JOURNAL OF BASHIR INSTITUTE OF HEALTH SCIENCES

RESEARCH ARTICLE

OPEN ACCESS

ARTICLE INFO
Date Received:
Jyly 11, 2020
Date Revised:
October 12, 2020
Date Published Online
December 24, 2020

Effectiveness of glucose-insulin–potassium infusion for myocardial protection in non-diabetic patients during adult cardiac surgery

[a]Attiya Hameed Khan*, [a]Hafsa Rasool, [b]Hammad Ahmed, [c]Khawaja Ahsen Faheem, [d]Aamir Naveed, [e]Shabir Hussain

[a]*Department of Cardiac Perfusion, Bashir Institute of Health Sciences, Baharakahu Islamabad, Pakistan.*
[b]*Department of Allied Health Sciences, Bashir Institute of Health Sciences, Islamabad, Pakistan.*
[c]*Department of Emergency and intensive care, Bashir Institute of Health Sciences, Islamabad, Pakistan.*
[d]*Department of Psychiatry, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.*
[e]*Department of Pharmacology, Banu Medical College, Banu Khyber Pakhtunkhwa, Pakistan.*

*CORRESPONDENCE
Attiya Hameed Khan
Email:
attiyahameed864@gmail.com
Phone:
+923465780929

ABSTRACT

Background: Glucose-insulin-potassium (GIK) infusion is most commonly used in diabetic patients during cardiopulmonary bypass. Many studies suggest that the use of GIK infusion has beneficial outcomes mainly in myocardial protection, as myocardial protection is the main goal of Perfusionist during bypass surgery. In Pakistan, GIK is used normally in the diabetic patient as it has a good effect on insulin maintenance. Most surgeons use GIK in diabetic patients but many of the studies suggest that it has good post-op outcomes especially in myocardial protection. **Method:** This was an observational cross-sectional study conducted for 6 months, from November 2019 to April 2020 at the Pakistan Institute of medical sciences department of Cardiac surgery. Ethical approval was taken from the hospital ethical committee. It was consisting of 80 patients, 40 from group A (GIK infused) and 40 from group B (GIK non-infused) by using the Non-probability convenient sampling technique. Data was collected through pre-structured Performa. **Results:** In the early postoperative period, peak CKMB levels were high in the Non-GIK group (62.7375± 19.75393IU/L) versus (54.0005±11.41493IU/L) in the GIK group (p-value 0.000). Mean ventilation time in the GIK group was (10.85 ±6.302) hours versus (12.15 ±7.814) hours in the non-GIK group (p< 0.001). Similarly, ICU stay period was also shorter in the GIK group is (3.50 ±1.013) and in the non-GIK group is (3.50 ±0.906) (p>0.001). **Conclusion:** Glucose-insulin-potassium (GIK) infusion has a beneficial role in myocardial protection and is associated with better post-operative outcomes without increasing the risk of non-cardiac complications.

Keywords: Glucose-insulin-potassium (GIK) solution, Myocardial Protection, cardiac enzymes CKMB.

INTRODUCTION

Cardiovascular diseases possess a major cause of fatality and disability all over the world. Since the last several decades, the rates of cardiovascular disease-related deaths have decreased in many high-income countries but increased in low- and middle-income countries with around 80% of the burden (1). Despite the seriousness of cardiovascular diseases in low- and middle-income countries, minimal attention is given to the prevention of cardiovascular disease risk factors in South Asia, particularly in Pakistan. Besides, economic and political instability is accelerating the rates of cardiovascular diseases in the country.

Practical efforts are required to enhance the understanding of cardiovascular disease risk factors such as diet, physical activity, and tobacco-control policies to support prevention and control at the population level (2). Cardiovascular diseases remain the most common causes of death, responsible for 35% of all deaths, almost 1 million deaths each year. Approximately one-fourth of these deaths are sudden. Besides, cardiovascular diseases are highly prevalent, diagnosed in 80 million adults, or ~35% of the adult population. The growing prevalence of obesity, type 2 diabetes mellitus, and metabolic syndrome, which are important risk factors for atherosclerosis, now threatens to reverse the progress that has been made in the age-adjusted reduction in the mortality rate of coronary heart disease (3).

Since the 1990s, open-heart surgery has been performed using cardiopulmonary bypass that provides oxygen to the body while the heart is steadied and emptied of its blood, allowing for more complicated and protracted surgeries to be performed (4). At the same time, many surgeons were being trained on newer minimally invasive surgical techniques, which typically rely on laparoscopic and endoscopic tools to manipulate tissue via numerous small incisions; this is in contrast to open-heart surgery that requires a large enough access route to fit the surgeons' hands (5). When noninvasive imaging techniques became clinically established and used on a widespread scale, minimally invasive cardiac procedures, focusing on the heart or surrounding vascular structures, became an active area of research and clinical interest (6).

The use of glucose-insulin and potassium (GIK) solution for myocardial protection was 1st time Introduced by Sodi-Pollares and colleagues. They used this solution in patients with acute myocardial Infarction and concluded that GIK solution limited electrocardiographic changes in these patients (7). Several studies have shown reduced morbidity and mortality in patients of acute MI with the use of GIK Solution (8).

Many studies suggest that the use of GIK infusion has beneficial outcomes mainly in myocardial protection, as myocardial protection is the main goal of Perfusionist during bypass surgery. In the setting of Islamabad and Rawalpindi GIK is used normally in diabetic patients as it has a good effect on insulin maintenance. Most surgeons use GIK in diabetic patients but many of the studies suggest that it has good post-op outcomes especially myocardial protection. In this study, we used GIK in non–diabetic patients for assessment of myocardial protection, treatment of patients with cardiac dysfunction during episodes of ischemia and reperfusion.

METHODOLOGY

This was an observational cross-sectional study conducted for 6 months, from November 2019 to April 2020 at the Department of Cardiac Surgery, Pakistan Institute of Medical Sciences, Islamabad Pakistan. It was based upon to assess the effectiveness of glucose-insulin potassium infusion in non-diabetic patients. 5% dextrose containing 70 IU/L regular insulin and 70 meq/L of potassium was administered. The infusion was started at a rate of 30 ml/hour after induction of anesthesia and before the start of cardiopulmonary bypass. The infusion was started again after the removal of an aortic cross-clamp and was continued for six hours after the operation. Data was collected through pre-structured Performa which contains both open and close-ended questions. The sample was collected by using the Non-probability convenient sampling method. Ethical approval was taken from the ethical committee of Bashir Institute of Health Sciences, Islamabad Pakistan. Verbal informed consent was taken from patients. The trial was conducted in compliance with the International Harmonization guidelines for good clinical practices and according to the declarations of Helsinki [7]. Independent T-test was applied to compare pre-and postoperative outcomes in GIK and Non-GIK Groups, respectively.

Statistical analysis:

In the present study, we used SPSS version 25, and an independent t-test was applied to compare pre and post-operative outcomes in GIK and non GIK groups respectively.

RESULTS

Demographic Profile and outcomes

In the present study, a total of eighty (n=80) patients of both genders age between 50-75 years were enrolled, who were planned for undergoing isolated ON pump bypass. Patients were divided into two groups, Group A and B. Group A were those who were infused with GIK and group B were those who were non-GIK infused. The mean ages of GIK infused were (57.70±8.483SD) and non GIK infused (57.00±8.578SD). It depicts that 40 patients were infused with GIK and 40 were not. Diabetic patients were excluded from the study. As shown in table 1.

Table 1. Socio demographic Profile and baseline characters. (n=80).

Table 1. Socio demographic Profile and baseline characters. (n=80).

Socio-demographic profile		
Variables	GIK	Non-GIK
	Mean±SD	Mean±SD
Age of patients	57.70±8.483	57.00±678
	Number (%age)	**Number (%age)**
Female	20 (50 %)	15 (37.5%)
Male	20 (50 %)	15 (37.5%)
Smoker	12(30 %)	14 (35.5%)
Non-smoker	28 (70 %)	26 (65%)
GIK-infused	40 (100%)	40 (100%)
Non-diabetic	40 (100%)	40 (100%)
Previous medical history		
Yes	19 (47.5%)	20 (50%)
No	21 (52.5%)	20 (50%)
Underlying cardiac pathology		
Septal	5 (12.5%)	4 (10 %)
Coronary heart disease	25 (62.5%)	25 (62.5%)
Valvular Disease	10 (25.0%)	11 (27.5%)
Surgical Procedure		
AS/VSD	5 (12.5%)	4 (10%)
CABG	25 (62.5%)	25 (62.5%)
Valve replacement	10 (25%)	11 (27.5%)
Post-operative arrhythmia		
Yes	28 (70%)	33 (82.5%)
No	12 (30%)	7 (17.5%)
Levels of inotropic support		
Mild	15 (37.5%)	10 (25%)
Moderate	17 (42.5%)	13 (32%)
Severe	8 (20%)	17 (42.5%)
Non-cardiac perfusion		
Yes	9 (22.5%)	7 (17.5%)
No	31 (77.5%)	33 (82.5%)
Mean±SD of pre- and post-outcomes	**Mean±SD**	**Mean±SD**
Bypass time	83 (42.5%)	
Pre-op CKMB levels	29.9500±5.30578	29.2250±5.84627
Post-op CKMB levels	54.0005±11.41493	62.7375±19.75393
Ejection fraction	53.65±9.026	52.58±8.788
Cross clamp time	60.98±16.175	57.65±17.243
Pre-op potassium Levels	4.2850±0.38997	4.1920±0.34776
Post-op potassium Levels	4.6925±0.30667	4.5785±0.40251
Ventilation time (hours)	10.85±6.302	12.15±7.814
ICU stay in days	3.50±1.013	3.50±0.906

CABG (Coronary artery bypass grafing), CKMB (Creatinine Kinase Myoglobin), ASD (Atrial Septal Defect), VSD (Ventricular Septal Defect)

Comparison of Pre and Post-operative outcomes

In the early postoperative period, peak CKMB levels were high in the Non-GIK group (62.7375± 19.75393IU/L) versus (54.0005±11.41493IU/L) in the GIK group (p-value 0.000). Mean ventilation time in the GIK group was (10.85 ±6.302) hours versus (12.15 ±7.814) hours in the non-GIK group (p< 0.001). Similarly, the ICU stay period was also shorter in the GIK group is (3.50 ±1.013) and in the non-GIK group is (3.50 ±0.906) (p>0.001). We did not find any detrimental effect of GIK infusion on non-cardiac complications e.g. renal, pulmonary, and neurologic complications, as shown in table 2.

Table 2. Comparison of Pre and post–op outcomes of both group (Independent t-test): n=80.

Variables	GIK Infused	Non GIK infused	95% Confidence Interval		
	Mean±SD	Mean±SD	t	df	p
Patients Age	57.70± 8.483	57.00± 8.578	0.367	78	0.631
Pre-op CKMB levels	29.9500±5.30578	29.2250±5.84627	0.581	78	0.266
Post-op CKMB levels	54.0005±11.41493	62.7375±19.75393	-2.422	78	0.000
Ejection fraction	53.65±9,026	52.58±8.788	0.540	78	0.657
Pre-op potassium levels	4.3850±0.38997	4.1920±0.34776	1.126	78	0.254
Post-op potassium levels	4.6925±0.30667	4.5785±0.42051	1.385	78	0.413
Vantilation time (hours)	10.85±6.302	12.15±7.814	-0.819	78	0.178
Bypass time (mins)	77.58±14.863	82.70±20.294	-1.289	78	0.027
ICU stay (days)	3.50±1.013	3.50±0.906	0.000	78	0.387

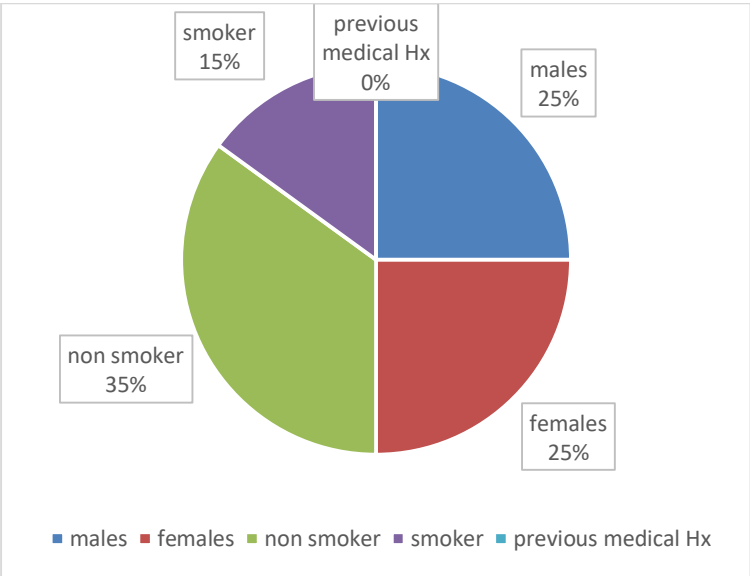

Figure 1. Previous smoking History and Gender group (GIK infuse group).

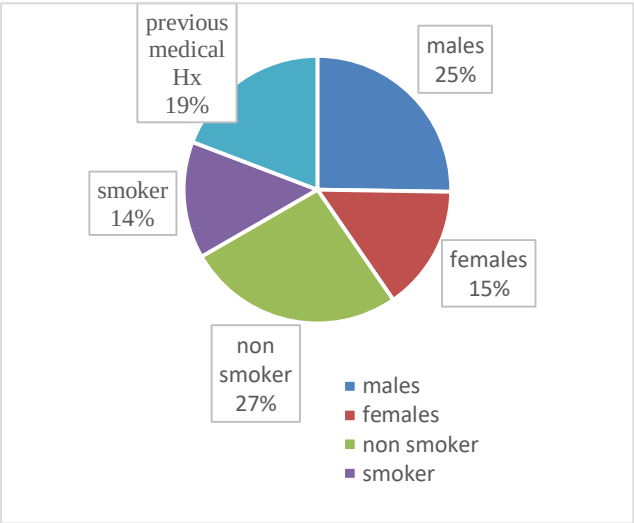

Figure 2. Previous smoking History and Gender group (Non-GIK infuse group).

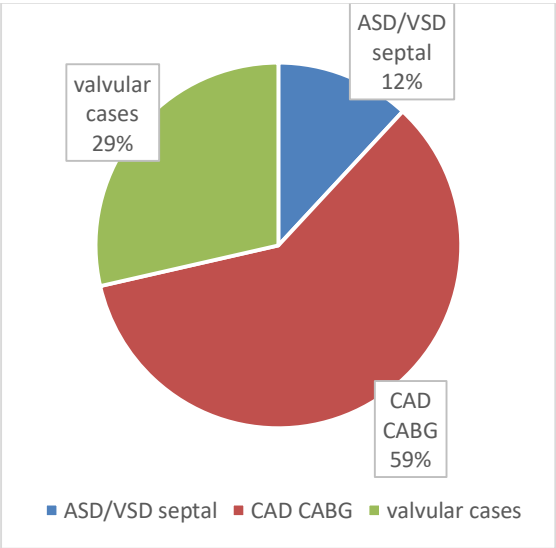

Figure 3. Corrective surgeries (GIK group).

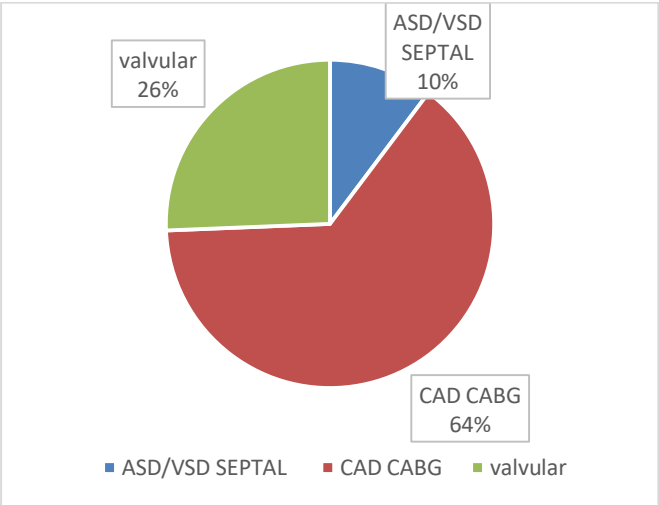

Figure 4. Corrective surgical procedures (non -GIK group).

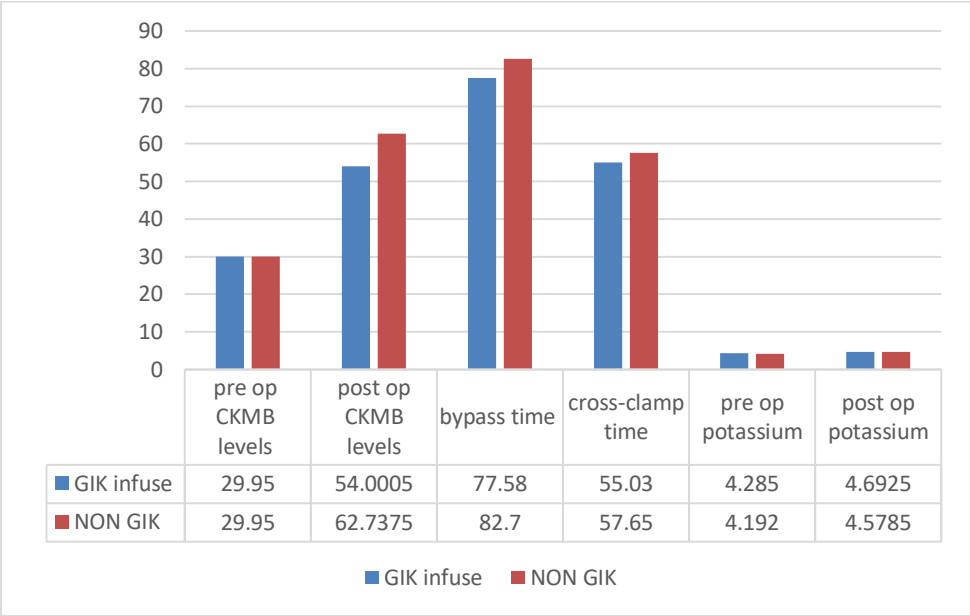

Figure 5. Pre and post-op outcomes of both groups (n=80).

DISCUSSIONS

This observational cross-sectional study was carried out to access the effectiveness of glucose-insulin-potassium infusion for myocardial protection in non-diabetic patients during adult cardiac surgery. GIK infusion is most commonly used in diabetic patients during cardiopulmonary bypass. Many studies suggested that the use of GIK infusion has beneficial outcomes mainly in myocardial protection, as myocardial protection is the main goal of Perfusionist during bypass surgery.

GIK is used normally in diabetic patients as it has a good effect on insulin maintenance. Most surgeons use GIK in diabetic patients but many of the studies suggest that it has good post-op outcomes especially myocardial protection. In our study, we use GIK in non–diabetic patients for assessment of myocardial protection, treatment of patients with cardiac dysfunction during episodes of ischemia and reperfusion.

In the GIK group, 5% dextrose containing 70 IU/L regular insulin and 70 meq/L of potassium was administered. The infusion was started at a rate of 30 ml/hour after induction of anesthesia and before the start of cardiopulmonary bypass. The infusion was started again after the removal of the aortic cross-clamp and was continued for six hours after the operation.

In this study the mean age of both groups which, in GIK infused (57.70±8.483) as compared to non-GIK infused (57.00±8.578). It also showed the lower percentages of smokers in GIK were lower as compared to Non-GIK if we discuss the previous medical history, we can assess that in GIK group the percentage was higher as compared to non-GIK, and most of the patients were undergone for CABG and few of them for ASD/VSD and valvular replacement. Most of them had previously coronary artery diseases and septal defects.

In the non-GIK group, most patients had previous coronary artery disease and valvular abnormality but few of them had septal defects. In the non-GIK group, most of the patients were undergone for CABG and valvular replacement. The effect of glucose-insulin infusion on a patient shows a good postoperative outcome. Many studies suggest that infusion of glucose in diabetic patients during cardiac surgery had a beneficial role in the maintenance of insulin requirement because in diabetic patient's insulin deficiency could be managed through this administration (9).

In another study by Bunger and colleagues showed that, during the change from anaerobic to aerobic metabolism, activation of glycolytic activity can show critical effect for the recovery of functional heart and in this sense, GIK can serve as a substrate (10). In another study conducted by Xu and their colleague, according to them, GIK shows beneficial effects in the scavenging activity of free radicals (11). According to the result of their study which shows that if we infused GIK before starting surgery and continued for 12±48h after surgery as suggested by other studies (9).

If we discuss nonmyocardial effects of ischemia and myocardial tissues, the main source of energy in their protection is a free fatty acid and provide 60-70% for their myocardial demand. During ischemia, these fatty acids can be provided by fatty acids. After all, it shows crucial effects because it can increase O_2consumption (12), also inhibit glucose consumption, and predispose

myocardium to arrhythmias during ischemia and reperfusion, e.g. it can also reduce the free fatty acid (13). After the provision of exogenous glucose substrate, it can be used as an improvement of the myocardium during ischemia and reperfusion (14). GIK can also play an important role in insulin signaled K-ATP channel activation. All estimates of the subgroup analysis supported GIK as cardioprotection. However, effect modification related to LVEF and CPB duration could not be excluded due to the low power of the tests for interaction (15). In conclusion, we demonstrated that pre bypass GIK infusion coupled with tight glycemic control improves Post bypass ventricular function, attenuates myocardial injuries, reduces ventilation timings and reduces the incidence of cardiac and respiratory complications after CABG and valvular and septal surgeries. Given its safety profile and effectiveness, this simple and low-cost metabolic cocktail might be considered a valuable adjuvant to the current myocardial protective strategy, particularly in moderate- and high-risk patients undergoing open-heart surgery (16).

CONCLUSION

Glucose-insulin-potassium (GIK) infusion has a beneficial role in myocardial protection and is associated with better post-operative outcomes without increasing the risk of non-cardiac complications. According to the results of this study, it is concluded that GIK infusion in adult cardiac surgery patients, there was good myocardial protection and better post-operative outcomes in GIK infused patients as compared to non GIK infused patients. It was also assessed that there was a low requirement for inotropic support, lesser ventilator time and a shorter length of ICU stay in the GIK group.

CONFLICT OF INTEREST STATEMENT

We hereby confirm that there is no conflict of interest which can effect the current work.

ACKNOWLEDGMENT

The authors wish to thank the Department of Cardiac Surgery, Pakistan Institute of Medical Sciences, Islamabad Pakistan for their support during data collection.

AUTHOR CONTRIBUTIONS

AHK conceptualized the whole study, wrote the first draft of the manuscript, performed the statistical analysis and supervised the whole study. HR collected the data and helped in revising the manuscript. HA helped in study design and conceptualization. KHF helped in editing the final version of the manuscript. All Authors have read and approved the final version of the manuscript.

FUNDING

This study did not receive any funding.

REFERENCES

1. Turin TC, Shahana N, Wangchuk LZ, Specogna AV, Al Mamun M, Khan MA, et al. Burden of cardio-and cerebro-vascular diseases and the conventional risk factors in South Asian population. Global heart. 2013;8(2):121-30.
2. Laslett LJ, Alagona P, Clark BA, Drozda JP, Saldivar F, Wilson SR, et al. The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy issues: a report from the American College of Cardiology. Journal of the American College of Cardiology. 2012;60(25 Supplement):S1-S49.
3. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Executive summary: heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation. 2016;133(4):447-54.
4. Ritsinger V, Malmberg K, Mårtensson A, Rydén L, Wedel H, Norhammar A. Intensified insulin-based glycaemic control after myocardial infarction: mortality during 20 year follow-up of the randomised Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI 1) trial. The lancet Diabetes & endocrinology. 2014;2(8):627-33.
5. Fath-Ordoubadi F, Beatt KJ. Glucose-insulin-potassium therapy for treatment of acute myocardial infarction: an overview of randomized placebo-controlled trials. Circulation. 1997;96(4):1152-6.
6. Maroko P, Libby P, Sobel B, Bloor C, Sybers H, Shell W, et al. Effect of glucose-insulin-potassium infusion on myocardial infarction following experimental coronary artery occlusion. Circulation. 1972;45(6):1160-75.

7. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, et al. Predictors of atrial fibrillation after coronary artery surgery: current trends and impact on hospital resources. Circulation. 1996;94(3):390-7.
8. Heng M, Norris R, PETER T, NISBET HD, Singh B. The effects of glucose-insulin-potassium on experimental myocardial infarction in the dog. Cardiovascular Research. 1978;12(7):429-35.
9. Straus S, Gerc V, Kacila M, Custovic F. Glucosa-Insulin-Potassium (GIK) solution used with diabetic patients provides better recovery after coronary bypass operations. Medical Archives. 2013;67(2):84.
10. Lazar HL, Chipkin S, Philippides G, Bao Y, Apstein C. Glucose-insulin-potassium solutions improve outcomes in diabetics who have coronary artery operations. The Annals of thoracic surgery. 2000;70(1):145-50.
11. Lazar HL, Philippides G, Fitzgerald C, Lancaster D, Shemin RJ, Apstein C. Glucose-insulin-potassium solutions enhance recovery after urgent coronary artery bypass grafting. The Journal of Thoracic and Cardiovascular Surgery. 1997;113(2):354-62.
12. BÜNGER R, Mallet RT, HARTMAN DA. Pyruvate-enhanced phosphorylation potential and inotropism in normoxic and postischemic isolated working heart: Near-complete prevention of reperfusion contractile failure. European journal of biochemistry. 1989;180(1):221-33.
13. Hess ML, Okabe E, Poland J, Warner M, Stewart JR, Greenfield L. Glucose, insulin, potassium protection during the course of hypothermic global ischemia and reperfusion: a new proposed mechanism by the scavenging of free radicals. Journal of cardiovascular pharmacology. 1983;5(1):35-43.
14. Jeppsson A, Ekroth R, Kirnö K, Milocco I, Nilsson B, Nilsson F, et al. Insulin and amino acid infusion after cardiac operations: effects on systemic and renal perfusion. The Journal of thoracic and cardiovascular surgery. 1997;113(3):594-602.
15. Bolli R, Jeroudi MO, Patel BS, Aruoma OI, Halliwell B, Lai EK, et al. Marked reduction of free radical generation and contractile dysfunction by antioxidant therapy begun at the time of reperfusion. Evidence that myocardial" stunning" is a manifestation of reperfusion injury. Circulation Research. 1989;65(3):607-22.
16. Ali-Hassan-Sayegh S, Mirhosseini SJ, Zeriouh M, Dehghan AM, Shahidzadeh A, Karimi-Bondarabadi AA, et al. Safety and efficacy of glucose–insulin–potassium treatment in coronary artery bypass graft surgery and percutaneous coronary intervention. Interactive CardioVascular and Thoracic Surgery. 2015;21(5):667-76.