Original Article

Evaluation of the effect of infusion of GIK (Glucose-Insulin-potassium) solution on serum lactate and central VO_2 during CABG surgeries

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ABSTRACT

Introduction: Prescription of glucose insulin potassium (GlK) affects the heart function with different mechanisms. GIK leads to metabolic support of myocardial muscle, reduced ischemia, and increased heart function reconstruction. Since lactate is a marker susceptible for heart function and saturation of central venous oxygen (SCVo2) is also useful in evaluating heart muscle perfusion, this study was conducted to evaluate the effect of injection of GIK solution on heart function using the indicators of serum lactate and saturation of central venous oxygen. Methodology: This double-blind clinical trial was performed on 74 patients aged 30-85 years undergoing coronary artery bypass grafting surgery. Patients were divided into two groups of GIK and control, and atrial fibrillation variables, the need to use inotropic, discharge time, serum lactate and SCVO2 levels 24 and 48 hours after surgery were compared in two groups using independent t-test, paired t-test, chi-square, and ANOVA. Results: the use of inotropic (P <0/01), incidence of AF (P = 0.003), discharge time of patients (P = 0.005) and death rate (P = 0.5) were higher in GIK group than those in the control group. In addition, serum lactate was higher in the control group (P <0.001) and CVO2 was higher in the GIK group 24 hours after surgery and 48 hours after surgery (P <0.001).

Keywords: Glucose-Insulin-potassium, lactate, CABG surgeries.

Introduction

Coronary artery disease is one of the main causes of death in the world nowadays [1]. One of the ways to reduce death caused by this disease is to use of Coronary Artery Bypass Grafting (CABG) surgery outlet technique. This surgery is the most common surgery performed nowadays by heart surgeons [2]. Approximately, 60 % of patients with coronary artery disease experience this surgical technique [3]. The use of the GIK (Glucose-Insulin-Potassium) solution was first used by Sodi-Pallares in the 1960s for treatment of acute myocardial infarction for electrical myocardia stabilizing in the ischemic phase [4]. Despite the extensive studies conducted on this solution and its use in various studies, the results of its use are still being questioned.

Different studies have shown that GlK prescription affects the heart function with different mechanisms. GIK causes metabolic support of myocardial muscle [5]. It also reduces ischemia and increases the heart function reconstruction [6]. In the ischemia phase, the carbohydrate aerobic metabolism alters metabolism of free fatty acids, leading to production of free radicals and metabolites in the heart muscle [7]. The use of GIK in cardiovascular diseases reduces the level of free fatty acids in the blood and reduces their absorption in myocardium and improves the function of the heart muscle [8]. Studies have reported its useful effects with regard to morbidity and the reasons for its association with GIK reagents [9], while some studies have suggested other contradictory results and have reported that the use of GIK is associated with increased morbidity (phlebitis, increased potassium levels and congestive heart failure) [10]. A protective effect has also been observed in patients undergoing cardiac surgery [11]. Although it is believed that heart takes major part of its required energy from fatty

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acids, recent studies have shown that lactate is also an important element for the heart [12]. Evidence suggests that lactate is a marker susceptible for cardiac function that can predict the level of left ventricular perfusion and post-CABG complications .Another study showed that SVO2 is a market predicting the short-term and long-term outcomes in patients with coronary artery bypass graft surgery [13]. The objective of this study was to evaluate the effect of using GIK on perfusion of ischemic tissues, including myocardial muscle, in patients undergoing elective coronary artery bypass grafting surgery. In this study, lactate was used as a marker for evaluation of myocardial function. As SVO2 is proportional to the rate of saturation of central venous oxygen (SCVO2), COV2 has also been used as an indicator in evaluation of heart muscle perfusion. If its results are proven to be useful and beneficial, given the cost-effectiveness and availability of GIK solution, it can be used to improve heart function in coronary artery bypass grafting surgery.

Methodology

This double-blinded clinical trial was conducted on 30-85-year-old patients admitted to the Shahid Faghihi Hospital of Shiraz for coronary artery bypass grafting surgery. Patients who met the inclusion criteria of study (age range of 30-80 years and ejection fraction of less than 40%) were included into study after obtaining their informed consent. Patients were randomly assigned to case and control groups .After induction of anesthesia, the case group received GIK solution with combinition of 00cc dextrose 10% and 40 units of insulin and 40 m equivalent of potassium chloride at a rate of 1 cc per kg per hour for up to 24 hours after anesthetic induction and normal saline as a placebo was used in the control group. The anesthetic induction method was the same in both groups and the demographic information and data needed before and after the surgery were collected by anesthesiologist nurse and nurse of intensive care unit. Data were analyzed before and after surgery by anesthesiologist nurse and nurse of intensive care unit .Data were analyzed using SPSS 20 software. In data analysis, in addition to descriptive statistics of SD ± Mean and Frequency (percentage), t-test, paired t-test, chi-square, and repeated-measures analysis of variance (RANOVA) were used to compare the groups. P value less than 0.05 was considered as acceptable level.

Results

Out of the 72 patients in the study, 37 patients (51.4%) were male and 35 patients (48.6%) were female .The mean age of patients was 59.8 ± 11.13 years and their age range from 38 to 85 years. The mean age of the group received the GIK was 57.34 ± 8.77 and the mean age of control group was 62.58 ± 12.94, which means no difference between two groups. In addition, the ejection fraction (EF) in the GIK group and in the control group was 41.31 ± 6 and 40.91 ± 5.25, respectively, which two groups did not differ significantly .The underlying characteristics of the patients in the GIK and control groups are presented in Table 1. As seen, by comparing the mean of quantitative variables in the two groups by using independent t-test and by comparing the number (percentage) of the qualitative variables using the Chi-square test, no significant difference was found between them in this regard. In this study, in order to assess the effect of GIK in patients, the level of serum lactate and saturation of venous oxygen 24 and 48 hours after the surgery was measured and compared in two groups. As shown in Table 2, the comparison of serum lactate level 24 hours after surgery using independent t-test showed a significant difference between the two groups of GIK and control with a mean of 0.31 ± 0.82 and P <0 / 001. This comparison was also significant between the two groups 48 hours after the surgery (P <0.001). At this time, the mean serum lactate level in the control group was 0.44 ±.07 higher than that in the control group (Table 2). ANOVA Repeated Measurement showed that means of serum lactate level were significantly different between the two groups (P = 0.001), considering the measurement repeat times (P = 0.001). Additionally, the intra-groups mean differences were also significant in the studied groups (P <0.001). As shown in Table 2, the rate of saturation of venous oxygen 24 hours after the surgery in the GIK group with a mean of 12.13 ± 2.09 was higher than that in the control group, which this difference was statistically significant (P </ 001). The mean difference 48 hours after surgery with value of 16.12 ± 2.21 in the GIK group was higher than that in the control group significantly (P <0.001). ANOVA Repeated Measurement test showed a significant intra-group and inter-group differences in terms of rate of saturation of venous oxygen by considering the repeat times of the measurements (P <0.001). Extubation time, patient discharge, rate of inotropic dependency, ventricular fibrillation, and postoperative morbidity were compared in two groups (Table 3). Extubation time after surgery in the control group was significantly higher than that in the GIK group (P = 0.001), so that the mean of this index was 7.68 ± 2.59 in the GIK group and 13.52 ± 8.79 in the control group. The patients discharge time in both groups showed a significant difference (P = 0.005). The mean of this index in the control group was 11.18 ± 3.81. The mean dependency on inotropic drugs in the control group was significantly higher than that of GIK group with a mean difference of 5.21 ± 1.02% (P <0.001). Chi-square test showed that the rate of incidence of ventricular fibrillation and morbidity after the surgery in the control group was not significantly different. (With P = 0.1 and P = 0.5, respectively).

Discussion

This study was conducted on 72 patients underwent elective coronary artery bypass grafting surgery in Shahid Faghihi Hospital of Shiraz to evaluate the effect of GIK solution on heart

function. The mean age of the patients was 59.8 ± 11.3 and there was no significant difference between the two groups of GIK and control in terms of the underlying variables at the beginning of the study .Arrhythmias are common side effects after heart surgery, which can be seen in 30 to 50% of cases. In this regard, AF is the most common arrhythmia found in clinical studies, and accounts for one third of patients hospitalized due to heart rhythm abnormalities [14]. In the present study, the rate of incidence of AF in the GIK group was not significant. In the study conducted by Agha Davoudi, the rate of incidence of arrhythmia in the control group was significantly higher than that of the GIK group [15]. Based on the study conducted by Golestani in Zanjan in 2012, GIK caused significant reduction in arrhythmia. Although the incidence of AF in the GIK group was reduced, this reduction was not significant [14]. The study conducted by Lazar also showed that the incidence of AF was reduced in the group received GIK and underwent heart surgery in an emergency [16]. GIK prescription may increase myocardial glycogen and cause atrial ischemia, leading to reduced arrhythmias [17], as in the study conducted by Lazar, patients of GIK group had a higher glycogen level and lower AF. [16] In a meta-analysis study conducted by Doreen, after GIK injection in patients undergoing CABG surgery, a greater percentage of patients were affected by AF [10]. In this study, the dependency and the need for inotropic use in GIK group was not significant. In the study conducted by Golestani, the rate of inotropic intake in patients who did not receive GIK was slightly higher than that in GIK group, while this difference was not significant [14]. The study conducted by Wistbacka on CABG patients did not showed significant difference between two groups in terms of need for inotropes after surgery [18]. However, it should be noted that in the study conducted by Wistbacka, the effect of GIK consumption before connection to pump was examined, so the time of GIK receiving was shorter, and this might justify for lack of the difference. The other result of the present study suggests the longer extubation time in control group than that of GIK group. Moreover, the patients' discharge time in the control group was significantly higher than that of control group (11.18 ± 3.81). Since GIK prescription may reduce cell death and size of the area affected by infraction, the ischemia and its complications would also decrease and heart performance would improve. In the study conducted by Agha Davoudi et al, a similar result was obtained, indicating shorter hospitalization time in ICU in the GIK group compared to that in the control group [15]. In the study conducted by Lazar, patients who received GIK solution had shorter discharge time than control group [16]. In the study conducted by Shim et al on patients with ACS underwent surgery, the duration of hospitalization in ICU and the duration of hospitalization in the control group were higher, but this difference was not significant [19]. In the study conducted by Smith, in which receiving the GIK with methods of off pump and cardiopulmonary bypass were compared, no difference in the duration of hospitalization in ICUs was seen [20]. The other result of the study suggests that morbidity rate in the GIK group is not low. Some studies have shown that receiving the GIK does not have an effect on the survival of patients, and they have even indicated that GIK can increase the morbidity, especially phlebitis, increased blood potassium, and congestive heart failure [10]. In the study conducted by Shim, as our study, the rate of morbidity in patients receiving GIK was higher, but this difference was not significant [19]. The main and important result of this study suggests the lower serum lactate level 24 hours after surgery, with a mean of 0.31 ± 0.82 and lower serum lactate level 48 hours after surgery, with a mean of 0.44 ± 0.77 GIK in the GIK group. Based on these results, receiving the GIK would decrease the serum lactate level and as duration of receiving the GIK increases, the serum lactate level would decrease. Thus, it can be stated that not only receiving the GIK but also the time to receive this solution affect the serum lactate level .As serum lactate level predicts the left ventricular perfusion and postoperative complications of CABG [13], it can be stated that receiving the GIK increases left ventricular perfusion, leading to decreased ischemia and improved heart function .In this study, 24 hours after surgery, the levels of SCVO2with a mean of 12.13 ± 2.09 and 48 hours after surgery, the levels of SCVO2 with mean of 16.12 ± 2.21 were significantly higher in GIK group. In this study, the SCVO2 levels 24 hours after the surgery was significantly lower than the initial SCVO2 in the case group, and after discontinuation of GIK, its level increased 48 hours after surgery compared to that 24 hours after the surgery, although this difference was not significant. As the level of Sov2 is proportional to SCVO2, in the study conducted by Szabo on diabetic patients undergoing CABG, the level of Sov2 was higher in the GIK group than that in the control group at all stages of measurement, but this difference was not significant [21].

Conclusion

Thus, based on the results of the present study, using GIK reduces the use of inotropes, reduces the duration of hospitalization, and reduces serum lactate level, and increases SCVO2 after CABG to some extent. Although, it is a for long time that the possible effect of GIK on heart function has been suggested and several studies have been carried out on different groups over the past years, conflicting results have been reported in this regard. Thus, the benefits of this solution cannot be completely approved. However, this study suggests the beneficial effects of this solution in patients undergoing coronary artery bypass grafting surgery .Therefore, it is recommended that complementary studies with larger sample sizes using different doses and different GIK prescription times to be conducted on different patients in order to reduce the inconsistencies and make more complete conclusion on the effects of this solution on the heart function.

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