Oxygenated multidose delivery of crystalloid esmolol cardioplegia as an alternative to high potassium cardioplegia

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Cardioplegia is used as a myoprotective agent for the alleviation of surgically induced ischemic injury, incurred during cardiac operative procedures, to allow the functional preservation of the myocardium. These solutions allow for the rapid electromechanical arrest of the myocardium through alteration of cellular electrochemical gradients.¹ Most cardioplegic solutions use a high potassium content to arrest the heart.² The use of hypothermic potassium cardioplegia in adult cardiac surgery increases the safely available intraoperative time and has been correlated with improved postischemic myocardial functional recovery and reduced postoperative mortality.³

Potassium-induced arrest maintains the heart in a depolarized state, significantly decreasing the energy demand of the myocardium, but basal metabolic energy requirements are sustained and thus still constitute a significant energy expenditure.⁴ The advantages of cardioplegic arrest in providing a bloodless field are tempered by the fact that depolarization also leads to the alteration of ion flux across the sarcolemmal membrane and is associated with both increased cytosolic calcium accumulation and the significant depletion of cellular high-energy (adenosine triphosphate) reserves.⁵⁻⁹

The use of blood cardioplegia is currently the criterion standard with which all cardioplegic formulations must be compared, and its benefits relative to crystalloid cardioplegia have been extensively reported.¹⁰⁻¹³ Similarly, the relative contributions of hypothermia (cold, warm, and tepid cardioplegia) and the route of administration of cardioplegia (retrograde, antegrade, and combined retrograde and antegrade delivery) have been examined.¹⁴⁻¹⁸ The applicability of high-potassium cardioplegia to the neonatal and immature heart remains poorly defined and will not be addressed here, but the reader is directed to reviews by del Nido¹⁹ and Hammon²⁰ and the recent reviews of Allen and colleagues²¹ and Ihnken²² for further information.

Despite continuous improvements in surgical technique and cardioplegic formulations, the inadequacies of current intraoperative myocardial protection protocols and formulations, most of which maintain as their basis high-potassium depolarizing arrest, remain a concern. Novel myoprotective protocols to allow enhanced functional recovery of the myocardium after ischemia and reperfusion continue to be needed. In this issue of the *Journal*, Bessho and Chambers²³ present evidence in favor of the use of oxygenated multidose crystalloid esmolol cardioplegia to induce cardiac arrest as an alternative to St Thomas' Hospital cardioplegic solution No. 2.

Esmolol is an ultra-short acting (9-minute half-life) cardioselective β -blocker that is rapidly hydrolyzed by an esterase in the blood cell cytosol to an inactive form, thus avoiding the negative inotropic and chronotropic effects of prolonged β -block-

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Received for publication Oct 22, 2001; accepted for publication Oct 31, 2001.

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J Thorac Cardiovasc Surg 2002;124:219-20

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0022-5223/2002 \$35.00+0 12/1/121762

doi:10.1067/mtc.2002.121762

ade. Bessho and Chambers²³ present a well-designed set of studies with appropriate controls to investigate the role of oxygenation of crystalloid esmolol cardioplegia and the effects of single and multidose delivery in providing enhanced cardioprotection in an isolated buffer-perfused rat heart model of global ischemia and reperfusion. Comparisons with deoxygenated control solutions and with St Thomas' Hospital cardioplegic solution No. 2 are provided. Bessho and Chambers²³ also investigate the efficacy of oxygenated multidose crystalloid esmolol cardioplegia in providing cardioprotection after 60, 75, 90, and 120 minutes of global ischemia and 60 minutes of reperfusion.

Intrinsic to the development of new myoprotective protocols for use in cardiac surgery is the requirement that these protocols be as good as or better than traditional cardioplegia in providing enhanced postischemic functional recovery and myocellular preservation. In their article, Bessho and Chambers²³ show that the oxygenation of multidose crystalloid esmolol cardioplegia is essential to provide effective cardioprotection. They further show that multidose crystalloid esmolol cardioplegia must be delivered at a constant pressure (45 mm Hg) rather than a constant flow. They show—as evidenced by recovery of left ventricular developed pressure, left ventricular end-diastolic pressure, coronary flow, and heart rate—that delivery of oxygenated multidose crystalloid esmolol cardioplegia at a constant pressure provides complete myocardial protection for as long as 90 minutes at 37°C and is superior to St Thomas' Hospital cardioplegic solution No. 2.

The short half-life of esmolol (9 minutes) necessitates 3 minutes of infusion every 15 minutes at a constant pressure of 45 mm Hg to maintain pharmacologic effectiveness, however; this protocol is not significantly different from current cardioplegic readministration protocols for intermittent cardioplegia and provides for rapid cardiac arrest similar to traditional cardioplegia. Bessho and Chambers³² speculate that the effects of esmolol cardioplegia include enhanced balance of myocardial oxygen supply and demand through the reduction of inotropic and chronotropic actions and may be associated with increased blood flow to ischemic areas or the redistribution of blood flow from the subepicardium to the subendocardium. They concede that further studies with a larger animal model are needed for determination of surgical relevance, as is investigation of delivery routes, temperature, and applicability to neonatal, immature, and aged patients. The current inability to deliver esmolol in blood cardioplegia because of inactivation also requires further study.

In this issue of the *Journal*, Bessho and Chambers²³ present a well-designed study that closely examines a surgically relevant issue in an experimental model. Although the cardioprotective mechanisms remain to be elucidated, the benefits of esmolol cardioplegia offer the potential to

provide a needed alternative to traditional high-potassium depolarizing cardioplegia.

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