Dopamine Depletes Minute Ventilation in Patients With Heart Failure

Philippe van de Borne, MD, PhD; Ron Oren, MD; Virend K. Somers, MD, PhD

Background—Low-dose dopamine is frequently used in patients in the intensive care setting. Dopamine may inhibit chemoreceptor afferents and hence decrease chemoreflex sensitivity to hypoxia.

Methods and Results—In a double-blind, randomized, crossover study, we determined the effects of dopamine (5 μg · kg⁻¹ · min⁻¹) and placebo infusion on oxygen saturation, minute ventilation, and sympathetic nerve activity during normoxia and 5 minutes of hypoxia in 10 normal young subjects. We further investigated the effects of dopamine and placebo on minute ventilation during normoxic breathing in 8 patients with severe heart failure and in 8 age-matched control subjects. Dopamine did not decrease minute ventilation during normoxia in normal subjects. During hypoxia, minute ventilation was 12.9±1.3 L/min on dopamine and 15.8±1.5 L/min on placebo (P<0.0001). Oxygen saturation during hypoxia was lower with dopamine (78±3%) than placebo (84±2%; P<0.0001). Sympathetic nerve activity during hypoxia was not enhanced with dopamine despite the lower O₂ saturation. Subjects were able to maintain a voluntary apnea to a lower oxygen saturation on dopamine than on placebo (P<0.05). In heart failure patients breathing room air, but not in age-matched control subjects, dopamine decreased minute ventilation despite decreased oxygen saturation and increased PETCO₂ during dopamine (all P≤0.02).

Conclusions—Dopamine inhibits chemoreflex responses during hypoxic breathing in normal humans, preferentially affecting the ventilatory response more than the sympathetic response. Dopamine also depletes ventilation in normoxic heart failure patients breathing room air. Ventilatory inhibition by low-dose dopamine may adversely influence outcome in hypoxic patients, especially in patients with heart failure. (Circulation. 1998;98:126-131.)

Key Words: ventilation ■ dopamine ■ heart failure ■ nervous system, sympathetic

Peripheral chemoreceptors in the carotid body respond to hypoxia by reflex increases in both minute ventilation and sympathetic neural discharge to muscle blood vessels.¹ The increase in minute ventilation, acting via thoracic afferents, has an inhibiting influence on the sympathetic neural response.¹² Therefore, with apnea during hypoxia (and hence attenuation of the influence of pulmonary afferents), sympathetic activation is potentiated.¹²

Dopamine receptors are present in the carotid bodies.³⁴ Activation of the dopamine receptors is thought to have an inhibitory influence on chemoreceptor afferent activity in cats.⁵ Previous studies have suggested that infusion of dopamine during hypoxia results in a decrease in minute ventilation during hypoxia.⁶⁷ Domperidone (a dopamine antagonist) increases the ventilatory responses to hypoxia.⁵

Low-dose dopamine infusion is widely used in the intensive care setting, often in patients on ventilators and in patients with impaired oxygenation.⁹ The most frequent rationale underlying the use of low-dose dopamine is as an empirical therapy to improve renal function or outcome in critically ill patients with oliguria.¹⁰–¹⁶ This rationale has been used to support the use of low-dose dopamine in patients with heart failure¹⁶ and in cardiac surgical patients with left ventricular dysfunction admitted to the intensive care unit after cardiopulmonary bypass.¹⁷ Dopamine has also been recommended for use during discontinuation of mechanical ventilation in patients with postoperative heart failure.¹⁸ In addition, it has been suggested that dopamine agonists (ibopamine) may be of benefit in patients with heart failure.¹⁹

An inhibitory effect of low-dose dopamine on the chemoreceptor reflex may adversely affect attempts to wean patients from mechanical ventilatory support. In addition, in patients with impaired oxygenation (for example, those with cardiac and respiratory dysfunction), inhibition of chemoreceptor sensitivity may further impair oxygenation status. This could significantly influence clinical outcome in patients in whom cardiorespiratory function is already tenuous.

Using a double-blind, randomized, placebo-controlled crossover design, we therefore tested the hypothesis that low-dose dopamine would inhibit the chemoreflex responses to hypoxia. We examined the effects of hypoxia on minute ventilation, sympathetic nerve responses, blood pressure, and heart rate...
during a low-dose (5 \( \mu \)g \cdot kg\(^{-1}\) \cdot min\(^{-1}\)) infusion of dopamine or placebo in healthy young subjects. We also examined the effects of dopamine and placebo on the sympathetic responses to apnea during normoxia and responses to apnea during hypoxia. We further investigated the effects of low-dose dopamine on minute ventilation in patients with heart failure (New York Heart Association class III and IV) breathing room air.

**Methods**

**Subjects**

We studied the effects of dopamine on responses to hypoxia in 10 normal subjects (8 men, 2 women) 30±6 years old. None were receiving any medications. During 4 visits to the University Hospitals, medical and surgical intensive care units, we noted that at any given time, between 10% and 25% of patients in intensive care were receiving a low-dose dopamine infusion (between 2 and 6 \( \mu \)g \cdot kg\(^{-1}\) \cdot min\(^{-1}\)). Hence, to determine the effect of low-dose dopamine on ventilatory variables in patients with cardiopulmonary compromise, we also studied 8 patients with stable chronic heart failure (3 men, 5 women, 57±12 years old) and 8 control subjects (5 men, 3 women, 67±7 years old). All patients had clinical, radiographic, and echocardiographic evidence of impaired ventricular function and had heart failure for >60 days. The etiology of heart failure was ischemic heart disease (n=5) or idiopathic (n=3). All patients were in NYHA functional class III/IV and were on various combinations of diuretics, digitalis, nitrates, and ACE inhibitors. Normal subjects were recruited by advertisements in the local newspaper. Informed written consent was obtained from all subjects. The study was approved by the Institutional Human Subjects Review Committee.

**Measurements**

Mean blood pressure was measured with a Physio-Control Lifesat 200 sphygmomanometer. ECG, respiration (pneumograph), oxygen saturation (Nellcor N-100 C pulse oximeter), and \( \text{PETCO}_2 \) (Hewlett-Packard 47210A capnometer) were recorded on a Gould 2800 S recorder. Ventilatory rate and minute ventilation were determined with a Bourns LS-75 monitor. Breathing was via a mouthpiece with a nose clip to ensure exclusive mouth breathing. In the normal subjects, sympathetic nerve activity to muscle was measured continuously by obtaining multunit recordings of postganglionic sympathetic activity to muscle, measured from a nerve fascicle in the peroneal nerve posterior to the fibular head as described previously. Electrical activity in the nerve fascicle was measured with tungsten microelectrodes (shaft diameter, 200 \( \mu \)m, tapering to an uninsulated tip of 1 to 5 \( \mu \)m). A subcutaneous reference electrode was first inserted 2 to 3 cm away from the recording electrode, which was itself inserted into the nerve fascicle. The neural signals were amplified, filtered, rectified, and integrated to obtain a voltage display of sympathetic nerve activity.

**Protocol and Interventions**

**Normal Subjects**

The protocol used to test chemoreflex responses to hypoxia during breathing and apnea in the normal subjects was identical to that used in previous studies. Measurements were taken during a 3-minute baseline period of stable ventilation. Infusion of either dopamine or placebo (equal volumes of normal saline) was then started according to a double-blind randomized protocol. Dopamine or placebo (identical volumes) was first administered at a dose of 2 \( \mu \)g \cdot kg\(^{-1}\) \cdot min\(^{-1}\) for 2 minutes and then increased to 5 \( \mu \)g \cdot kg\(^{-1}\) \cdot min\(^{-1}\) for 8 minutes of baseline recordings. The last 3 minutes of the baseline was used for the analysis of the effects of dopamine on ventilation and sympathetic nerve activity during normoxia. The dopamine or placebo infusion was continued throughout the rest of the protocol. This consisted of 5 minutes of exposure to isocapnic hypoxia (10% \( \text{O}_2 \) in \( \text{N}_2 \) with \( \text{CO}_2 \) titrated to maintain isocapnia), a recovery period of 15 minutes, and a subsequent cold pressor test. The cold pressor test is a nonspecific stimulus for ventilation and sympathetic excitation.

**Figure 1.** Effects of dopamine on responses to hypoxia. Values are mean±SEM for placebo (\( \square \)) and dopamine (\( \bullet \)). Measurements are shown for baseline values before start of infusion (Bsl), during infusion (Inf), and during all 5 minutes of hypoxia. Measurements are shown for minute ventilation (\( V_E \), left) and oxygen saturation (\( \text{O}_2\text{ Sat.} \), right). Dopamine depressed ventilatory response to hypoxia and was associated with lower levels of oxygen saturation during hypoxia vs placebo (*\( P < 0.008 \)).

**Table 1.** Effects of Dopamine and Placebo on Mean Pressure, Heart Rate, and Sympathetic Nerve Activity During Normoxia and Hypoxia in Normal Subjects

<table>
<thead>
<tr>
<th></th>
<th>Mean BP, mm Hg</th>
<th>HR, bpm</th>
<th>( \text{PETCO}_2 ), mm Hg</th>
<th>( \Delta\text{SNA} ), %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Dopamine</td>
<td>Placebo</td>
<td>Dopamine</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>81±2</td>
<td>81±2</td>
<td>59±3</td>
<td>59±2</td>
</tr>
<tr>
<td><strong>Infusion</strong></td>
<td>81±2</td>
<td>82±2</td>
<td>59±3</td>
<td>65±2*</td>
</tr>
<tr>
<td><strong>Hypoxia, min</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>82±2</td>
<td>84±2</td>
<td>70±4</td>
<td>73±3</td>
</tr>
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<td>2</td>
<td>84±2</td>
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<td>4</td>
<td>83±3</td>
<td>85±2</td>
<td>72±3</td>
<td>77±2*</td>
</tr>
<tr>
<td>5</td>
<td>83±2</td>
<td>86±2</td>
<td>73±3</td>
<td>78±3*</td>
</tr>
</tbody>
</table>

**BP** indicates blood pressure; **HR**, heart rate; and **SNA**, sympathetic nerve activity.

*Pairwise contrast of effects of dopamine vs placebo, significant at *\( P < 0.008 \) (Bonferroni correction).
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**Table 2. Effects of Dopamine and Placebo on Mean Blood Pressure, Heart Rate, Minute Ventilation, \( O_2 \), and Sympathetic Nerve Activity During the Cold Pressor Test in Normal Subjects**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Dopamine</th>
<th>Placebo</th>
<th>Dopamine</th>
<th>Placebo</th>
<th>Dopamine</th>
<th>Placebo</th>
<th>Dopamine</th>
<th>Placebo</th>
<th>Dopamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BP, mm Hg</td>
<td>80±2</td>
<td>83±2</td>
<td>59±3</td>
<td>61±2</td>
<td>7.5±0.8</td>
<td>6.4±0.5</td>
<td>98.5±0.4</td>
<td>97.1±0.6</td>
<td>38±1</td>
<td>41±1</td>
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<tr>
<td>Cold pressor test, min</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>91±4</td>
<td>95±4</td>
<td>68±4</td>
<td>70±4</td>
<td>11.1±2.1</td>
<td>9.0±1.2</td>
<td>98.2±0.4</td>
<td>97.2±0.7</td>
<td>38±1</td>
<td>41±1</td>
</tr>
<tr>
<td>2</td>
<td>96±5</td>
<td>96±4</td>
<td>64±4</td>
<td>69±3</td>
<td>13.2±3.4</td>
<td>11.3±2.2</td>
<td>99.6±0.2</td>
<td>99.2±0.4*</td>
<td>35±2</td>
<td>39±2</td>
</tr>
<tr>
<td>( \Delta SNA, % )</td>
<td></td>
<td></td>
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</table>

Abbreviations as in Table 1.

*Pairwise contrast of effects of dopamine vs placebo, significant at \( P<0.017 \) (Bonferroni correction).

Heart Failure Patients

In the patients with heart failure, we again used a randomized, double-blind, placebo-controlled crossover design. However, we tested only the effects of a dopamine infusion on minute ventilation during room air breathing. With safety reasons, heart failure patients were not exposed to the hypoxic gas mixture. In a double-blind design, dopamine or placebo was administered for 10 minutes during room air breathing, with a 10-minute recovery period between dopamine and placebo infusion. We measured minute ventilation, oxygen saturation, \( P_E T C O_2 \), blood pressure, and heart rate. Measurements taken during the last 5 minutes of dopamine infusion were compared with measurements during the last 5 minutes of placebo infusion. The same protocol was carried out in 8 age-matched control subjects breathing room air.

Analyses

Sympathetic bursts were identified by a careful inspection of the mean voltage neurogram. The amplitude of each burst was determined, and sympathetic activity was calculated as bursts per minute multiplied by mean burst amplitude. Measurements of nerve activity during the baseline periods for hypoxia and the cold pressor test were expressed as 100%. Changes in nerve activity during the interventions were expressed as a percentage of changes from baseline. For the apneas, sympathetic activity was expressed as a percentage increase from the preceding minute. Results are expressed as mean±SEM. Statistical analysis was performed by an independent statistician. A repeated-measures ANOVA determined whether dopamine affected the cardiovascular and ventilatory responses to hypoxia and the cold pressor test compared with the changes occurring during the infusion of placebo. Bonferroni adjustments were performed for multiple comparisons during hypoxia and the cold pressor test (respective levels of statistical significance, \( P<0.008 \) and \( P<0.017 \)). Other comparisons were performed with Student’s paired \( t \) tests (two-tailed) (significance assumed at \( P<0.05 \)).

**Results**

**Normal Subjects**

**Effects of Dopamine During Normoxia**

Dopamine had no significant effect on minute ventilation, oxygen saturation, \( P_E T C O_2 \), mean blood pressure, or sympathetic nerve activity when normal subjects were breathing room air (Table 1, Figure 1). However, during dopamine, heart rate increased to 65±2 bpm, compared with 59±3 bpm during placebo infusion (\( P<0.008 \)).

The normal subjects performed a maximal voluntary end-expiratory apnea during both placebo and dopamine infusion. While breathing room air, subjects were able to maintain apnea until oxygen saturation fell to 93±1% during placebo infusion, but during dopamine, apnea was able to be maintained until oxygen saturation fell to 88±4% (\( P<0.008 \)). Despite the greater fall in oxygen saturation with apnea during dopamine infusion, sympathetic nerve activity during apnea increased from baseline by 144±36% with placebo and by 99±23% (\( P=NS \)) during dopamine.

Dopamine did not affect the responses to the cold pressor test (Table 2).

**Effects of Dopamine on Responses to Hypoxia**

Dopamine significantly attenuated the ventilatory response to hypoxia (Figure 1). During the last minute of hypoxia, minute ventilation was 12.9±1.3 L/min on dopamine and 15.8±1.5 L/min on placebo (\( P<0.0001 \)). As a consequence of the impaired ventilatory response to hypoxia, oxygen saturation during dopamine was also much lower than that seen during placebo infusion (falling to 78±3% with dopamine and to 84±2% with placebo; \( P<0.0001 \)) (Figure 1 and 2). Despite the lower levels of ventilation and oxygen saturation, symp-

\[
V_e = 10.4 \, \text{L/min} \quad V_e = 5.5 \, \text{L/min} \\
O_2 = 75\% \quad O_2 = 59\%
\]

**Figure 2.** Example recording of sympathetic nerve activity (MSNA) and minute ventilation during placebo (left) and dopamine (right) during minute 5 of exposure to hypoxia. In this study, dopamine depressed ventilatory response to hypoxia (5.5 L/min) especially severely vs placebo (10.4 L/min). Oxygen saturation during dopamine was 59% vs 75% on placebo. Despite greater oxygen desaturation and lower minute ventilation, sympathetic nerve activity was similar during dopamine and placebo.
oxygen saturation with dopamine infusion during hypoxia are not accompanied by increased sympathetic activity (right).

pathetic nerve responses to hypoxia were similar for dopamine and placebo (Table 1; Figures 2 and 3). Dopamine did not affect the blood pressure response to hypoxia, although heart rate was slightly faster during minutes 4 and 5 of hypoxia with dopamine infusion (Table 1).

At the end of minute 5 of hypoxia, subjects carried out a maximal voluntary end-expiratory apnea. Apnea was able to be maintained until oxygen saturation fell to 78±3% during placebo and was maintained until oxygen saturation fell to 70±4% during dopamine (P=0.0004, Figure 4). Despite the greater fall in oxygen saturation with apnea during hypoxia and dopamine infusion, sympathetic nerve activity increased from baseline by 330±75% during placebo and by 248±43% during dopamine (P=NS).

Heart Failure Patients
Dopamine depressed ventilation even during normoxic breathing in the heart failure patients (Figure 5) but did not affect ventilation in age-matched controls. Minute ventilation was 6.8±0.6 L/min during placebo and 5.7±0.7 L/min during dopamine (P=0.02) in the heart failure patients, but in the age-matched controls, it was 5.0±0.4 L/min during placebo and 5.3±0.6 L/min during dopamine. The decrease in minute ventilation during dopamine was accompanied by a modest fall in oxygen saturation (P=0.006) and an increase in PetCO₂ (P=0.0004) in the patients with heart failure breathing room air. Dopamine had no significant effects on mean blood pressure (83±4 mm Hg during dopamine versus 86±5 mm Hg during placebo) or heart rate (88±5 bpm during dopamine and 89±5 bpm during placebo in these patients).

Discussion
This randomized, double-blind, placebo-controlled study investigated the effects of dopamine on minute ventilation in (1) normal humans during normoxia and hypoxia and (2) heart failure patients during normoxia. The goals of this study were first, to examine whether dopamine inhibited chemoreflex responses to hypoxia in normal subjects and second, to determine whether this effect of dopamine would result in a depression of minute ventilation in patients with severe heart failure. Although we confirm that in normal subjects, dopamine decreases minute ventilation during hypoxic breathing, our novel findings are that (1) dopamine does not decrease minute ventilation in normal subjects breathing room air; (2) dopamine allows prolongation of voluntary apnea to significantly greater levels of oxygen desaturation during both normoxia and hypoxia; and (3) in patients with severe heart failure, but not in age-matched controls, dopamine decreases minute ventilation, even during normoxic breathing.

Studies in Normal Subjects
Accompanying the ventilatory inhibition during hypoxia, oxygen saturation is also much lower during dopamine infusion. Lower oxygen saturation during dopamine may be in part secondary to dopamine increasing pulmonary arteriovenous shunting.22 Our data show that during a dopamine infusion, despite the lower oxygen saturation with dopamine during hypoxia, and hence an increased stimulus to minute ventilation, minute ventilation is lower and sympathetic activation is not increased. Hyperventilation, acting via pulmonary afferents, inhibits the sympathetic response to hypoxia, whereas chemoreflex stimulation by hypoxia increases sympathetic nerve activity.1,2 Thus, with lower levels of ventilation and lower oxygen levels (Figure 3), one would expect greater sympathetic activity. In contrast, with dopamine infusion during hypoxia, the lower levels of ventilation are not accompanied by increased sympathetic activity. Nevertheless, the inhibitory effects of dopamine are more marked.
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for ventilation than for sympathetic activation. Thus, dopamine exerts a preferential inhibitory influence, affecting mainly the ventilatory response, compared with the sympathetic response to hypoxia. While breathing room air and during hypoxia, normal subjects are able to maintain apnea to a significantly lower level of oxygen saturation during dopamine than during placebo infusion. Despite a greater oxygen desaturation with apnea during dopamine, the sympathetic response is not increased. Thus, the preferential effect of dopamine on the ventilatory compared with the sympathetic response to hypoxia is evident both during hypoxic breathing and during breath-hold. During breath-hold, the differential effect of dopamine on hypoxic ventilatory drive is indicated by the lower oxygen saturation at break point of apnea.

Dopamine stimulates α- and β-adrenergic as well as dopaminergic receptors. It is likely that the inhibitory effect on chemoreflex responses to hypoxia is mediated by dopamine receptors in the carotid bodies inhibiting chemoreflex afferent discharge. Neither α- nor β-blockade affects the ventilatory response to dopamine and hypoxia. Our findings apply to low-dose dopamine infusion only. Higher doses of dopamine have differential effects on chemoreflexes.

Our findings support earlier studies showing that dopamine inhibits ventilatory responses to hypoxia. In contrast to the findings of Welsh et al., in our double-blind, randomized, placebo-controlled study, we were unable to detect any significant depression of minute ventilation during normoxia in our normal subjects. It is possible that in normal subjects, there is a lower tonic chemoreceptor drive to ventilation. Thus, any inhibition of chemoreceptor afferent activity during normoxia does not induce significant decreases in minute ventilation. During hypoxia, however, dopamine has a striking effect on minute ventilation, even in healthy young subjects. Thus, in hypoxic patients in intensive care, inhibition of chemoreceptor drive by low-dose dopamine infusion may adversely affect minute ventilation and hence clinical outcome.

It is unlikely that alterations in other variables influenced our findings. PETCO₂ in minute 1 of hypoxia was slightly higher during dopamine than during placebo, despite our efforts to maintain isocapnia. If anything, the slightly higher PETCO₂ would have potentiated the ventilatory and sympathetic nerve responses to hypoxia during dopamine.

The absence of any significant effect of dopamine on the sympathetic and ventilatory responses to the cold pressor test indicates that our findings do not reflect a nonspecific depression of ventilatory and sympathetic responses by dopamine infusion.

Studies in Patients with Heart Failure

Patients with heart failure have increased chemoreflex sensitivity. In these patients, our findings indicate that dopamine depresses minute ventilation by >1 L/min (=16%), even during normoxic breathing. Inhibition of chemoreceptor drive in these patients may have subtle but significant effects on oxygen saturation that may negatively affect cardiovascular homeostasis. Our findings are consistent with a prior uncontrolled study by Huckauf et al. who showed that low-dose dopamine elicited a 10 mm Hg fall in PO₂ and a small but significant rise in PCO₂ in patients with moderate heart failure. In their study, the primary cause of the low PO₂ during dopamine was impaired ventilation-perfusion matching, but this was aggravated significantly by the lack of a normal compensatory increase in ventilation, as evidenced by the increase in PCO₂. Minute ventilation was not measured. Our data, showing that dopamine depresses ventilation in heart failure patients, complement these earlier findings by Huckauf and colleagues. This ventilatory depression occurs despite reductions in oxygen saturation and increased PETCO₂ during the dopamine infusion. Thus, there appears to be important synergistic mechanisms by which dopamine may contribute to hypoxemia in patients with heart failure: first, by direct impairment of gas exchange and second, by impaired ventilatory compensation.

An alternative mechanism by which dopamine may have reduced minute ventilation may be by reduction of lung water (by augmentation of either cardiac output or urine output), thus decreasing stimulation of pulmonary J receptors, which constitute an important mechanism for hyperventilation in heart failure. This effect might also help explain the difference in responses to dopamine between the healthy subjects and heart failure patients in normoxic conditions.

Our findings may have implications for an understanding of the effects of dopamine receptor agonists in heart failure. The dosage of the dopamine receptor agonist ibopamine in heart failure patients is directed at stimulation of dopaminergic receptors only, without stimulation of α- or β-receptors, similar to the effects of a low-dose dopamine infusion (3 to 5 μg · kg⁻¹ · min⁻¹). Preliminary studies suggested that ibopamine may be beneficial in heart failure. However, a randomized, placebo-
controlled trial of ibopamine in heart failure patients was terminated early because of an unexplained increased mortality rate in ibopamine-treated patients compared with those receiving placebo.26,27 Nevertheless, there is no evidence that respiratory depression contributed to the excess mortality, and at this time, any such supposition is speculative.

A limitation of our study is the absence of measurements of arterial blood sampling to determine the relative contributions of ventilatory depression and ventilation-perfusion mismatching to hypoxemia during dopamine infusion. Measurements of arterial oxygen tension would also more accurately quantify the degree of hypoxemia than would measurements of oxygen saturation, as was done in this study. However, regardless of the causes of the decrease in oxygen saturation and increased PETCO₂, the key finding in this study was that dopamine decreased minute ventilation, despite the fall in oxygen saturation and the increase in PETCO₂, both of which would be expected to increase minute ventilation.

In conclusion, this study demonstrates that dopamine attenuates chemoreflex responses to hypoxia in normal subjects. This inhibitory effect of dopamine more profoundly affects the ventilatory limb of the chemoreflex responses. Inhibition by dopamine of autonomic responses to chemoreflex activation are less striking. Dopamine allows maintenance of voluntary apnea to greater levels of oxygen desaturation. We also report that dopamine depresses minute ventilation and oxygen saturation in heart failure patients even when they are breathing room air. This reduction in ventilation occurs despite a fall in oxygen saturation and a rise in PETCO₂. Increased chemoreflex drive in patients with heart failure and a ventilatory depressant effect of dopamine in hypoxic normal subjects and in normoxic heart failure patients suggests that inhibitory effects of dopamine on minute ventilation are likely to be especially marked in patients with heart failure who are also significantly hypoxic. Low-dose dopamine is widely used in the intensive care setting, most frequently as empirical therapy to improve renal function.10–17 Recognition of the ventilatory effect of low-dose dopamine is important, especially when dopamine is used in hypoxic patients, in patients with tenuous cardiorespiratory status, or in patients being weaned off ventilatory support.

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