Dobutamine

Too Dangerous for “Routine” Administration?

RISK factors associated with the administration of positive inotropic drugs (PIDs) have often been studied; the indications for which dobutamine and other PIDs are administered to patients undergoing cardiac surgery are less well defined.1–4 Depending on the center in which the surgery takes place, PIDs may be administered to as few as 5% or to as many as 100% of patients undergoing elective coronary artery bypass surgery. Prescribing habits vary markedly by physician and by center. Some initiate therapy with dobutamine, others with epinephrine, dopamine, dopexamine, milrinone, enoximone, olprinone, norepinephrine, or levsimendan.4,5 Even when practicing with the same set of surgeons within the same center, individual anesthesiologists may demonstrate a widely varying threshold for initiating therapy with PIDs.2 These seemingly haphazard prescribing habits seem consistent with a belief that patients who are given PIDs have no worse outcome than patients who do not receive them. In this issue of Anesthesiology, Fellahi et al.6 attempt to test this assumption.

Most PIDs (including dobutamine, inamrinone, and milrinone) were licensed by drug regulatory agencies for treatment of acute heart failure or acute exacerbations of chronic heart failure. If we assume that clinicians prescribe PIDs appropriately, the patients receiving them should be “sicker” and have a worse outcome than those who do not receive them. Nevertheless, in a small sample of patients that provided inadequate statistical power, a negative outcome from the decision to administer PIDs was not detected.1

In any case, the critical hypothesis must be properly stated. For patients with low cardiac output syndrome after heart surgery, the alternatives to PIDs include intraaortic balloon counterpulsation, ventricular assist devices, or death. None of these are attractive alternatives. Unlike the case for patients with severe chronic heart failure who are not transplant candidates, there is no consensus that assist devices are safer than PIDs for patients with acute heart failure after cardiac surgery.7 Therefore, a critical and testable hypothesis must be that patients who can be appropriately managed without PIDs will have a worse outcome if they receive PIDs. Fellahi et al.6 used a propensity scoring technique to approach this hypothesis. They attempted to compare the outcome after coronary artery surgery in otherwise similar patients who either did or did not receive a PID (nearly always dobutamine). Their conclusion was that, all other things being the same, patients had worse outcome when they received PIDs. But what do these results mean for the practicing clinician?

First, these results relate almost exclusively to the use of dobutamine and may not apply to other PIDs. Although often used, dobutamine may not be the best agent. We know that dobutamine has different hemodynamic actions from other β-adrenergic agonists. For example, dobutamine has a marked tendency to produce tachycardia, much more so than epinephrine, inamrinone, or milrinone, and elevated heart rate has long been associated with worsened outcome in patients with coronary artery disease.8–12 Dobutamine differs from phosphodiesterase inhibitors in how it interacts with the calcium salts that some clinicians administer at the time of separation from cardiopulmonary bypass.13 Dobutamine is also a partial agonist with the potential for inhibiting the response to other β-adrenergic agonists.14

Second, these authors have not excluded from their analysis those patients to whom nearly every clinician would administer a PID. That is, there are patients who require PIDs, and there really is not a suitable alternative (other than an alternative PID). Until suitable options are available, we will continue to administer PIDs to these patients.

Third, there may come a time when we can identify which patients may derive benefit and which patients may derive harm from dobutamine and other PIDs. Genetic studies have already identified a particular β-adrenergic receptor polymorphism in patients undergoing coronary artery bypass surgery that associates with the use of larger doses of β-adrenergic agonists.15

I think the most important lesson to be gleaned from this report is that no patient should receive dobutamine after heart surgery unless there is a medical indication. There are centers where it is routine practice to initiate an infusion of 5 μg·kg⁻¹·min⁻¹ dobutamine at the time of separation from cardiopulmonary bypass in all patients, not just those with depressed cardiac function. The data of Fellahi et al., consistent with previous work...
in chronic heart failure patients, provide a very strong argument against administering dobutamine to any patient who does not require the agent to improve the odds of survival. The authors argue that there should be guidelines and protocols by which dobutamine should be administered. I would have the more mundane hope that patients will receive this agent only for an indication, rather than based on a whim or a routine practice.

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References