Glucose-Insulin-Potassium Infusion in Acute Myocardial Infarction: A Prospective Randomized Double Blinded Placebo Controlled Multi-Center Interventional Clinical Trial

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A. Study Purpose & Rationale

Cardiovascular disease is the leading cause of morbidity and mortality in the United States. Coronary artery disease, including acute myocardial infarction, is the largest component of these diseases. Every year 1,500,000 patients experience acute MI, 500,000 die, and significantly more experience serious sequelae including arrhythmia, heart failure, and cardiogenic shock. Any adjunct therapy proven to reduce the incidence of death or these sequelae in acute MI with minimal risk is of great interest to the general patient population.

Studies have demonstrated the harmful effects of FFA on myocardial tissue in acute ischemia. The protective effects of glucose infusion on arrhythmia and ejection fraction have all been demonstrated in animals and humans over short time periods. Meta-analysis has suggested a mortality benefit to glucose infusion. Small pilot randomized controlled trials have identified an ad hoc subgroup requiring thrombolysis that demonstrates a mortality benefit. These studies warrant a new trial focusing on this subgroup, looking for mortality benefit in acute MI.

B. Study Design and Statistical Analysis

This is a prospective randomized double-blind placebo controlled multi-center interventional clinical trial. Enrolled patients will be randomly administered either study drug or placebo infusion and followed for end-points of in-hospital mortality, arrhythmia, heart failure, and cardiogenic shock. Data will be pooled from multiple participating centers to obtain approximately 162 patients for each arm, and data will be analyzed by Chi-square analysis for an expected mortality difference of 15% to 5% with a power=0.8 and an alpha=0.05.

C. Study Subjects

All patients presenting to participating heart centers with the diagnosis of acute MI who meet criteria for thrombolysis will be screened. This is generally defined as chest pain >30 mins and EKG changes including ST elevation in 2 contiguous leads or new onset LBBB. Patients with a history of renal failure, or admission Cr>1.8, K+>5.5 will be excluded as being at higher risk for hyperkalemia.

D. Study Procedure

These patients will be approached by a research coordinator for informed consent after confirmation of the inclusion/exclusion criteria. This research coordinator will only approach patients after consent for thrombolysis/catheterization is obtained and identify themselves as NOT part of the medical care team. A clear distinction will be expressed between the therapeutic value of catheterization, and the investigational nature of the study drug.

After informed consent is obtained, the research coordinator will randomly assign the subject to either treatment or placebo arms. The research pharmacy will be contacted to provide a blinded form of

the appropriate infusion. The research coordinator alone will be aware of the subject status and will no longer be involved in patient care.

E. Study Drugs

A research pharmacy blinded formulation of either study infusion [25% glucose solution, 50 IU insulin/Liter, and 80 meq potassium/Liter in water] or placebo will be started by the medical team @ 1.5cc/kg/hr x 48 hours as an adjunct to standard medical treatment. Serial labs will be monitored for glucose, potassium, and magnesium starting 1 hour after infusion. FFA level measurements will be followed for confirmation purposes.

The infusion will be stopped for K+>5.8, or glucose <60 >300. Otherwise, patient progress will be monitored for the following in-hospital endpoints: mortality, arrhythmia (monitored by telemetry, defined as VT>10 beats or Vfib), heart failure (monitored clinically, defined as Killip class>2 requiring diuretic treatment) , and cardiogenic shock (monitored by BP, defined as SBP<80 requiring inotropic support). Troponin peak and TTE ejection fraction during acute MI and after will be followed for adjunct information regarding infarct size/effect.

F. Confidentiality of Study Data

All personal identifiers of patient data will be replaced with anonymous study identifiers, and strict confidentiality kept. Identification of which arm subjects were randomized to will be kept confidential solely by the research coordinator until all data is collected and ready for analysis.

G. Potential Risks & Benefits

Prior studies have identified only minimal risks to subjects including thrombophlebitis, hyperkalemia, hypokalemia, hyperglycemia, and hypoglycemia. Routine medical care involves careful monitoring of all these possibilities, as well as additional study related blood draws. These risks will be explained to subjects, and will be promptly treated according to the standards of care. Potential benefits to individual subjects are yet unknown.