CON: Propofol Is Better Than Etomidate for Induction in Cardiac Surgical Patients

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Abstract

There is an ongoing debate regarding the choice of ideal induction agent between propofol and etomidate for cardiac surgical patients. Etomidate appears to be better than propofol as the induction agent due to the superior hemodynamic stability. However, the adrenal suppression due to etomidate can pose challenges to the anesthesiologist in certain clinical situations.

Keywords
- cardiac surgical
- etomidate
- induction
- propofol

Introduction

The choice of an ideal induction agent in cardiac surgical patients is not always straight forward. The comparison between propofol and etomidate as the preferred induction agent in cardiac surgical patients is difficult and the evidence is varied. There are only a few published studies comparing the perioperative effects of etomidate and propofol in cardiac surgical patients.[1,2] The evidence in this area is conflicting, possibly reflecting different experimental setups along with variations in anesthetic techniques, drug dosages, and variations in timing and techniques of measuring clinical data.[3,4] Furthermore, a few studies have some degree of methodological drawbacks such as retrospective design, selection biases, small sample sizes, and failure to blinding.

Propofol is undoubtedly one of the most popular intravenous anesthetic agents for induction and maintenance of anesthesia.[5,6] In a recent survey, propofol in combination with an opioid was the most popular choice of anesthetic techniques for off-pump coronary artery bypass grafting operation.[7] However, etomidate is an induction agent known for its smooth intubating conditions and cardiovascular stability. It has a very high therapeutic index of safety, among all the other available induction agents. It has a favorable kinetic profile of producing rapid onset and offset of action. In comparative studies with other anesthetic drugs, etomidate is usually described as the drug that causes the least changes in all hemodynamic variables.[1,2,8] Patients who have hypovolemia, cardiac tamponade, or low cardiac output probably represent the population for whom etomidate is better than propofol. In certain situations, the advantages of etomidate outweigh those of propofol like emergency use situations in which rapid induction is essential in cardiac surgical patients.[9]

Various studies have evaluated the hemodynamic effect of propofol and etomidate.[1-3]The hemodynamic effects of propofol have been investigated in American Society of Anesthesiologists class I (normal and healthy) and class II (mild systemic disease) patients, elderly patients, patients with coronary artery disease and good left ventricular function, and patients with impaired left ventricular function. Most studies have demonstrated significant reductions in systemic vascular resistance (SVR) (9–30%), cardiac index (CI), stroke volume, and left ventricular stroke work index after propofol. Although controversial, the evidence points to a dose-dependent decrease in myocardial contractility.[2] Transient hypotension after propofol administration is common. Most anesthesiologist can manage this hypotension

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with fluids and small dose of vasopressors. However, the effects of such postinduction hypotension on patient outcome need to be determined. Reich et al observed in a study including 2,406 patients that those who had postinduction hypotension had prolonged postoperative stay and/or death in comparison to those without postinduction hypotension. It was concluded in this study that propofol be avoided for induction in patients who present with baseline mean arterial pressure (MAP) < 70 mm Hg and to avoid severe hypotension, alternatives to propofol anesthetic induction be considered like etomidate.[10] Alcock et al found that in patients treated with antiplatelet agents for cardiovascular comorbidities undergoing major noncardiac surgery, intraoperative hypotension was identified as one of three independent predictors of intraoperative myocardial ischemia and necrosis assessed using postoperative troponin T levels.[11] Given the high risk of poor outcome after postinduction and intraoperative hypotension, the ideal induction agent would avoid any major deviation from baseline hemodynamic parameters.[1] The use of etomidate in doses of 0.15 to 0.30 mg/kg both in healthy subjects or patients who have compensated ischemic heart disease did not produce any significant change in variables such as heart rate, pulmonary artery pressure, pulmonary capillary wedge pressure, left ventricular end-diastolic pressure, right artery pressure, CI, SVR, pulmonary vascular resistance, and left ventricular dP/dt. Compared with other anesthetic agents, etomidate produces the least change in the balance of myocardial oxygen demand and supply.[12] Systemic blood pressure remains unchanged in most studies. In a randomized controlled trial by Hannam et al found that propofol caused a 34% greater reduction in MAP-time integral from baseline after induction of anesthesia than etomidate, despite more frequent use of vasopressors with propofol, confirming the superior hemodynamic profile of etomidate in this context.[1] Haessler et al compared the effect of etomidate with propofol combined with fentanyl, respectively, in patients with severe coronary artery disease. The study was terminated early owing to myocardial ischemia in two patients who were induced with propofol.[13] Seitz et al randomly assigned 20 patients scheduled for coronary artery bypass grafting to induction with propofol and fentanyl or etomidate and fentanyl plus midazolam. Even with a slow titration of propofol, 5 of 10 patients needed active treatment for hypotensive episodes.[14]

In patients with valvular heart lesions, the maintenance of preload is desired for stenotic and regurgitant lesions. Preservation or even increasing afterload is the therapeutic goal for stenotic lesions, such as aortic stenosis, hypertrophic obstructive cardiomyopathy, and mitral stenosis. Etomidate in comparison to propofol would appear to be the ideal induction agent in such patients. In a randomized controlled, double-blind, prospective study of anesthesia induction, in patients with severe aortic stenosis by Bendell et al, it was found that propofol is twice as likely as etomidate to evoke hypotension in anesthesia induction with severe aortic stenosis.[3] Propofol can have negative effect on the myocardial contractility but etomidate does not have such negative effect.

Patients with congestive heart failure have two specific concerns: they are dependent on high sympathetic tone and often are treated with angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers.[15] Angiotensin-converting enzyme inhibitors decrease the sympathetic nervous system reactivity and put patients at high risk of postinduction hypotension. Compared with propofol, etomidate has been shown to maintain the sympathetic tone after usual induction doses, whereas propofol decreases this tone. Ebert et al studied the sympathetic response to induction of anesthesia with propofol and etomidate by using microneurography to measure the sympathetic tone.[16] Propofol-induced hypotension is mediated by inhibition of sympathetic nervous system and impairment of baroreflex regulatory mechanism. Etomidate maintains hemodynamic stability through preservation of both sympathetic outflow and autonomic reflexes. There is, however, emerging evidence that propofol may enhance antioxidant activity in the heart and may prevent lipid peroxidation after ischemia and reperfusion, offering a potential protection of the heart. There is no evidence of such role by etomidate.

Hence, it is an established fact that etomidate often is the favored induction agent for patients who are hemodynamically compromised because of its relative cardiovascular stability. However, there is ongoing debate about its use in critically ill patients because of its inhibition of adrenal steroidogenesis.[6,9]Etomidate infusion and single injections directly suppress adrenocortical function, which interferes with the normal stress response.[17] Blockade of 11β-hydroxylation mediated by the imidazole radical of etomidate results in decreased biosynthesis of cortisol and aldosterone.[18,19] There is universal agreement and strong evidence that etomidate causes adrenal suppression even at low blood levels and even after a single bolus. There is also reasonable evidence that the duration of adrenal suppression lasts significantly longer than the hypnotic effect. However, the intensity of this suppression and its clinical significance remain inconsistent and inadequately quantified in cardiac surgery. Several studies have observed that due to the adrenal steroid synthesis inhibition by etomidate, its use in trauma patients or patients with sepsis translates to increase in morbidity and mortality.[17-20] Such patients often have a minimal physiologic reserve and may develop hemodynamic perturbations because of suppression of the adrenal axis. Cardiac surgery and the initiation of cardiopulmonary bypass are known stimulators of the inflammatory response.[21] Catecholamine and stress hormone levels are increased in patients undergoing bypass. These endogenous cytokines, such as cortisol, are thought to play a role in the maintenance of vascular tone. The anesthetist using etomidate often wonders whether the impairment of these stress hormones will contribute to the increase in the vasopressor/inotropic requirement in the postoperative period, will the consequences of vasoconstriction, such as ischemia, lead to increased morbidity, will the duration of mechanical ventilation increase, will there be more ischemia-reperfusion injury, and ultimately will all this lead to increased mortality.

Few studies have found that the use of etomidate was associated with a substantially increased risk for 30-day mortality, cardiovascular morbidity, and prolonged hospital stay in noncardiac surgery like Komatsu et al, but the factors in cardiac surgery vary from that in noncardiac surgery.[22] The evidence of postoperative adverse outcomes by using etomidate as an induction agent in noncardiac surgery cannot be extrapolated

to cardiac surgery. Wagneret al studied the postoperative outcomes of the use of etomidate in patients undergoing cardiac surgery and found that single use etomidate is not associated with severe hypotension, longer mechanical ventilation hours, longer length of hospital stay, or in-hospital mortality.[23] Basciani et al found that in patients undergoing elective cardiac surgery, laboratory indicators of etomidate-induced adrenal insufficiency do not translate into increased vasopressor requirement or inferior early outcomes.[8] Similarly, Komatsu et al found that etomidate was not associated with increased incidence of postoperative atrial arrhythmia or increased intensive care unit or hospital stay.[24] Evidence for postoperative systemic inflammatory response syndrome (SIRS) due to adrenal insufficiency is of particular relevance for patients after on-pump cardiac surgery. It is well known that on-pump cardiac surgery per se is a risk factor for postoperative SIRS and infection. Heinrich et al found that there is no evidence for differences in key clinical outcome in cardiac surgery patients based on anesthesia induction with or without administration of a single dose of etomidate.[4]

Summary

Etomidate appears to be better than propofol as the induction agent due to the superior hemodynamic stability. Hypotension after induction of patients with valvular heart disease and congestive heart failure has been associated with increased morbidity and mortality. In the current era, when the cardiac anesthesiologist encounters patients with severe comorbidities, the maintenance of a stable hemodynamic profile during the induction of anesthesia is very important. Although it is established that etomidate causes adrenal suppression, there is little evidence for differences in key clinical outcome in cardiac surgical patients based on anesthesia induction with a single dose of etomidate.

Conflict of Interest
None.

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