Alpine Anesthesia: Can Pretreatment with Clonidine Decrease the Peaks and Valleys?

This issue of Anesthesiology contains two articles1,2 which champion the use of oral clonidine premedication as an effective method to decrease the frequency and severity of hypertension and tachycardia in patients who are especially vulnerable to the sequelae of these complications.

Clonidine is an antihypertensive agent which acts by multiple and complex mechanisms, including a prominent central alpha2-adrenergic agonist action combined with some reduction in peripheral adrenergic transmission. Overall, it reduces sympathetic nervous system activity and decreases circulating catecholamines, plasma renin activity, and aldosterone. The acute administration of clonidine produces modest reductions in blood pressure, heart rate, stroke volume, and cardiac output, and systemic vascular resistance is decreased in patients in the upright position. The pharmacology of clonidine is detailed in the discussion sections of these manuscripts, and it would be repetitive to also present that material here. Rather, this observer would prefer to comment on the experimental designs, the importance of the findings, and the possible applications for the results presented in these reports.

Flacke et al.1 studied two groups of patients before, during, and after coronary artery bypass graft operations performed under narcotic-oxygen anesthesia. One group received clonidine, a single dose orally as premedication and a second dose by nasogastric tube intraoperatively, and efforts were made to manage both groups similarly thereafter. In brief, those who received clonidine required less sedation preoperatively, and they required approximately 40% less sufentanil for the maintenance of anesthesia. Plasma catecholamines were rather consistently reduced in those receiving clonidine, and intraoperative and postoperative hypertension which required treatment was also less frequent in those receiving clonidine.

Ghignone et al.2 studied the influence of clonidine premedication on perioperative hemodynamics in treated hypertensive patients undergoing a variety of operative procedures in whom anesthesia was maintained with nitrous oxide-oxygen-isoflurane supplemented with fentanyl. Premedication with clonidine resulted in moderate decreases in systolic and diastolic blood pressures and an increase in sedation preoperatively. Clonidine was more effective than intravenous lidocaine plus fentanyl for blunting the tachycardia associated with tracheal intubation. Clonidine also decreased the lability of heart rate and blood pressure in hypertensive patients (the anesthetic records of hypertensive patients have been described by some as “alpine anesthesia,” because the blood pressure pattern often looks like a series of mountains and valleys), and heart rate remained decreased in the early postoperative period. The requirement for isoflurane was decreased by approximately 40%, and narcotic supplementation was required less frequently in those treated with clonidine.

This observer was struck by two factors which were common to both of these reports. First, the remarkable complexity of the pharmacology of modern anesthetic practice is evident throughout. With the exception of clonidine pretreatment, the anesthetic care described in these reports probably does not differ fundamentally

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from that which is practiced by many anesthesiologists, and it is typified by the need to understand the pharmacology of a remarkable variety of drugs in addition to the anesthetics per se. In this context, the possibility for drug interactions cannot be overlooked, and it is likely that many such potential interactions would not be observed in the small sample sizes studied here. This is not to condemn the present studies, but it should serve as a reminder that there may well be interactions which were not identified in these initial studies.

A more important concern relates to the absence of double blind experimental protocols. Both reports place considerable importance on the observation that clonidine decreased the need for additional hemodynamic interventions, but the possibility for investigational bias is difficult to eliminate from such an approach. Indeed, the vigilance and foresight of the anesthesiologist could certainly influence the need for additional hemodynamic interventions, and the enthusiasm and interest of the investigative team might well be influenced by the knowledge that a specific patient was receiving clonidine treatment. Future studies will need to control for this insidious and subtle possibility, now that the relative safety of acute clonidine treatment combined with general anesthetics has been demonstrated.

One of the most interesting findings here is the potential value of clonidine pretreatment for the amelioration of postoperative hypertension and/or tachycardia which results from the sympathetic stimulation associated with emergence from anesthesia. All too often, hemodynamics are controlled precisely throughout an operation, but precise control is followed by a remarkably unstable interval between anesthetic emergence and the time that a fragile patient can be transported to, and stabilized in, the recovery room or intensive care unit. This would appear to be a fruitful area for further improvement in perioperative care, and these results suggest that clonidine may be quite useful for this purpose.

The results reported here apply directly to patients with hypertension or coronary artery disease requiring coronary bypass graft operations, but they may have important implications for other patients who are at risk for complications which might arise from tachycardia and hypertension in the perioperative interval. Possible uses for clonidine pretreatment might include patients undergoing neurosurgical procedures, such as intracranial aneurysm clipping, or vascular operations, such as carotid endarterectomy or abdominal aortic aneurysmectomy; procedures which are often accompanied by postoperative hypertension, which is both undesirable and difficult to control without aggressive antihypertensive measures. However, each of these potential applications will require carefully designed and well-controlled studies to document the relative merits of this therapy. Finally, the two studies reported here should stimulate further evaluations of this antihypertensive agent (which is limited by the lack of availability of an intravenous formulation that is approved for use in this country), and of a variety of others which might serve as well or better to provide improved perioperative, and not just intraoperative, care to patients who are at risk for the complications which are associated with hypertension and tachycardia.

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References