**Case Reports**

**Excellent Outcomes in a Case of Complex Re-do Surgery Requiring Prolonged Cardioplegia Using a New Cardioprotective Approach: Adenocaine**

James J. O’Rullian, CCP,* Stephen E. Clayson, MD;† Raul Peragallo, MD‡

*Department of Perfusion, †Department of Surgery, and ‡Department of Anesthesiology, Intermountain Medical Center (Intermountain Health Care), Murray, Utah

**Abstract:** A 71-year-old high-risk fourth-time redo male patient was diagnosed with prosthetic valve endocarditis of both aortic and mitral valves, and subsequently required a re-operative aortic and mitral valve replacement. He was placed on cardiopulmonary bypass (CPB) and arrested with normothermic hyperkalemic all-blood cardioplegia (microplegia) containing adjunctive adenosine-lidocaine-magnesium (adenocaine); aerobic arrest was maintained with near-continuous retrograde low potassium (∼2 mEq/L) adenosine microplegia. After 4 hours of arrest on CPB, the aortic valve was found to be incompetent and was resected. A root replacement was required utilizing a Medtronic Freestyle Root prosthesis. Four separate periods of cross-clamp were required during the course of the entire operation. The patient was on CPB for 9.8 hours with a total cross-clamp time of 7 hours, during which he received 72 liters of all-blood adenosine microplegia. After a terminal “hot shot” with adenosine microplegia and no added potassium, CPB was discontinued with no systemic hyperkalemia (5.1 mmol/L), no hemodilution (hematocrit, 24%), no balloon pump, no antiarrhythmic agents, and modest inotropic support. The patient was hemodynamically stable, was extubated in 12 hours, and was transferred out of the cardiac ICU after 48 hours with a subsequent uneventful recovery. **Keywords:** myocardial protection, microplegia, adenosine, lidocaine, polarized arrest, cardioplegia.

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Surgeons are operating on increasingly higher-risk patients from an aging population with more challenging co-morbidities and complex demographic, ethnic, sex, and metabolic profiles. Independent risk factors of surgical mortality and poor outcomes include low pre-operative ejection fraction (1), re-do operation (1), and prolonged cardiopulmonary bypass (2) and cross-clamp times (3). In patients with pre-operative left ventricular ejection fraction <25%, the risk of perioperative mortality after coronary artery bypass graft (CABG) increases significantly from 1% to 3% and up to 11% (4). Currently, re-do operations represent 6–8% of all patients undergoing CABG. Poor pre-operative left ventricular function is another risk factor and predictor of outcomes. Operative risk is additionally increased in those patients with infective endocarditis (IE) after re-do valvular surgery, whose mortality may be as high as 40% (5). Poor outcomes that appear acutely or 5–10 years after surgery have been inexorably linked with inadequate myocardial protection during surgery (1).

The following case report presents an extremely high-risk patient with multiple physiological co-morbidities as well as the surgical risk factors of re-do operation, prolonged bypass and cross-clamp times, and infective endocarditis for which the outcome was excellent using a new adjunct to myocardial protection, adenosine-lidocaine-magnesium cardioplegia (adenocaine [Hibernation Therapeutics, Townsville, Queensland, Australia]).

**CASE REPORT**

In 1996, a 60-year-old man presented to the hospital for a six-vessel CABG and closure of a patent foramen ovale (PFO), with no aortic regurgitation. He presented again in early 2007 for a re-do three-vessel CABG, combined with...
aortic and mitral valve replacements for mild regurgitation, and closure of the re-opened PFO. One week later, an aortic perivalvular leak was detected, and the patient had a second aortic valve replacement and reconstruction of the aortic valve annulus. In June 2007, the patient was seen at a community hospital for gastrointestinal bleeding where routine blood work tested positive for gram-negative bacteria. He was again transferred to the hospital for a fourth operation with severe IE of the mitral valve, prosthesis and 4+ regurgitation. The patient was placed on cardiopulmonary bypass (CPB) at systemic perfusion flow rates ranging between 4.5 and 5.5 L/min. Elective arrest was induced using antegrade normothermic all-blood cardioplegia (mini-plegia (6) or microplegia) infused through the aortic root at a flow rate of 350–450 mL/min. The induction cardioplegia contained 25 mEq/L KCl in the arrest cassette and adjunctive adenosine-lidocaine-magnesium (7,8) (12 mg adenosine, 25 mg lidocaine, and 4 g magnesium) in the additive cassette, delivered at a rate of 10 mL/L of cardioplegia using the myocardial protection system (MPS; Quest Medical, Allen, TX). Normothermic induction was followed by 7°C cardioplegia delivered at 200–300 mL/min; arrest was maintained with near continuous retrograde microplegia containing adenocaine delivered at a rate of 2 mL/min (lower dose) and 2 mEq/L KCl. Systemic temperature was 30–32°C. The aortic root appeared intact and well preserved, and a root replacement was deemed unnecessary. The ascending aorta was opened, and infection was discovered on the aortic valve sewing ring, and the mitral valve was almost completely unseated with a large abscess on the posterior annulus. Both valves were replaced with bioprosthetic valves. After 4 hours of arrest under a single cross-clamp, the patient was rewarmed to 37°C, and the cross-clamp was removed, but was reapplied because of continued bleeding from the base of the aorta. A root enlargement using a Gore-Tex (W.L. Gore & Assoc., Flagstaff, AZ) patch was required. After the second cross-clamp removal, perivalvular bleeding persisted, and the entire aortic valve and root were replaced with a Medtronic (Minneapolis, MN) freestyle root with concomitant root enlargement. A total of four periods of cross-clamp were required, during which continuous cold retrograde cardioplegia was given with only brief interruptions. After each cross-clamp period, the patient was re-warmed, and the heart was re-animated with a terminal “hot-shot” comprised of 2 L of high-dose adenocaine cardioplegia without KCl. The patient was weaned from CPB without requiring an intra-aortic balloon pump. The patient was on CPB for 9.8 hours, with a total cross-clamp time of 7 hours. The heart was perfused with a total of 72 L of adenocaine microplegia delivered over 4 hours and 55 minutes of infusion time. However, the total volume of crystalloid used from the additive cassette was 250 mL. There was no post-operative systemic hyperkalemia (5.1 mmol/L), no hemodilution (hematocrit, 24%), and no appreciable edema. During the case, the patient received 4 units of packed red cells, 9 units of fresh frozen plasma, and 23 units of salvaged autologous blood. In addition, 7 L of ultrafiltrate was removed. Although exact values were not obtained, follow-up transesophageal echocardiography demonstrated that post-operative left ventricular function looked at least equal if not better than pre-operative observance. The patient was transferred to the intensive care unit on 4 units/h vasopressin, .05 μg/kg/min levophed, and .04 μg/kg/min epinephrine, but no anti-arrhythmic agents, and was hemodynamically stable. The patient was extubated in 12 hours. He was transferred out of the thoracic intensive care unit after 48 hours with no apparent neurologic sequelae, and there was an uneventful recovery thereafter. He was discharged from the cardiothoracic service after 5 days but remained in-house for an additional 11 days to complete the antibiotic regimen for endocarditis. This was followed by prolonged home intravenous antibiotic administration.

**DISCUSSION**

In this case, near-continuous all-blood microplegia (6) was chosen because it optimizes aerobic conditions during arrest with continual oxygen delivery and limits crystalloid additives and secondary hemodilution. In addition, it reduces the accumulation of fluid, especially during prolonged bypass, as evidenced by the lack of hemodilution with a decrease in hematocrit. Adenocaine was used as an adjunct to microplegia because the combination of adenosine, lidocaine, and magnesium has been shown to effectively induce cardiac quiescence by arresting the heart at more natural resting membrane voltages (non-depolarized arrest) (7,8) and for maintaining arrest at very low to no additional potassium added to blood. Hyperkalemia can be pro-arrhythmic, vasoconstrictive, and can activate the vascular endothelium to increase vascular permeability. In addition, dysfunction of the post-bypass vascular endothelium can show pro-inflammatory, pro-oxidant, prothrombotic, and pro-atherogenic characteristics that have been linked to post-ischemic injury and myocardial stunning. Reducing the potassium and fluid load using adenocaine microplegia has the additional benefit of reducing water shifts by improving electrolyte and metabolic balances, particularly during long cross-clamp times. In this case, the patient received only 250 mL crystalloid (diluent for adenocaine), which is <2% of the 14.4 L of crystalloid that would have been delivered if 4:1 blood cardioplegia had been used under similar circumstances.

The two pharmacological components of adenocaine, adenosine and lidocaine, individually and in combination inhibit the inflammatory response to CPB, attenuate microvascular injury, and reduce post-ischemic myocardial infarction, arrhythmias, and mortality in experimental
models (9). Adenosine has well-known anti-inflammatory effects that are relevant to both the systemic response to CPB and to myocardial ischemia reperfusion (10), which are enhanced by lidocaine. Lidocaine inhibits voltage-sensitive Na⁺ channels and may inhibit L-type calcium channels and open cardioprotective mitochondrial K_ATP channels through non-Na⁺ channel-dependent effects. Lidocaine also exerts anti-inflammatory effects and free-radical scavenger effects. The combination of adenosine and lidocaine in cardioplegia has been used in both experimental models of CPB (7) and in clinical pediatric cardiac surgery (11), the latter showing superiority over hyperkalemic crystalloid cardioplegia.

In conclusion, this case showed that strategic use of adenosine all-blood microplegia for induction, maintenance of arrest at low levels of hyperkalemia, and re-animation without potassium in high-risk patients requiring prolonged CPB may offer advantages over traditional hyperkalemic and hemodiluted cardioplegia protocols. Based on this case and other excellent outcomes over the last 3 years, we now use adenosine microplegia exclusively in our practice.

REFERENCES