

Cardioprotection with glucose insulin potassium (GIK) during non cardiac surgery in a patient with stress induced myocardial ischemia: A case report

ABSTRACT

The administration of glucose-insulin-potassium (GIK) has demonstrated cardioprotective effects in cardiac surgery. A 58-year-old male with severe disabling back pain due to posterolateral lumbar pseudarthrosis was scheduled for spine surgery. He previously experienced two episodes of acute coronary syndrome that required percutaneous coronary interventions (PCIs). Coronary angiogram showed intrastent occlusions and multiple coronary lesions that were not suitable for percutaneous or surgical revascularization. During pharmacological stress imaging, myocardial ischemia developed in 19% of the ventricular mass and was reduced to 7% when GIK was administered. After anesthesia induction, the GIK solution was also infused and surgery was uneventful, with no signs of postoperative myocardial injury. Four days later, the patient was successfully discharged to a rehabilitation center. This is the first clinical report of GIK pretreatment during non-cardiac surgery in a patient with ischemic heart disease (IHD).

Key words: Coronary artery disease, general anesthesia, myocardial infarct, postoperative complication

Background

In Western countries, spinal surgery has increased considerably over the last 20 years and is associated with low postoperative morbidity and mortality.^[1] Although myocardial infarct, heart failure, and arrhythmias occur in less than 6% after spinal surgery, these major adverse cardiac events (MACEs) represent the leading cause of death and prolonged hospital stay.^[2] Myocardial revascularization by the percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is recommended in patients with

severe ischemic heart disease (IHD).^[3] Whenever coronary lesions are not suitable for revascularization, perioperative cardioprotective interventions are aimed to provide adequate gas exchange and stable hemodynamic conditions, to avoid anemia and to modulate the surgery-induced prothrombotic state.^[4] Unfortunately, administration of antiplatelets, alpha-2 agonists, and beta-blockers has not been associated with better clinical outcomes in high-risk patients undergoing non-cardiac surgery.^[5]

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ROSA TESORO¹, ANDRES HAGERMAN¹, GRANIT MOLLIQAJ², CHRISTOPH ELLENBERGER¹, MARC LICKER^{1,3}

¹Department of Acute Medicine and ²Neuroscience, Neurosurgical Unit, Geneva University Hospitals, Geneva, ³Faculty of Medicine, University of Geneva, Geneva, Switzerland

Address for correspondence: Dr. Marc Licker, Department of Acute Medicine, Faculty of Medicine, Geneva University Hospitals and University of Geneva, Geneva, Switzerland.
 E-mail: Marc-joseph.licker@hcuge.ch

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Interestingly, the infusion of glucose-insulin-potassium (GIK) has been shown to enhance the tolerance to myocardial ischemia in cardiac surgery and thereby reduce the occurrence of MACEs.^{6,7]}

Herein, we report a 58-year-old man with stress-induced cardiac ischemia who was treated with GIK during spinal surgery with the aim to protect the heart.

Case Report

A 58-year-old male complained of severe back pain due to pseudarthrosis that developed 3 to 6 months after spinal lumbar decompressive surgery. He had IHD, insulin-dependent diabetes, hypertension, moderate renal failure, and peripheral arterial disease. In 2010 and 2017, he presented non-ST segment myocardial infarctions (NSTEMIs) and underwent PCIs with sirolimus-eluting stent insertion in the left anterior descending (LAD) artery and the posterior interventricular (PIV) artery. His current medications included beta-blockers (metoprolol 50 mg bid), rosuvastatine (20 mg qid), aspirin (100 mg qid), non-steroidal anti-inflammatory drugs, acetaminophen (1 g qid), pregabalin (200 mg bid), and tramadol (100 mg bid).

The electrocardiogram (ECG) showed an inferior myocardial infarction and transthoracic echocardiography hypokinesia of the apical and inferior ventricular segments. Coronary angiography revealed intrastent occlusion in the LAD artery, 70% intrastent stenosis in the PIV artery, 50% stenosis of the left main artery, and non-stenotic atheroma deposits in the right coronary and circumflex arteries [Figure 1]. Positron emission computed tomography (PET-CT) with a pharmacological stress agent (regadenoson) showed ischemia in the basal inferior, mid-anterior, and apical inferior segments [respectively 8%, 5%, and 6% of the left ventricular mass; Figure 2a]. Two days later, the PET-CT myocardial stress test was repeated after infusing 50 ml of GIK (0.4 g glucose/ml, 0.4 U insulin Actrapid®/ml, and 0.5 mEq potassium chloride [KCl]/ml) and it demonstrated a reduction of myocardial ischemia (0%,

4%, and 3% in basal inferior, mid-anterior, and apical inferior segments, respectively, Figure 2). As the coronary lesions were not amenable for PCI or CABG treatment, the multidisciplinary board recommended proceeding to surgery using GIK infusion as a cardioprotective intervention.

On the day of surgery, the patient received metoprolol 50 mg orally and was equipped with a 5-lead ECG, oxygen pulse oximetry, two peripheral intravenous (IV) catheters, and an arterial line for blood pressure monitoring (IntelliVue MP70, Philips Medical Systems, Philips Healthcare, 5680 DA Best, Netherland). After anesthesia induction with propofol and tracheal intubation, the lungs were mechanically ventilated and balanced anesthesia was established with inhaled sevoflurane, low IV doses of sufentanyl (150 mcg), ketamine (50 mg), and clonidine (150 mcg). The patient was installed in the prone position and a 100 ml GIK infusion (40 g glucose, 40 U insulin Actrapid®, and 20 mEq KCl) was started and continued over 60 min. Transforaminal interbody fusion extending from L4 to S1 with posterolateral fusion was performed over 5 h 20 min. A restrictive normovolemic fluid strategy was applied using IV fluids to compensate perspiration (4 ml.kg⁻¹.h⁻¹ Ringer-lactate) and blood losses (~500 ml) while low-dose norepinephrine was infused to target a mean arterial pressure between 70 and 90 mmHg and heart rate between 66 and 75 beats/min [Table 1]. The patient was successfully extubated at the end of the surgery and then transferred to the post-anesthesia care unit and 3 h later to the neurosurgical unit. Patient-controlled analgesia with IV morphine was initiated and the administration of beta-blockers, aspirin, and statins was resumed orally. On the first and second postoperative days, serum creatinine levels and ECG tracings were comparable to preoperative measurements and ultra-sensitive troponin T levels were less than 30 ng/l [Table 1]. As the patient experienced no postoperative complications (cardiovascular, renal, respiratory, and infectious) and had recovered satisfactory walking capacity with minimal pain, he was discharged to a rehabilitation center 4 days after surgery.

Discussion

In this patient with severe IHD and disabling back pain, repeated myocardial PET-CT imaging demonstrated the effectiveness of a GIK solution to reduce stress-induced ischemia. As coronary lesions were not suitable for PCI or CABG, the same GIK regimen was administered during spinal surgery as a means to protect the heart and reduce the risk of MACE.

Given the increased life expectancy, the number of surgical candidates with IHD will continue to grow as well as the

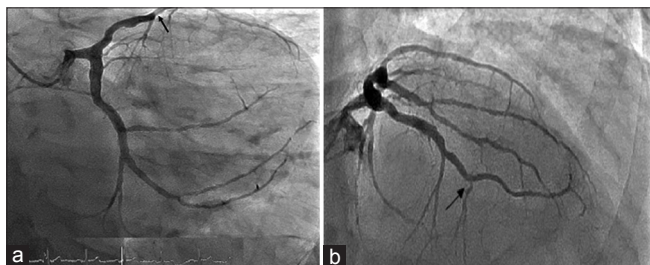


Figure 1: Coronary angiogram showing intrastent occlusion in the left descending artery (Figure 1a, arrow) and 70% stenosis in the stent in the posterior interventricular artery (Figure 1b, arrow)

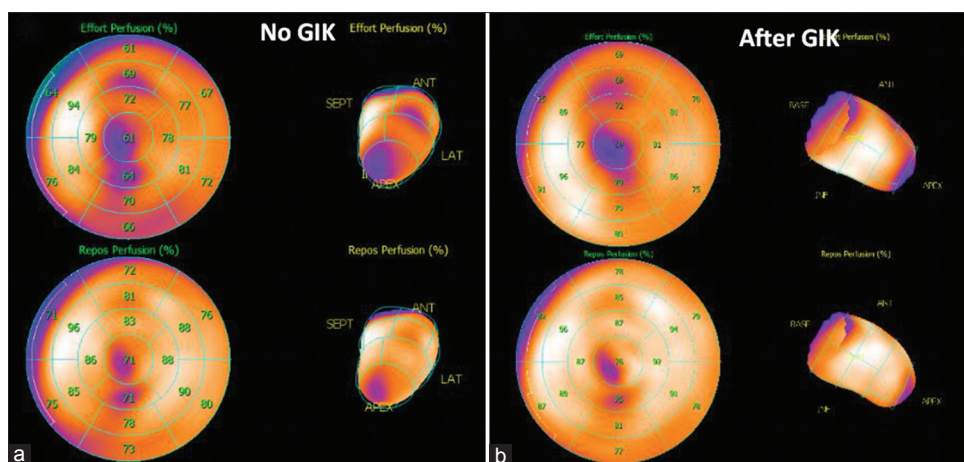


Figure 2: Myocardial positron emission computed tomography showing stress-induced ischemia (purple color) in basal inferior, mid-anterior, and apical inferior ventricular segments (Figure 2a) and the effect of glucose-insulin-potassium (GIK) infusion in reducing the extent of myocardial ischemia

Table 1: Perioperative hemodynamic, respiratory and biologic parameters

Parameters	Preop	Start of Surgery	1 h Intraop	End of surgery	POD 0	POD 1
HR, beats/min	69	65	64	70	75	69
BP, mmHg	155/87	120/69	109/64	132/74	110/55	126/71
NE infusion, mcg/h	0	0	0.2 mg/h	0.1 mg/h	0	0
Pain at rest on VAS	8/10	n.a.	n.a.	n.a.	0/10	2/10
Hb, g/l	113	110	103	108	109	106
SaO ₂ /FIO ₂	96/0.21	99/0.4	98/0.4	99/0.4	96/30	94/0.21
Glycemia, mmole/l	9.5	8.8	11.4 (4 IU AR)*	14.5 (6 IU AR)*	12.7 (4 UI AR)*	9.1
Creatinine, mmol/l	98	n.a.	n.a.	n.a.	93	96
cTn-T ng/l	17	n.a.	n.a.	n.a.	22	29
NT-proBNP, pg/ml	178	n.a.	n.a.	n.a.	-	155
CRP, mg/l	11	n.a.	n.a.	n.a.	-	128

BP, blood pressure; CRP, C-reactive protein; cTn-T, cardiac troponin T; FIO₂, inspiratory fraction in oxygen; Hb, hemoglobin; HR, heart rate; NE, norepinephrine; NT-proBNP, NT-pro-brain natriuretic peptide; n.a., not applicable; POD, postoperative day; SaO₂, arterial oxygen saturation; VAS, visual analog scale. * Actrapid® (AR) expressed in the international unit (IU)

need for innovative cardioprotective techniques to manage high-risk patients who might benefit from an invasive procedure.^[4,8] Tachycardia, hyper- or hypotension, anemia, hypoxemia, and pro-inflammatory condition during the perioperative period all could trigger myocardial ischemia as a result of an imbalance between myocardial oxygen delivery and metabolic needs.^[3]

This patient had a history of IHD with stress-induced myocardial ischemia that increased his risk of perioperative MACEs. Besides providing stable hemodynamic and adequate oxygenation, there is no “silver bullet” for perioperative cardioprotective interventions. All patient’s cardiovascular medications— aspirin, beta-blockers, and statin—were continued preoperatively and resumed early after surgery.^[5] General anesthesia using volatile anesthetics that have shown organ-protective effects was associated with intravenous ketamine and clonidine to facilitate anesthesia emergence and as part of multimodal analgesia.^[9] Hemodynamic management using a restrictive fluid approach and vasopressor titration

was aimed to maintain safe levels of blood pressure and heart rate.^[10]

In this high-risk patient, the cardioprotective effects of GIK were confirmed during stress imaging as evidenced by more than 50% reduction in myocardial ischemic burden. In agreement with this observation, Di Marco *et al.*^[11] used ECG and echocardiographic stress tests coupled to ²⁰¹Thallium myocardial perfusion scintigraphy, demonstrating that GIK pretreatment resulted in increased ventricular contractility, improved exercise tolerance, and enhanced recovery of post-ischemic reperfusion. As the time window of GIK-induced cardiac protection may extend up to 72 h,^[12] we elected to administer the GIK solution following anesthesia induction and therefore to minimize the risk for myocardial ischemia due to critical mismatch in oxygen supply–demand and prothrombotic conditions in the early postoperative period. The lack of myocardial injuries based on ECG recordings and cardiac biomarkers lend support for a successful perioperative cardioprotective strategy.

This is the first clinical report of the administration of GIK in non-cardiac surgery to prevent myocardial ischemia and stabilize the hemodynamic condition. Yet, a strong body of evidence supports the efficacy of GIK in reducing the size of myocardial infarct and the occurrence of arrhythmias in animal models of myocardial ischemia-reperfusion.^[12] Likewise, fewer myocardial infarcts and atrial fibrillation along with faster weaning from cardiopulmonary bypass and discharge from the hospital have been reported in GIK pretreated patients undergoing cardiac surgery.^[6,13] Moreover, GIK infusion has been demonstrated to enhance ventricular function with a lesser need for inotropic and vasopressor drugs.^[14] Hence, our patient could benefit from the GIK-induced shift of lipid oxidation to an “oxygen-sparing” pathway of glucose oxidation resulting in more efficient cardiac mechanical work and optimized hemodynamic status.^[15]

This proof-of-concept clinical report supports the effectiveness of GIK infusion in minimizing stress-induced myocardial ischemia and its potential utilization during non-cardiac surgery that warrants further prospective controlled trials.

Abbreviations

CABG: Coronary artery bypass grafting surgery
 GIK: Glucose-insulin-potassium
 IHD: Ischemic heart disease
 LAD: Left anterior descending
 MACE: Major adverse cardiac event
 PCI: Percutaneous coronary intervention
 PET-CT: Positron emission tomography-computed tomography
 PIV: Posterior interventricular.

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Conflicts of interest

There are no conflicts of interest.

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