Administration of Dopexamine, A New Adrenergic Agent, in Cardiorespiratory Failure*

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The short-term effects of dopexamine hydrochloride, a new synthetic adrenergic agent with predominant β2-adrenergic and dopaminergic properties, were studied in nine patients with inadequately cardiac output during the course of an episode of respiratory failure associated with lung infection. Dopexamine at doses up to 5 μg/kg/min had no significant effect on arterial pressure or cardiac filling pressures, but increased cardiac index from 2.0±0.2 to 2.6±0.2 L/min/m². Left ventricular stroke work increased from 17.3±15 to 22.1±5.4 gm/m² (p<0.01) and systemic vascular resistance index decreased from 3,792±1,035 to 2,194±523 dynes·cm⁻²·m⁻² (p<0.01). The increase in cardiac output was in part related to an increase in heart rate from 91±6 to 102±7 beats/min. Under a mean inspiratory oxygen fraction of 0.48, the PaO₂ decreased from 105±15 to 91±11 mm Hg (p<0.05) as venous admixture increased from 15.8±1.0 to 18.1±1.4 percent (p<0.05). Accordingly, the combination of inotropic, afterload-reducing and renal vasodilating effects of dopexamine can be useful acutely to increase cardiac output in critical conditions. However, its administration can be limited by a dose-related increase in heart rate. Dopexamine, like other catecholamines, alters blood oxygenation and increases venous admixture.

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Dopexamine hydrochloride is a new synthetic catecholamine that has β2-agonist and dopaminergic activities but only weak β1-agonist activity and no α-agonist activity.1 The drug also inhibits the active reuptake of neuronally released norepinephrine (uptake-1). Dopexamine has been shown to exert strong vasodilating effects and also to improve various indexes of myocardial contractility without significantly altering myocardial oxygen balance. Hence, the combination of inotropic, afterload-reducing and renal vasodilating effects can be useful in the management of heart failure.

The cardiovascular effects of dopexamine have been documented in patients with congestive heart failure or after cardiac surgery but less well in critically ill patients with more complex problems. In a recent experimental study, we observed that dopexamine infusion in septic shock could significantly increase cardiac output without altering blood pressure. In these conditions, the drug also appeared to improve arterial oxygenation.12

In this study, we evaluated the hemodynamic and gasometric effects of dopexamine in a selected group of critically ill patients with cardiac respiratory failure associated with an episode of acute respiratory tract infection.

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PATIENTS AND METHODS

The study included nine patients with underlying cardiomyopathy who had an inadequate cardiac output during the course of an episode of acute respiratory failure. Clinical data are presented in Table 1. Each patient had a cardiac index below 2.5 L/min/m² or a disproportionate increase in peripheral oxygen extraction. In each patient, mixed venous oxygen saturation was below 60 percent in the absence of hypoxemia (arterial oxygen saturation ≥92 percent) or anemia (hemoglobin ≥10 g/dl). Patients did not present signs of acute circulatory failure. Acute respiratory failure was primarily due to pulmonary infection as manifested by fever, purulent tracheobronchial secretions, and abnormal chest roentgenogram. In each case, hypoxemia was present, requiring an inspiratory oxygen fraction (FiO₂) of at least 0.4 to maintain a PaO₂≥65 mm Hg. No patient had evidence of bronchospasm. Mean FiO₂ was 0.48 (Table 1). Four patients were already treated with adrenergic agents and seven patients were mechanically ventilated. Four patients survived the ICU stay (Table 1).

In each patient, a Swan-Ganz catheter (7 or 7.5 F, Edwards Laboratories) and an arterial catheter had been previously inserted for routine management of their acute illness. Intravascular pressures and heart rate were recorded on a polygraph (recorder 7404A, Hewlett-Packard). Values were measured at end-expiration. Cardiac output was measured by the thermodilution technique (computer 9520A, Edwards Laboratories) at least in triplicate using cold water and a closed system (Co-Set system, Edwards Laboratories). In mechanically ventilated patients, the bolus injection was started at end-inspiration. After baseline measurements, dopexamine was infused at progressively increased doses of 1 to 5 μg/kg/min, each dose being increased after 20 min. At baseline and at the end of the study period, arterial and mixed venous blood gases were withdrawn to assess blood oxygenation and venous admixture. Derived parameters were obtained by standard formulas.
Table 1—Clinical Data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex/Age</th>
<th>Type of Cardiomyopathy</th>
<th>Associated Treatment*</th>
<th>Mechanical Ventilation</th>
<th>FIO₂</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/50</td>
<td>Ischemic</td>
<td>Dobu 6</td>
<td>+</td>
<td>0.5</td>
<td>Survived</td>
</tr>
<tr>
<td>2</td>
<td>M/66</td>
<td>Ischemic</td>
<td>Dobu 4</td>
<td>–</td>
<td>0.4</td>
<td>Died</td>
</tr>
<tr>
<td>3</td>
<td>M/62</td>
<td>Ischemic</td>
<td>–</td>
<td>+</td>
<td>0.6</td>
<td>Survived</td>
</tr>
<tr>
<td>4</td>
<td>M/64</td>
<td>Ischemic</td>
<td>–</td>
<td>+</td>
<td>0.5</td>
<td>Died</td>
</tr>
<tr>
<td>5</td>
<td>F/64</td>
<td>Ischemic</td>
<td>–</td>
<td>–</td>
<td>0.4</td>
<td>Survived</td>
</tr>
<tr>
<td>6</td>
<td>M/66</td>
<td>Ischemic</td>
<td>–</td>
<td>+</td>
<td>0.4</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>F/71</td>
<td>Dilated</td>
<td>Dobu 15/Dopa 2</td>
<td>+</td>
<td>0.6</td>
<td>Died</td>
</tr>
<tr>
<td>8</td>
<td>F/82</td>
<td>Dilated</td>
<td>Dobu 4</td>
<td>+</td>
<td>0.5</td>
<td>Died</td>
</tr>
<tr>
<td>9</td>
<td>F/62</td>
<td>Dilated</td>
<td>–</td>
<td>+</td>
<td>0.4</td>
<td>Survived</td>
</tr>
</tbody>
</table>

*Dobu = dobutamine; Dopa = dopamine (dosage as μg/kg/min).

Data were analyzed using a one-way analysis of variance followed by a Student's t test for paired data, using the Bonferroni adjustment for repeated measurements. A p value <0.05 was considered statistically significant. Data are presented as mean ± SEM.

RESULTS

The dopexamine administration did not significantly influence arterial pressure (Fig 1) or pulmonary arterial pressure. Pulmonary artery balloon-occluded pressure slightly decreased from 19.6 ± 2.1 to 17.8 ± 1.7 mm Hg (change not statistically significant). Cardiac index increased significantly from 2.0 ± 0.2 to 2.6 ± 0.2 L/min/m². Accordingly, left ventricular stroke work increased from 17.3 ± 1.5 to 22.1 ± 2.4 gm² (p<0.01) and systemic vascular resistance index decreased from 3,792 ± 1,035 to 2,194 ± 823 dynes/cm²-m² (p<0.01). The increase in cardiac output was in part due to a dose-related increase in heart rate from 91 ± 6 to 102 ± 7 beats/min (Fig 1). However, no significant arrhythmia was observed. The increase of the infusion rate above 3μg/kg/min was not clearly beneficial, as only a further increase in heart rate was observed (Fig 1). Left ventricular function, as expressed by the relationship between left ventricular stroke work and pulmonary artery balloon-occluded pressure, improved in six patients, was unchanged in two patients but worsened in one patient who only developed hypotension (Fig 2). This patient (7) with the poorest cardiac function was already treated with catecholamines and died the following day.

During the dopexamine infusion, the increase in cardiac output was associated with an increase in PVO₂, but there was a concurrent increase in venous admixture, so that PaO₂ decreased significantly (Table 2).

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21604/ on 04/28/2017)

**Figure 1.** Effects of dopexamine on mean arterial pressure (MEAN ART.P), pulmonary artery balloon-occluded pressure (PA OCCL.P), cardiac index, heart rate, and stroke index in the 9 patients. *p<0.05.
In eight patients, the dopexamine infusion was continued for up to 60 h at various doses adapted to the clinical requirements and was well tolerated.

**DISCUSSION**

The two adrenergic agents most commonly used today in the critically ill are dopamine and dobutamine. Dopexamine is structurally related to dopamine, but has no \( \alpha \)-adrenergic activity. Therefore, its potential advantage over dopamine is the lack of vasoconstrictive effects which in the otherwise non-hypotensive patient may counteract the beneficial effects of the \( \beta \)-stimulation by an increase in ventricular afterload. With a profile of hemodynamic response closer to dobutamine, dopexamine could have the additional advantage over dobutamine of selectively increasing renal blood flow by its dopaminergic properties.13 Dopexamine has been shown to increase urine output and sodium excretion in patients with heart failure.8 Case reports suggest that urine output could increase also in postoperative patients.14

With such a pharmacologic profile, dopexamine appears to combine the properties of dopamine and salbutamol,9 and is expected to have stronger vasodilating properties than dobutamine. In patients with heart failure, Bayliss et al.9 observed that dopexamine and dobutamine had comparable effects, except for a larger increase in heart rate with dopexamine. More recently, Baumann et al.10 observed that dopexamine produced cardiovascular effects between those produced by dobutamine and sodium nitroprusside. In experimental septic shock, we observed that systemic vascular resistance decreased more with dopexamine and that left ventricular stroke work increased more with dobutamine, consistent with a stronger inotropic effect of dobutamine but the stronger vasodilating effect of dopexamine.12

The present study included a homogeneous group of critically ill patients with insufficient cardiac output during an episode of acute respiratory failure. In these patients, systemic vascular resistance is not as high as may be expected in the absence of infection; thus, the vasodilating effects of dopexamine could be poorly tolerated. We observed that dopexamine usually had no significant effect on arterial pressure but substantially increased cardiac output, indicating a fall in systemic vascular resistance. This effect is similar to that observed in patients with chronic heart failure.5,9,10,14 Despite these vasodilating effects, dopexamine did not significantly alter cardiac filling pressures. In patients with heart failure receiving dopexamine, cardiac filling pressures have been seen both to decrease5,9,10 and to remain constant.7,9 Although arterial and pulmonary artery balloon-occluded pressures remained constant, the significant increase in left ventricular stroke work supported a positive inotropic effect of dopexamine. The left ventricular function did not improve in only one patient with terminal cardiomyopathy. Dopexamine consistently induced a dose-related increase in heart rate as has been consistently observed in other studies.5,11 This chronotropic response may limit its rate of infusion.

In a previous study on dopexamine administration in experimental septic shock, we observed that venous admixture did not increase despite the increase in cardiac output and \( \text{PaO}_2 \) increased significantly. In this previous study, we hypothesized that the improvement in oxygenation may be related to the counteracting effects of dopexamine on some degree of endotoxin-induced bronchoconstriction. In the present study, however, dopexamine increased venous admixture, as has been described with other adrenergic agents.15 Hence, dopexamine does not have a beneficial effect on gas exchange in respiratory failure, at least in the absence of clinically recognized bronchospasm.

The present study indicates that dopexamine can acutely increase cardiac output in the critically ill. Administration of higher doses can be limited by the dose-related increase in heart rate.

We explored only the short-term effects of dopexamine. Although the drug appeared well tolerated when its administration was prolonged, the assessment of

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**Table 2—Effects of Dopexamine on Gas Exchange**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Baseline</th>
<th>Dopexamine, 5 μg/kg/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{PaO}_2 ), mm Hg</td>
<td>105 ± 12</td>
<td>91 ± 11*</td>
</tr>
<tr>
<td>( \text{SaO}_2 ), %</td>
<td>96.1 ± 0.7</td>
<td>95.2 ± 0.8</td>
</tr>
<tr>
<td>( \text{PvO}_2 ), mm Hg</td>
<td>29 ± 1</td>
<td>33 ± 1*</td>
</tr>
<tr>
<td>( \text{SV} ), %</td>
<td>51.0 ± 3.0</td>
<td>56.2 ± 3.7*</td>
</tr>
<tr>
<td>( \text{Qw/Qr} ), %</td>
<td>15.8 ± 1.0</td>
<td>18.1 ± 1.4*</td>
</tr>
</tbody>
</table>

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**Figure 2.** Effects of dopexamine on the left ventricular function (left ventricular stroke work index vs pulmonary artery balloon-occluded pressure).

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**References:**


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**Note:** The references are not included in the natural text representation.
the effects was precluded by the unstable course of these critically ill patients. Two recent reports on the prolonged use of dopexamine in heart failure patients have yielded conflicting results. 16,17

ACKNOWLEDGMENTS: The authors are thankful to Fisons Pharmaceuticals for the generous dopexamine supply and to Michael Pinsky, M.D., for his thoughtful comments.

REFERENCES
16 Murphy JJ, Hampton JR. Failure of dopexamine to maintain haemodynamic improvement in patients with chronic heart failure. Br Heart J 1986; 60:45-49