Is Gaining Control of the Autonomic Nervous System Important to Our Specialty?

IN this issue of Anesthesiology, Parlow et al. report the effects of clonidine in a group of hypertensive patients with known impaired baroreflexes. Clonidine administration improved early postoperative baroreflex function compared with a control group of hypertensive patients that received a placebo. Perioperative hemodynamic variations were reduced in the patients receiving clonidine. Improved baroreflex function and less perioperative hemodynamic variability are not necessarily independent of one another, but they are most likely closely related.

The arterial baroreflex operates as a rapid control system to adjust cardiac output and peripheral resistance to maintain arterial pressure around a homeostatic “set point.” Surgical stimulation or blood volume losses lead to changes in blood pressure (BP) that are subsequently opposed or corrected by baroreflex compensatory mechanisms. A reduced baroreflex “gain” or sensitivity impairs the compensatory response and results in greater hemodynamic fluctuations. Not surprisingly, it is well documented that patients with impaired autonomic reflexes (e.g., patients with diabetes) have greater intraoperative BP lability compared with autonomically intact patients. In addition, it now is recognized that many of the sedative, hypnotic drugs used for induction of anesthesia and all of the potent inhaled anesthetic gases in clinical use impair autonomic reflex responses. Thus, surgical patients with an underlying impairment of the autonomic nervous system (ANS), such as patients with hypertension, who receive a general anesthetic are likely to have substantial intraoperative BP lability during surgical stress or blood loss.

The statement that clonidine, or other α₂ agonists, improves hemodynamic “stability” perioperatively is correct but needs clarification. The primary effect of clonidine is to reduce sympathetic activity or “tone.” This lowers BP and often reduces heart rate (HR). In the majority of studies that evaluated α₂ agonists during anesthesia, hypotension was common, and vasopressors, inotropes, and more fluid administration were necessary to support BP. These effects can be magnified with volatile anesthetics that directly relax vascular smooth muscle. The reported improved hemodynamic “stability” associated with clonidine should be more specifically described as smaller hemodynamic fluctuations (especially tachycardia and hypertension) around a lower basal BP (and sometimes a lower resting HR) in the perioperative period.

The question remains, how does clonidine contribute to smaller hemodynamic variations when its common effect is to inhibit sympathetic vasoconstrictor outflow? To answer this question, a greater depth of knowledge about human baroreflex physiology and about the influence of clonidine on the ANS is required. The efferent limb of the baroreflex consists of the parasympathetic (vagal) and sympathetic nervous systems. The sympathetic component is primarily involved in adjusting peripheral vascular tone and plays a lesser role in the reflex regulation of HR and cardiac output. The vagal component is primarily involved in regulating HR. For example, reflex slowing of HR during baroreceptor loading is virtually abolished after administration of atropine, but it is not appreciably altered after blocking cardiac sympathetic innervation with a thoracic epidural anesthesia. A similar predominance of vagal control of HR can be demonstrated during baroreceptor unloading, although the sympathetic nervous system is involved to a degree.

Parlow et al. used a sequence technique test to provide insight into the vagal component of the baroreflex. They provided further insight into cardiac vagal function by demonstrating an increase in the high frequency component (0.15–0.5 Hz) of the HR power spectrum in


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the clonidine-treated patients. Previous work has substantiated the ability of clonidine to potentiate vagally mediated responses, presumably via a central effect on vagal motoneurons.9,10

Clonidine also decreases basal levels of sympathetic activity and decreases the sympathoexcitation associated with a painful stimulus.11 Although Parlow et al.1 did not evaluate the effect of clonidine on reflex sympathetic activation, our previous work has demonstrated that clonidine does not interfere with the ability of the baroreflex to increase sympathetic outflow during hypotension.11 Thus, although clonidine changes the ANS “set point” so that HR and BP are decreased at rest, the sensitivity of the sympathetic component of the baroreflex is maintained, and the sensitivity of the vagal component of the reflex is either maintained or increased. Consequently in most studies, the use of perioperative clonidine has resulted in a lower BP and HR and in fewer intraoperative hemodynamic variations. Based on the study of Parlow et al.,1 the latter effect can be attributed to the ability of clonidine to maintain reflex cardiac-vagal responsiveness perioperatively.

The ability of clonidine to improve the sympathovagal balance by decreasing sympathetic tone and increasing vagal control in surgical patients has a broader and still emerging importance to our specialty. This balance may have important effects on cardiac morbidity and mortality in surgical patients intra- and postoperatively. We have already learned that short-term β-adrenergic blockade improves short-term morbidity and 2-yr mortality in coronary artery disease (CAD) patients undergoing non-cardiac surgery.12,13 Similarly, preliminary data have suggested that low HR variability (HRV), an index of impaired cardiac-vagal tone, is an independent predictor of mortality after non-cardiac surgery.14,15 The use of α2 agonists in CAD patients undergoing both cardiac and noncardiac surgery has improved cardiac morbidity and is likely a result of their effect of improving the sympathovagal balance.16-18 Thus, there appears to be an important association between the ANS and cardiac outcomes after anesthesia and surgery.

This association is well established in the field of cardiology, where the focus has been on understanding the factors involved in survival of patients after myocardial infarction (MI).19-21 There is a strong experimental basis for attributing a decreased sympathetic-increased vagal tone to an improved cardiac outcome after MI.20 In dogs with a previous MI, the occurrence of malignant arrhythmias during subsequent ischemic episodes was significantly less in the animals with preserved vagal-cardiac reflexes. Moreover, when cardiac vagal tone was enhanced, either pharmacologically or by direct cardiac vagal nerve stimulation, ischemia-induced ventricular fibrillation was reduced.20 A similar benefit has been noted in dogs subjected to an exercise program that resulted in an improvement in cardiac–vagal reflexes. Presumably, preserved cardiac vagal tone or vagal reflexes opposed the sympathetically mediated malignant arrhythmias.

There also is strong evidence in patients that autonomic balance and vagal reflexes influence morbidity and mortality after MI. For example, a recent prospective, multicenter study has documented that the resting cardiac vagal tone and the “gain” or sensitivity of cardiac vagal reflexes have a prognostic value for long-term survival after MI.21 This was independent of known predictors of adverse outcomes, including low ejection fraction and ventricular arrhythmias. Patients surviving MI who had either low HRV or low baroreflex sensitivity had an increased risk of subsequent sudden cardiac death. It is theorized that a favorable autonomic balance (i.e., decreased sympathetic or increased vagal activity) restrains the genesis of malignant arrhythmias that are so often responsible for sudden cardiac death. In addition, the pattern of myocardial ischemia also might be influenced by autonomic “tone.” Patients with CAD and impaired cardiopulmonary reflex regulation of coronary vascular resistance have more frequent and more prolonged daily episodes of ischemia than patients who have preserved cardiopulmonary reflex function.22 Preserved vagal reflexes (e.g., the Bezold-Jarisch reflex, which is initiated from sensory receptors in the inferior-posterior regions of the heart during ischemia) have been associated with slowing of the HR, reduced myocardial oxygen demand, and a suppression of sympathetic hyperactivity.

Therefore it seems that we should consider autonomic balance in our surgical patients with, or at risk for, coronary artery disease. The current study by Parlow et al.1 used the α, agonist clonidine to reduce basal sympathetic outflow and to maintain vagally mediated baroreflex control of HR. This resulted in better perioperative hemodynamic control in these patients. The bigger picture may be that an intervention that favorably modifies sympathovagal balance has additional benefits in improving morbidity and mortality from anesthesia and surgery in “high-risk” patients. Of course, there are other approaches to influence sympathovagal balance in our patients. Thoracic epidurals have been used to block cardiac sympathetic outflow, and this has decreased the

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incidence of ischemia and the severity of angina in patients with CAD. Pharmacologic interventions that block β-receptors or enhance vagal outflow (e.g., scopolamine) also are available to the practitioner. Thus, we need to consider the importance of “gaining” control of the ANS in our “at risk” patients to improve short-term outcome (as demonstrated by Parlow et al.) and, potentially, long-term cardiac morbidity and mortality. The latter possibility awaits an adequately powered, prospective evaluation.

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References


