Comparison of intralipid with saline for ejection fraction, serum lactate and hemodynamic changes after coronary artery bypass graft

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Abstract

Background and Aims:

One of the complications of coronary artery bypass graft is reperfusion injury and myocardial damage. In vitro, intralipid has been able to reduce the size of the infarct area. In this study, intralipid was compared to saline for ejection fraction, lactate, and hemodynamic parameters of patients.

Materials and Methods:

This study was conducted on 60 patients undergoing coronary artery bypass graft with age<70 years and with an ejection fraction > 35%. The induction of anesthesia was performed in a similar manner and by a same surgeon for all patients. After intensive care unit transfer and the extubation, saline and 20% intralipid solutions were injected into the subjects in the control and intervention groups, respectively, on three hours. Before and after the injection of solutions, ejection fraction and serum lactate level were assessed by a special cardiologist. Moreover, heart rate and mean blood pressure were measured every 30 min from the onset of infusion to the end of the study. Data was analyzed with SPSS software version 16. P-value less than 0.05 were considered statistically significant.

Results:

Sixty patients were divided into two same groups. Both groups were homogeneous for demographic characteristics and euroscore. Although, there was a significant increase in ejection fraction for two groups during the study (P=0.00 in both groups). But, no significant difference was observed between the two groups regarding EF (P=0.26). Lactate serum level decreased significantly in both groups; that was more in the intralipid group (P=0.001). In addition, mean arterial pressure significantly decreased in both groups (P=0.001 and P=0.00 in control and intralipid groups, respectively), that was higher in the intralipid group, compared with the control group (P=0.001). Also, the patients' heart rate decreased in both groups, and it was more in the intralipid group (P=0.01).

Conclusion:

In our study, intralipid infusion improved the hemodynamic status of patients and was better than saline group. Also the level of serum lactate was lower in patients of the intralipid group. There was no significant difference between the two groups regarding the ejection fraction level. Given the low complications of intralipid administration and improved nutrition of patients, it is suggested that this method can be used for patients after CABG.

Keywords: intralipid, saline, ejection fraction, coronary artery bypass graft.

Introduction

High incidence of coronary artery disease has increased the invasive therapies, there such as heart stents and open heart surgery. One of complications following these invasive treatments include reperfusion injury, rapid release of acid and potassium compounds into the bloodstream through mitochondrial permeability (mPTP), can reduce cardiac function (1,2).

In recent years, researchers have paid great attention to fats, especially unsaturated fatty acids, due to their effects on heart disease, cardiac protection, and reperfusion injury (3,4,5). Intravenous intralipid is a combination of fatty acids that have been used for decades. In some studies, it has been shown that intralipid reduces the infarct size in reperfusion injury (6,7). This compound is used in local anesthetics (especially bupivacaine) cardiac toxicity (8,9). On the other hand, some studies have reported the insignificant impact of intralipid on cardiac function after heart valve surgery (3).

Due to lack of human studies and conflicting results, we aimed to compare the effect of intralipid and saline on patients undergoing CABG and cardiopulmonary bypass. We assessed its effects on the ejection fraction, lactate, and hemodynamic changes of patients.

Materials and Methods

This randomized double-blinded prospective study was conducted on candidates of coronary artery bypass graft (CABG) who admitted to ICU. The patients were enrolled in the study after approvals of the ethics committee and research deputy of the university (code: 930285) and written informed consent from the patients. The inclusion criteria were age below 70 years and ejection fraction (EF) above 35. The Exclusion criteria included the need for mechanical ventilation and inotrope before surgery, body mass index (BMI) above 30, the need for balloon pump, inherited metabolic disease, dysrhythmia, and the history of cardiac surgeries.

60 patients were randomly divided into two equal groups using the envelope sampling technique. At first, patients were assessed with Euroscore model. Then, EF was measured for all patients by a cardiologist who had no information about the groups. Afterwards, all patients underwent anesthesia and surgery through a similar method. Induction of anesthesia was carried out with intravenous injection of midazolam 40 µg/kg, propofol 1-2 mg/kg, pancuronium 0.1 mg/kg, and fentanyl 2-5µg/kg.

Patients were intubated and underwent cardiopulmonary bypass surgery under moderate systemic hypothermia (28-32°C).The surgeon had no information about the study group. To protect the heart during surgery, a cold cardioplegic solution (below 4°C),which was a combination of saline with 14 mEq of potassium chloride and 80 milligrams of lidocaine and 1 gram of magnesium sulfate, was utilized. This solution was used after the onset of heart bypass and aortic clamping.

The patients were transferred to the ICU and after the endotracheal tube was removed, saline and 20% intralipid solutions (in 1cc/kg/hour) were injected in the control and intervention groups for three hours, respectively. Before and after the administration of the solution, the EF was rechecked by the same cardiologist. Hemodynamic variables, such as heart rate and blood pressure, were evaluated every half hour from the onset of infusion to the end of the study. In addition, lactate level was measured before and after intralipid and saline infusions.

Statistical analysis

Due to lack of similar studies on human, the present study was carried out as a pilot study on 60 patients. Data analysis was performed in SPSS (version 16) using Kolmogorov-Smirnov test (to assess the normal distribution of the data), t-test, and ANOVA (to evaluate the parametric data, including age, BMI, ejection fraction, lactate, and hemodynamic changes [blood pressure and heart rate]), as well as the Chi-square test, Fisher's exact test, and Mann-Whitney U test (to analyze the non-parametric data). P-value less than 0.05 was considered statistically significant.

Results

In this study 60 patients were divided to same groups, the intervention group (intralipid group) and the control group (normal saline group). Table 1 shows the demographic characteristics and euroscore of the patients, no apparent statistical difference was observed between the groups.

Ejection fraction (EF): The levels of EF in the control and intralipid groups before the injection of relevant solutions were44.3±3.6 and 45.3±4.9, respectively (P=0.49). After 3hours and injection of normal saline, the EF level was 47.7±3.1, which showed a significant increase (P=0.00). In the intralipid group, the EF after three hours of injection was estimated at 48.7±3.9, which was also significant (P=0.00). However, the comparison of the two groups showed no significant difference (P=0.26).

Mean arterial pressure (MAP): The level of MAP before infusion was 96.7±4.1 mmHg and 94.3±8.2 mmHg in the saline and intralipid groups, respectively, showing no significant difference in this regard (P=0.28). During the study, MAP deceased in all patients. Reduction of MAP was significant in both groups (P=0.001 and P=0.00 in the control and intralipid groups, respectively). Moreover, the reduction of mean arterial pressure was more significant in the intralipid group, compared to the control group (P=0.001).

Heart rate: The heart rate of patients in the saline and intralipid groups before infusion was 97.4±6.463 per min and 96.3±9.7 per min, respectively, showing no significant difference between the two groups (P=0.59). During the study, the heart rate of all patients decreased, more significantly in the intralipid group (P=0.01).

The lactate level: Arterial blood lactate before infusion was 2.9±0.3 mmol/L and 2.8±0.2 mmol/L in the saline and intralipid groups, respectively. There was no significant difference between the two groups (P=0.42). After the solutions infusion, the level of lactate decreased in both groups. After 3 hours, lactate levels were 2.2±0.3 mmol/L and 1.2±0.1 mmol/L in the control and intralipid groups, respectively (P=0.001 and P=0.00, respectively). In this regard, the decrease of lactate level was more significant in the intralipid group, compared to the control group (P=0.001).

Discussion

The intravenous fat emulsion, with the commercial name of intralipid, is a sterile, isotonic, and non-pyrogenic solution that causes no fever. Moreover, it has been used as a source of energy for many body tissues and for essential fatty acid deficiencies in patients requiring intravenous feeding for many years.

In the present study, there were two groups of patients, one group received saline and the other group received intralipid infusions. The patients in the two groups were compared for performance of cardiac indicators (e.g., lactate level, heart rate, mean arterial pressure, and ejection fraction).

A number of studies have shown that intralipid reduces cardiac injuries following ischemia-reperfusion, improves heart performance, and decreases the infarction size, compared to the control group (4,5,10). In this study, the lactate level decreased after intralipid infusion, compared to the control group. The lactate dehydrogenase is an enzyme with a special medical performance since it is frequently found in body tissues, including heart muscles. When heart muscles are injured, lactate dehydrogenase is released into the blood, which makes it an important indicator for the identification of myocardial injuries (11,12). Cardiac toxicity is correlated with excessive intravascular administration of local anesthetic drugs (especially bupivacaeine). On the other hand, the intravenous fat emulsion can reduce cardiac damage due to local anesthesia. Therefore, intralipid infusion can improve cardiac activities and

reduces side effects of local anesthesia drugs. Accordingly, the lower the lactate level is the more positive performance of intravenous fat emulsions (13,14).

In a study conducted by Eghbali, various cardioprotective effects were observed for intralipid in ischemia-reperfusion injuries, meaning that fat infusion increases aortic pressure and arterial pressure more than saline. Fat infusion in the heart leads to the increased number, pressure, and consumption of myocardial oxygen (15,16). In a previous study, fat emulsion positively increased the inotropic effect and tissue blood pressure (17).

In the current research, intravenous fat emulsion had a greater effect on the improvement of arterial pressure and heart rate, in a way that the mean arterial pressure and heart rate of patients decreased from 94.3 and 96.3 to 87.9 and 86.0, respectively. Also intralipid infusion enhanced cardiac function statistically significant, and the mean EF increased from 45.3 to 48.7. However, this increase was not clinically significant (P=0.26), which can be due to the properties of plasma dilatation caused by intralipid. Fatty acids enhance the calcium entry into heart cells and smooth muscle cells, which not only improves heart function but also increases blood pressure.

In an animal model of verapamil toxicity in rodents, intralipid was able to increase the heart rate. Gueret et al. reported that intralipid in verapamil toxicity led to the increased entry of calcium into the myocyte, thereby causing an inotropic improvement (18). In the present research, intralipid reduced the heart rate. It seems that the differences between the results of various studies might be due to the differences in the concentration and speed of intralipid administration and fat load.

With the rapid administration of high levels of intralipid and increased fat intake, the lipoprotein lipase enzyme also increases, resulting in an increase in the concentration of free fatty acids in the plasma. This high concentration leads to impaired endothelium-dependent vasodilation mechanisms, resulting in vascular contraction, decreased capacity of large and small arteries, increased vascular resistance, and high blood pressure (19). In the present study, there was a decrease in mean arterial pressure in both groups, which was more significant in the intralipid group. The reason might be a greater reduction in lactate and blood acidity, and its effect on cardiac refluxes with a lower rate of intralipid injection.

Martin Harvey et al. evaluated the effect of intralipid infusion on the improvement of blood pressure caused by propranolol in rabbits. In this study, animals were exposed to 6mg/kg of 20% intralipid and 6mg/kg 0.9% normal saline. Pulse and mean arterial pressure were recorded at intervals of 2.5-15 min. The results showed that the mean arterial pressure in the intralipid group (mean 69 mmHg) was higher than normal saline (mean 53 mmHg) in 15 min (P=0.029) (20). Moreover, Stojiljkovic et al. indicated that administration of $0.8ml.m^{-1}\ min^{-1}$ of intralipid and heparin solution to healthy individuals increased systolic and diastolic arterial pressure as well as the heart rate of subjects (21). Nevertheless, there was a reduction in the arterial pressure and heart rate in the current research, which might be due to the level of the consumption of intralipid and/or consumption of narcotics during or after surgery.

Conclusion

According to the results of the present study, the injectable fat emulsion can be considered as a factor in open heart surgery, which can improve hemodynamic parameters. However, as a new method in improving the treatment, there is a need to conduct more scientific research on different laboratory animals, doses and concentrations to assess intralipid efficacy on cardiac function after invasive cardiac therapies.

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Table 1- demographic and prestudy euroscore in two groups.

Basic parameters	Saline group (n=30)	Intralipid group (n=30)	P value
Age (year)	59.5±7.9	60.8±7.1	0.51
Sex (F/M)	8/22	11/19	0.41
BMI (Kg/m2)	27.9±1.5	27.5±1.5	0.23
Euro Score	3.6±1.6	3.6±1.4	0.64

Table 2- hemodynamic parameters and lactate level in two groups.

parameters	Study time	Saline group (n=30)	Intralipid group (n=30)	P value
Ejection fraction (%)	Before infusion	44.3±3.6	45.3±4.9	0.001
	After infusion	47.7±3.1	48.7±3.9	0.00
Mean blood pressure (mmHg)	Before infusion	96.7±4.1	94.3±8.2	0.00
	After infusion	93.3±4.3	87.9±5.5	0.001
Heart rate (pulse/min)	Before infusion	97.4±6.4	96.3±9.7	0.00
	After infusion	94.1±6.7	86±8.1	0.00
Lactate level (mmol/L)	Before infusion	2.9±0.3	2.8±0.2	0.001
	After infusion	2.2±0.3	1.2±0.1	0.00