The role of glucose, insulin, and potassium solution in protecting the myocardium during open heart surgery

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Abstract:
The purpose of this review was to verify the function and potential mechanisms of glucose-insulin-potassium (GIK) solution infusion in cardiac surgery concerning cardiac protection. Myocardial damage is associated with cardiac surgical procedures involving hypothermic cardiac arrest and cardiopulmonary bypass (CPB). One of the most critical targets for cardiac surgery during anesthesia is to reduce myocardial damage. In terms of cardiac morbidity and mortality, effective intraoperative cardiac protection primarily defines postoperative outcomes. Well studied techniques and recognized cardiac safety methods do have some drawbacks in their functions. One solution to this issue is increased metabolic assistance, intended to minimize perceived ischemic injury. In practical use, many modern techniques such as glucose insulin potassium infusion are still restricted in terms of their added efficacy in cardiac protection. Providing glucose and insulin to the critically ischaemic cell has been hypothesized to have several beneficial effects, it increases the production of anaerobic adenosine triphosphate (ATP) despite the inhibition of fatty acid metabolism while retaining a defensive role on the threatened cell membrane.

Keywords: Coronary artery bypass grafting (CABG), cardiac protection, GIK, myocardial injury.

Introduction
More than 1.5 million open-heart surgeries are conducted annually worldwide. (1) Despite the growing burden of associated diseases and more complicated surgical procedure, improvement in surgical methods, and anesthetic management as well as cardioprotective techniques has led to decrease operational mortality. (2,3)
Several procedures have been developed in conjunction with myocardial protection, such as the use of whole-body hypothermia, local myocardial hypothermia, the use of antegrade and retrograde cardioplegic injection methods, the use of cold and warm blood in cardioplegic solutions, and the use of drugs such as calcium channel blocking agents. (4)
Glucose insulin and potassium (GIK) solution for myocardial protection was presented by Sodi-Pallares and colleagues for the first time. They used that solution in patients with acute myocardial infarction (MI) and concluded that GIK solution reduced electrocardiographic changes in these patients. (5)

Review of literature:
During coronary artery bypass grafting (CABG), the myocardium is subject to
bouts of ischemia and reperfusion, which can lead to post-ischemic contractile dysfunction. This is a significant contributor to early and late postoperative morbidity and mortality, as well as to increased pharmacological and mechanical circulatory support requirements. (6)

Despite all developments in myocardial protective techniques and methods, perioperative myocardial damage after technically successful CABG is still the most significant cause of cardiovascular morbidity and mortality. (7) By-myocardial glucose uptake and enhancing the combination of glycolysis and glucose usage, GIK infusion is believed to provide cardioprotective benefits. (8, 9)

Several experimental studies have documented that GIK therapy ad-ministration-as determined by intraoperative and postoperative hemodynamic parameters- can maintain myocardial perfusion and left ventricular function. (4, 10) One or a combination of GIK mechanisms has been proposed to produce cardiac defense in most studies. Insulin causes myocardial contractile benefits directly from the enhanced expression of glucose transporters and improved turnover of Na-K-ATPases in addition to the well-known metabolic insulin effects, facilitating positive inotropic effects. (11)

Preventive supply of GIK before periods of myocardial ischemia increases the content of myocardial glycogen, allowing prolonged synthesis-under anaerobic conditions- of ATP and crea-tine triphosphate. (12)

Accordingly, perioperative insulin application can improve both ischemia tolerance and contractile function recovery. (13) The increased release of stress-induced catecholamines not only reduces the beneficial effects of insulin but also causes systemic lipolysis, leading to increased levels of free fatty acids (FFA) with its harmful implications (14) like the production of oxygen free radicals, the efficiency of ATP production also declined with substantially higher oxygen consumption compared to glucose oxidation (15) and injury to the cell membrane because of elevated acyl-carnitine levels. (16)

Each of these effects can be avoided by adequate administration of insulin, which inhibits adipose tissue hormone-sensitive lipase as well as activation of mitochondrial acetyl-CoA-carboxylase, thus directly inhibiting the oxide-action of FFA. (17)

Improved polarization of the membrane was supposed to be the main impact of the GIK solution. (17, 18) Insulin likely increases the myocyte's potassium uptake (16) which leads to a quicker postoperative recovery of the sinus rhythm. (19) Infusion of GIK greatly decreases the occurrence of ventricular arrhythmia in addition to atrial fibrillation. (13, 20) These beneficial effects are significant because conduction abnormalities and postoperative arrhythmias are common complications following coronary revascularization surgery. (17, 21)

After ischemia, one of the essential myocardial metabolic reactions is transient insulin resistance. It is part of general hormonal stress reactions (22) and has been considered to have a high propensity for hyperglycemia. (12) However, by using postoperative insulin, this risk may be obviated. (25)

Some other GIK infusion impacts, which are not recorded so consistently and seem to play a role in cardiac preservation; Improved cardiac output and decreased overall peripheral resistance by vasodilation (24). Increased phagocytic activity in neutrophilic granulocytes, resulting in lower rates of infection and shorter surgical recovery times. (25)

On the other hand, GIK infusion has some limitations and jeopardies. The main concern with its use, swings in
blood glucose, and potassium levels. (26) High-concentration glucose infusion leads to hyperglycemia, which could damage the brain and worsen neurological outcomes. (27) There is an agreement that blood glucose concentration should be maintained within the normal range. (28,29) Measuring glucose and potassium concentrations regularly is necessary. (27) It is worth noting that several beneficial GIK implications are not yet completely known.

**Conclusion**

In summary, intraoperative cardiac protection protocols have not included many modern methods such as GIK infusion. The significant challenge is to determine adequate amounts of administered GIK and the duration of its application in patients undergoing cardiac surgery because variable concentrations have been described.

**References**

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