Low-Dose Dopamine and Oxygen Transport by the Lung

Robert L. Johnson, Jr MD

Dopamine is an endogenous catecholamine that preferentially reduces renal vascular resistance and increases glomerular filtration rate, urine flow, and solute excretion in normal subjects. In contrast to norepinephrine, it increases cardiac output and aortic pressure without raising systemic vascular resistance (Table) and increases rather than decreases renal blood flow. Hence, dopamine was suggested as a potentially valuable pharmacological agent for treatment of cardiogenic and septic shock, particularly in patients who were oliguric. Even at low doses (ie, <5 μg · kg⁻¹ · min⁻¹), at which hemodynamic effects are relatively small, it raises glomerular filtration and causes modest diuresis in normal subjects that might protect against acute renal failure in oliguric patients who are in shock or heart failure. The synthetic catecholamine dobutamine was introduced later and had many features similar to those of dopamine but without preferential renal vasodilation. However, at high infusion rates, dobutamine enhances cardiac output, stroke index, and O₂ transport more effectively than dopamine, and it also minimizes afterload on the left ventricle. Dobutamine now is more often used for hemodynamic support in heart failure or cardiogenic shock, although the 2 drugs are sometimes used together for their complementary effects. Low-dose or so called “renal-dose” dopamine, however, has become widely used in intensive care units for its presumed protective effect on renal function in patients undergoing major surgical procedures, patients with refractory heart failure, and patients with cardiorenal failure who are receiving ventilatory support. In these settings, it is often considered to be relatively free of serious adverse effects. However, as pointed out by van de Borne et al in this issue of Circulation, there are two potentially detrimental effects of low-dose dopamine on oxygen transport that are often overlooked. Dopamine has been shown (1) to impair the ventilatory response to hypoxemia and hypercapnia by a depressive effect on the carotid body and (2) to reduce arterial oxygen saturation at a given alveolar oxygen tension by impairing regional ventilation/perfusion (V/Q) matching in the lung (Table).

The article by van de Borne et al brings these observations into a clearer clinical perspective with better quantification and a more unified interpretation of the different effects of low-dose dopamine on gas exchange. They are not trivial. The effects on carotid body function and on efficiency of alveolar capillary gas exchange have been well documented in the past but are not widely recognized clinically. In the late 1960s, high concentrations of dopamine were measured in the carotid body, higher than any other catecholamine. It was later shown that dopamine inhibits chemoreceptor discharge from the carotid body and very likely has the same effect on aortic bodies. In 1975, Zapata reported that superfusion of isolated carotid bodies with dopamine in Locke solution depresses the frequency of chemoreceptor discharges recorded from the nerve trunk. Complete inhibition of chemoreceptor discharges from the in situ carotid body of the cat could be elicited by infusing a 2-μg bolus of dopamine into the carotid artery. Depression of the ventilatory response to hypoxia by intravenous dopamine infusion in normal humans was reported first in 1978 by Welsh et al. In their study, dopamine also caused a slight but significant decrease in ventilation and an increase in PaCO₂ in normal subjects breathing air.

Huckauf et al reported that dopamine infusions induced hypoxemia in patients with left heart failure, which was primarily explained by an increased alveolar-arterial O₂ tension difference (A-aPO₂), presumably from uneven regional matching of blood flow to alveolar ventilation (ie, uneven distribution of V/Q ratios). However, hypoxemia was aggravated by a small but statistically significant rise in arterial PCO₂. Shoemaker et al have reported a progressive decrease in arterial Po₂ with increasing rates of dopamine infusion in critically ill patients after major surgery, which was also attributed to uneven V/Q matching in the lung.

In summary, available data from multiple sources now indicate that dopamine infusions in critically ill patients can interfere with 2 important protective mechanisms against a fall in arterial O₂ saturation in the presence of uneven distribution of alveolar ventilation: (1) depress local vasoconstriction in response to alveolar hypoxia, which normally keeps perfusion appropriately matched to ventilation in the lung, and (2) depress the chemoreceptor drive to ventilation normally induced by arterial hypoxemia and probably hypercapnia. As pointed out by van de Borne et al, the 2 effects are synergistic. Both mechanisms can usually be counterbalanced by modest use of supplemental oxygen if substantial anatomic right-to-left shunts are not present. In mechanically ventilated patients, depression of ventilatory drive is not a problem. In some instances, reduced ventilatory drive during mechanical ventilation can be beneficial by reducing any tendency to fight the ventilator. However, problems can arise when the patient is taken off mechanical support. The patient in whom the carotid body is functionally ablated by a continuous dopamine infusion actually may be
Comparing Effects of Catecholamines on Hemodynamics and Gas Exchange

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<th>Norepinephrine</th>
<th>Low-Dose (&lt;=5 mg \cdot kg^{-1} \cdot min^{-1})</th>
<th>High-Dose (&gt;5 mg \cdot kg^{-1} \cdot min^{-1})</th>
<th>Dobutamine</th>
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A-aPO2 indicates alveolar-arterial O2 tension difference; <=, no change; <=, increase; <=, decrease; <=, more profound increase; <=, more profound decrease.

There is another intriguing aspect of the results obtained by van de Borne et al. in patients with heart failure that was not discussed in detail. Ventilation was significantly depressed in normoxic patients with heart failure by low-dose dopamine infusion, which resulted in a fall of arterial O2 saturation and a significant rise in end-tidal PCO2. The latter results suggest a significant depression of the ventilatory response not only to O2 but also to CO2. The data of Huckauf et al. also suggest that dopamine suppresses the carotid body response to hypercapnia as well as hypoxemia. This is consistent with observations in cats that dopamine significantly reduces chemoreceptor drive in response to both hypoxemia and hypercapnia. This has not been systematically examined in humans, particularly in patients with mechanically abnormal lungs. An increase in mechanical load imposed on respiratory muscles can amplify an impaired ventilatory response to CO2, whereas the effect may be difficult to detect in subjects with normal lung mechanics.

None of the data presented by van de Borne et al. imposes a contraindication to appropriate use of low-dose dopamine in critically ill patients as long as the possible side effects on gas exchange are recognized and avoided. It seems prudent to avoid low-dose dopamine when weaning patients from mechanical ventilation unless arterial O2 saturation is closely monitored. Perhaps the most important message that should be derived from the study by van de Borne et al. is an expanded need to define more clearly the appropriate clinical uses for renal-dose dopamine. Although there is a theoretical rationale for use of low-dose dopamine, its clinical efficacy remains largely unsupported by data. In view of the potentially detrimental effects, the clinical rationale for use of renal-dose dopamine should be more clearly defined, as pointed out in an excellent review by Denton et al.

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References


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