20 µg ⋅ kg⁻¹ ⋅ min⁻¹ (table 4) increased
PVRI at FiO₂ 0.4 but not at FiO₂ 0.1.
Neither dopamine nor dobutamine significantly de-
pressed 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-
DOPAMINE, DOBUTAMINE, AND PULMONARY CIRCULATION

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>$F_{iO_2} 0.4$</th>
<th>Dopamine 20 μg·kg⁻¹·min⁻¹</th>
<th>$F_{iO_2} 0.125$</th>
<th>Dopamine 20 μg·kg⁻¹·min⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td></td>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>$pH_s$</td>
<td>7.53 ± 0.02</td>
<td>7.28 ± 0.02*</td>
<td>7.36 ± 0.02*</td>
<td>7.30 ± 0.01†</td>
</tr>
<tr>
<td>$P_{aO_2}$ (mmHg)</td>
<td>187 ± 19</td>
<td>177 ± 17</td>
<td>48 ± 4‡</td>
<td>37 ± 3§</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg)</td>
<td>36 ± 1</td>
<td>40 ± 2†</td>
<td>33 ± 1*</td>
<td>39 ± 1‡</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg)</td>
<td>57 ± 4</td>
<td>64 ± 3*</td>
<td>37 ± 4‡</td>
<td>31 ± 2‡</td>
</tr>
<tr>
<td>CI (l·min⁻¹·m⁻²)</td>
<td>4.75 ± 0.58</td>
<td>7.65 ± 0.67‡</td>
<td>5.13 ± 0.58‡</td>
<td>8.12 ± 0.89‡</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>148 ± 13</td>
<td>158 ± 19</td>
<td>163 ± 12</td>
<td>219 ± 19†</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>118 ± 4</td>
<td>194 ± 12‡</td>
<td>133 ± 7*</td>
<td>153 ± 12</td>
</tr>
<tr>
<td>SVRI (dyne·s·cm⁻⁵·m⁻³)</td>
<td>2003 ± 216</td>
<td>2012 ± 212†</td>
<td>2080 ± 189</td>
<td>1553 ± 244*</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>8 ± 1</td>
<td>12 ± 2*</td>
<td>9 ± 2</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>8 ± 1</td>
<td>9 ± 1</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>MPAP (mmHg)</td>
<td>17 ± 2</td>
<td>24 ± 3†</td>
<td>23 ± 4†</td>
<td>27 ± 4†</td>
</tr>
<tr>
<td>PVR (dyne·s·cm⁻⁵·m⁻³)</td>
<td>151 ± 33</td>
<td>135 ± 25</td>
<td>215 ± 43†</td>
<td>193 ± 45</td>
</tr>
</tbody>
</table>

See text for abbreviations.

"Baseline" indicates the first series of determinations at $F_{iO_2} 0.4$ and at $F_{iO_2} 0.125$, respectively. Values are expressed as mean ± SEM.

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>$F_{iO_2} 0.4$</th>
<th>Dobutamine 20 μg·kg⁻¹·min⁻¹</th>
<th>$F_{iO_2} 0.125$</th>
<th>Dobutamine 20 μg·kg⁻¹·min⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td></td>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>$pH_s$</td>
<td>7.36 ± 0.02</td>
<td>7.29 ± 0.02‡</td>
<td>7.39 ± 0.02*</td>
<td>7.31 ± 0.02‡</td>
</tr>
<tr>
<td>$P_{aO_2}$ (mmHg)</td>
<td>201 ± 10</td>
<td>175 ± 15*</td>
<td>46 ± 1‡</td>
<td>38 ± 2*</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg)</td>
<td>35 ± 1</td>
<td>38 ± 1*</td>
<td>33 ± 1</td>
<td>36 ± 1†</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg)</td>
<td>54 ± 2</td>
<td>65 ± 4†</td>
<td>35 ± 1‡</td>
<td>31 ± 1*</td>
</tr>
<tr>
<td>CI (l·min⁻¹·m⁻²)</td>
<td>4.71 ± 0.47</td>
<td>9.37 ± 1.15‡</td>
<td>5.08 ± 0.54‡</td>
<td>9.13 ± 1.12‡</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>149 ± 9</td>
<td>215 ± 10‡</td>
<td>165 ± 9</td>
<td>204 ± 16‡</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>124 ± 8</td>
<td>120 ± 8</td>
<td>130 ± 7</td>
<td>129 ± 7</td>
</tr>
<tr>
<td>SVRI (dyne·s·cm⁻⁵·m⁻³)</td>
<td>2125 ± 277</td>
<td>1093 ± 98‡</td>
<td>2075 ± 256</td>
<td>1129 ± 130‡</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>7 ± 1</td>
<td>7 ± 1</td>
<td>7 ± 1</td>
<td>7 ± 1</td>
</tr>
<tr>
<td>MPAP (mmHg)</td>
<td>15 ± 1</td>
<td>23 ± 2‡</td>
<td>25 ± 4‡</td>
<td>25 ± 2§</td>
</tr>
<tr>
<td>PVR (dyne·s·cm⁻⁵·m⁻³)</td>
<td>154 ± 12</td>
<td>130 ± 15</td>
<td>255 ± 74†</td>
<td>153 ± 11*</td>
</tr>
</tbody>
</table>

See text for abbreviations.

"Baseline" indicates the first series of determinations at $F_{iO_2} 0.4$ and $F_{iO_2} 0.125$, 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: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$. 

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to increase and increased PVRI at FIO\textsubscript{2} 0.4 probably represent an increased pulmonary vascular tone, in agreement with above mentioned work on isolated lung lobes.\textsuperscript{11}

Repeated hypoxia has been reported previously either to enhance\textsuperscript{29,26} or not to affect\textsuperscript{27,28} HPV. In our intact dog preparation, repeatedly decreasing FIO\textsubscript{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.\textsuperscript{27}

Our dogs were anesthetized with pentobarbital. This agent does not affect HPV.\textsuperscript{29}

HPV has been observed to be variably affected by dopamine\textsuperscript{16-19} and inhibited bydobutamine.\textsuperscript{16,17} These discrepancies between studies and the present data may be accounted for by the misleading use of the present data and methodology.

In this study, at doses up to 20 μg·kg\textsuperscript{-1}·min\textsuperscript{-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\textsubscript{A,VO\textsubscript{2}}\textsuperscript{60}) and/or higher pulmonary vascular pressures \textsuperscript{51} did not seem to be implicated. It cannot be excluded that dobutamine at 20 μg·kg\textsuperscript{-1}·min\textsuperscript{-1} had some direct pulmonary vasodilating effect that was not significant at constant flow because of the small number of animals. An FIO\textsubscript{2} of 0.1 instead of 0.125 was imposed during the controlled cardiac output set of experiments, which resulted in more severe hypox-

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>FIO\textsubscript{2} 0.4</th>
<th>Dopamine 10 μg·kg\textsuperscript{-1}·min\textsuperscript{-1}</th>
<th>Dobutamine 10 μg·kg\textsuperscript{-1}·min\textsuperscript{-1}</th>
<th>FIO\textsubscript{2} 0.1</th>
<th>Dopamine 10 μg·kg\textsuperscript{-1}·min\textsuperscript{-1}</th>
<th>Dobutamine 10 μg·kg\textsuperscript{-1}·min\textsuperscript{-1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH\textsubscript{a}</td>
<td>7.32 ± 0.02</td>
<td>7.27 ± 0.02</td>
<td>7.30 ± 0.02</td>
<td>7.35 ± 0.02*</td>
<td>7.26 ± 0.02*</td>
<td>7.30 ± 0.02</td>
</tr>
<tr>
<td>P\textsubscript{a}CO\textsubscript{2} (mmHg)</td>
<td>175 ± 15</td>
<td>165 ± 14</td>
<td>169 ± 19</td>
<td>29 ± 2*</td>
<td>25 ± 1</td>
<td>27 ± 1</td>
</tr>
<tr>
<td>P\textsubscript{a}O\textsubscript{2} (mmHg)</td>
<td>56 ± 1</td>
<td>39 ± 2</td>
<td>39 ± 1</td>
<td>34 ± 2</td>
<td>40 ± 2*</td>
<td>39 ± 1*</td>
</tr>
<tr>
<td>F\textsubscript{IO\textsubscript{2}} (mmHg)</td>
<td>51 ± 4</td>
<td>58 ± 4*</td>
<td>59 ± 3*</td>
<td>20 ± 2*</td>
<td>15 ± 2*</td>
<td>16 ± 1</td>
</tr>
<tr>
<td>CI (l·min\textsuperscript{-1}·m\textsuperscript{-2})</td>
<td>4.21 ± 0.52</td>
<td>4.25 ± 0.49</td>
<td>4.35 ± 0.54</td>
<td>4.45 ± 0.56</td>
<td>4.35 ± 0.51</td>
<td>4.15 ± 0.53</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>166 ± 12</td>
<td>166 ± 13</td>
<td>172 ± 7</td>
<td>169 ± 9</td>
<td>207 ± 9*</td>
<td>185 ± 10</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>118 ± 8</td>
<td>120 ± 9</td>
<td>109 ± 9</td>
<td>120 ± 9</td>
<td>98 ± 8*</td>
<td>109 ± 8</td>
</tr>
<tr>
<td>SVRI (dyne·s·cm\textsuperscript{-5}·m\textsuperscript{-2})</td>
<td>2407 ± 330</td>
<td>2362 ± 260</td>
<td>2187 ± 332</td>
<td>2331 ± 346</td>
<td>1888 ± 234*</td>
<td>2216 ± 236</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>5 ± 1</td>
<td>4 ± 1*</td>
<td>3 ± 1*</td>
<td>4 ± 1</td>
<td>4 ± 1</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>3 ± 1</td>
<td>2 ± 1*</td>
<td>2 ± 1*</td>
<td>3 ± 1</td>
<td>3 ± 1</td>
<td>2 ± 1</td>
</tr>
<tr>
<td>MPAP (mmHg)</td>
<td>11 ± 1</td>
<td>12 ± 1*</td>
<td>12 ± 1*</td>
<td>21 ± 2*</td>
<td>20 ± 1</td>
<td>18 ± 2</td>
</tr>
<tr>
<td>PVRI (dyne·s·cm\textsuperscript{-5}·m\textsuperscript{-2})</td>
<td>134 ± 23</td>
<td>172 ± 26†</td>
<td>181 ± 20‡</td>
<td>346 ± 71‡</td>
<td>339 ± 64</td>
<td>333 ± 62</td>
</tr>
</tbody>
</table>

See text for abbreviations.

"Baseline" indicates the first series of determinations at FIO\textsubscript{2} 0.4 and FIO\textsubscript{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 Hypoxic and Hypoxic Conditions as Constant Flow

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Dopamine 20 μg·kg⁻¹·min⁻¹</th>
<th>Dobutamine 20 μg·kg⁻¹·min⁻¹</th>
<th>Baseline</th>
<th>Dopamine 20 μg·kg⁻¹·min⁻¹</th>
<th>Dobutamine 20 μg·kg⁻¹·min⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH&lt;sub&gt;S&lt;/sub&gt;</td>
<td>7.32 ± 0.01</td>
<td>7.29 ± 0.02</td>
<td>7.29 ± 0.02</td>
<td>7.36 ± 0.01†</td>
<td>7.27 ± 0.01‡</td>
<td>7.29 ± 0.02†</td>
</tr>
<tr>
<td>Pao&lt;sub&gt;2&lt;/sub&gt; (mmHg)</td>
<td>180 ± 17</td>
<td>161 ± 18*</td>
<td>165 ± 18*</td>
<td>30 ± 2‡</td>
<td>25 ± 1*</td>
<td>27 ± 1</td>
</tr>
<tr>
<td>Paco&lt;sub&gt;2&lt;/sub&gt; (mmHg)</td>
<td>36 ± 1</td>
<td>45 ± 2‡</td>
<td>44 ± 2‡</td>
<td>34 ± 2</td>
<td>42 ± 2‡</td>
<td>41 ± 2‡</td>
</tr>
<tr>
<td>PVO&lt;sub&gt;2&lt;/sub&gt; (mmHg)</td>
<td>49 ± 2</td>
<td>55 ± 3*</td>
<td>55 ± 3*</td>
<td>21 ± 2‡</td>
<td>16 ± 2*</td>
<td>15 ± 2*</td>
</tr>
<tr>
<td>CI (l·min⁻¹·m⁻²)</td>
<td>3.68 ± 0.5</td>
<td>3.70 ± 0.44</td>
<td>3.66 ± 0.47</td>
<td>3.72 ± 0.44</td>
<td>3.67 ± 0.45</td>
<td>3.81 ± 0.47</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>140 ± 11</td>
<td>186 ± 10†</td>
<td>209 ± 10†</td>
<td>164 ± 10*</td>
<td>246 ± 8‡</td>
<td>198 ± 10†</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>119 ± 3</td>
<td>144 ± 15</td>
<td>101 ± 7</td>
<td>124 ± 4</td>
<td>123 ± 16</td>
<td>112 ± 12</td>
</tr>
<tr>
<td>SVRI (dyne·s·cm⁻⁵·m⁻²)</td>
<td>2894 ± 447</td>
<td>3476 ± 638*</td>
<td>2264 ± 152</td>
<td>2845 ± 362</td>
<td>2764 ± 326</td>
<td>2925 ± 162</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>4 ± 1</td>
<td>2 ± 1</td>
<td>3 ± 1</td>
<td>4 ± 1</td>
<td>3 ± 1</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>2 ± 1</td>
<td>1 ± 1</td>
<td>2 ± 1</td>
<td>2 ± 1</td>
<td>2 ± 1</td>
<td>2 ± 1</td>
</tr>
<tr>
<td>MPAP (mmHg)</td>
<td>15 ± 1</td>
<td>14 ± 2</td>
<td>15 ± 1</td>
<td>20 ± 2‡</td>
<td>23 ± 2*</td>
<td>20 ± 2</td>
</tr>
<tr>
<td>PVR&lt;sub&gt;I&lt;/sub&gt; (dyne·s·cm⁻⁵·m⁻²)</td>
<td>221 ± 54</td>
<td>286 ± 56*</td>
<td>291 ± 54*</td>
<td>365 ± 67‡</td>
<td>467 ± 69*</td>
<td>404 ± 77</td>
</tr>
</tbody>
</table>

See text for abbreviations.

"Baseline" indicates the first series of determinations at F<sub>O₂</sub> 0.4 and F<sub>O₂</sub> 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<sub>2</sub> deprivation.

The systemic hemodynamic changes in our hypoxic dogs after dopamine and dobutamine were in keeping with previous work.¹² At constant flow, alpha-mediated vasoconstriction after dopamine was seen only at the highest dosage and in hypoxic 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<sub>O₂</sub>-dependent changes in vasocostricting and vasodilating activities of dopamine and dobutamine is available.

Both dopamine and dobutamine constrict capacitance vessels and so enhance venous return in experimental animal preparations³²,³³ 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

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**PVRI**

| dyne·s·cm⁻⁵·m⁻² |

**F<sub>O₂</sub> = 0.4**

**F<sub>O₂</sub> = 0.1**

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*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 hypoxic and hypoxic conditions at each dose (*P < 0.05).*
are\textsuperscript{20}: 1) an increase in venous admixture due to augmented pulmonary blood flow; 2) an inhibition of HPV; and 3) an increased O\textsubscript{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 Pao\textsubscript{2} in the presence of an increased PVO\textsubscript{2} at FIO\textsubscript{2} 0.4 (table 4) suggests an increased venous admixture. Oxygen consumption and CO\textsubscript{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

34. Marino RJ, Romagnoli A, Keats SA: Selective vasoconstriction by dopamine in comparison with isoproterenol and phenylephrine. Anesthesiology 43:570-572, 1975