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Renal Effects of Dopamine

OFTEN the clinician is faced with the situation in which cardiac output is compromised and urine output is minimal, despite adequate intravascular volume. What does the clinician do? He may decide to infuse dopamine with the anticipated result that both cardiac output and urine output will increase. But is the increase in urine output the result of the improved cardiac output or of specific renal effects of dopamine?

Goldberg and co-workers have studied the effects of dopamine in a variety of experimental animals as well as in humans.[1] Initial studies demonstrated that a sodium diuresis could be produced in patients in congestive heart failure by the infusion of dopamine.[2] Subsequent investigations over the past 20 years have shown that dopamine causes direct vasodilation in the canine renal vascular bed by action on specific dopaminergic receptors. But dopamine is known not only to affect dopaminergic receptors but also to stimulate alpha and beta receptors with the result that both cardiac output and peripheral resistance may be increased. Whether the effects of dopamine on the kidney are related to the combined effects of dopamine or specifically to the renal effect was investigated by Hilberman and associates as presented in this issue of ANESTHESIOLOGY.[3] They infused either dopamine or dobutamine in 12 patients who underwent cardiac operation. They chose the dose of either agent in order to produce an increase in cardiac output, with the net result that cardiac output was the same in both groups of patients. They found that with 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine, there was a significantly greater diuresis, natriuresis, and kaliuresis than when 3.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dobutamine was infused. However, both glomerular filtration rate and effective renal plasma flow were similar in both groups of patients.

The authors suggest that the data demonstrate that dopamine causes a direct tubular effect in these patients and no selective renal vasodilator effects are seen. While the number of patients is small, this well-done study would support the authors' contention. However, the authors, by process of elimination, believe that the direct action of dopamine on tubular solute transport is the most likely explanation for their results. While these experiments could not examine tubular function directly, neither could they examine distribution of blood flow within the kidney directly, another plausible explanation for their results.

The laboratory of Barger over the years has examined the role of blood flow alterations within the kidney. By using the inert gas washout technique and silicone cast studies, they were able to show that alterations in distribution of blood flow could alter kidney function.[4–6] However, the concept of alteration of intrarenal blood flow is not as simple as one might believe. Beeuwkes and Bonventre in a series of elegant experiments demonstrated that the vascular–tubular organization of the kidney is most complex.[7] They showed that sections of tubules had blood supplies that arose from other than the parent glomerulus and, therefore, function in one part of the tubule could be altered by blood flow from another glomerulus. How a dopamine infusion specifically acts on intrarenal vessels in patients after cardiac surgery has not been studied, but certainly small alterations in distribution that are not detectable by current techniques could occur without changes in total blood flow, resulting in significant alterations in solute excretion.

A second important consideration in an explanation of the results presented is the role of the adrenergic nervous system in renal sodium excretion independent of changes in systemic or renal hemodynamics induced by catecholamines. There is clear evidence that the direct infusion of alpha- and beta-adrenergic agonists alter sodium excretion and morphologic studies demonstrate adrenergic innervation of both proximal and distal tubules.[8] Whether the effects seen in this study

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are due to dopamine activation or to alpha- and/or beta-receptor stimulation is unknown.

More insight into the mechanism(s) responsible for the results of Hilberman *et al.* may be forthcoming. It was not until we had specific blockers of alpha- and beta-receptors that we could tell the importance of the adrenergic nervous system in cardiovascular control. Now, we not only have alpha- and beta-receptor agonists and antagonists, but beta-1, beta-2, alpha-1, and alpha-2 agents. Similarly, new synthetic blocking agents of the dopaminergic system are being developed.

Dopamine has not only DA-1 receptor activity (postsynaptic vasodilation, renal and mesenteric beds) and DA-2 activity (presynaptic inhibition of norepinephrine release) but also alpha- and beta-adrenergic receptor activity.[9] The use of a dopamine infusion with activation of multiple receptors makes the mechanism responsible for the diuresis and natriuresis seen in this study complex. Recently, specific agonists and antagonists of DA-1 and DA-2 have been synthesized, and some, even infused into humans.[10,11] The use of such specific agonists and antagonists of the dopaminergic system will allow better definition of the mechanism(s) responsible for the effects seen by Hilberman *et al.*

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