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The Use of Prophylactic Levosimendan in Patients with Left Ventricular Dysfunction Under Off-pump Coronary Artery Bypass Graft Surgery

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Abstract

Introduction: Levosimendan is a calcium sensitive inotrope and ATP-sensitive potassium channel opener that is effective in the prevention and treatment of low cardiac output syndrome (LCOS) after cardiac surgery. The purpose of this study was to investigate the need for inotrope during ICU admission, the incidence of myocardial infarction within 3 days after surgery, the need for insertion of intra-aortic balloon pump within 3 days after surgery, and examining the time of extubation of the endotracheal tube and the time of discharge from the ICU.

Methods: In this randomized clinical trial, 60 patients with mean age of 65 years with left ventricular ejection fraction (% 30 ≥) (LVEF), who were candidates of off pump coronary artery bypass graft surgery were examined. Patients were screened for 20 days before surgery and those with renal insufficiency or liver failure as well as those who simultaneously needed to use inotropic or vasopressor drugs or were candidates for cardiac surgery using a cardiopulmonary pump were excluded. Patients were randomly divided into experimental and control groups. After insertion of the arterial catheter and simultaneously with the skin incision in the experimental group, intravenous prophylactic levosimendan (0.1g / kg / min) was used from the start of surgery to 24 hours after surgery. The control group did not receive any inotrope. For statistical analysis of data U Mann-Whitney test and Chi-square test were used ($P< 0.05$).

Results: The use of levosimendan had no significant effect on the time of extubation of the endotracheal tube in the ICU ($p = 0.336$); Also, levosimendan had no significant effect on the time of discharge of patients from ICU ($p = 0.292$). However, the use of levosimendan had a significant effect on the need for insertion of intra-aortic balloon pump (IABP) ($p = 0.038$) as well as the incidence of myocardial infarction ($p <0.001$), and reduced the incidence of myocardial infarction ($p=0.001$) and the percentage of need for insertion of intra-aortic balloon pump (IABP).) ($p = 0.038$).

Conclusion: According to findings of the present study, it is recommended to use levosimendan to reduce the incidence of myocardial infarction and reduce the need for insertion of intra-aortic balloon pump in patients with left ventricular dysfunction in off pump coronary artery bypass graft surgery.

Keywords: Levosimendan, Coronary Artery Bypass Graft Surgery, Off pump.

Introduction

Open heart surgery is a common surgical procedure. Compared to the past, patients with open heart surgery are more likely to have higher age and associated illness (1). This is accompanied by complications and one of these complications is low cardiac output syndrome, which occurs in 3 to

14% of patients undergoing open heart surgery (2, 3). Patients with left ventricular dysfunction are accompanied with the low cardiac output syndrome (4). This syndrome has a high short-term mortality and can be managed using inotropic drugs and inserting intra-aortic balloon and heart pumps for facilitating left and right ventricular drainage (5, 6). The prevention of low cardiac output syndrome is an important therapeutic aspect in improving the outcome of patients undergoing off pump open heart surgery. Levosimendan is a calcium sensitizing inotrope and ATP-sensitive potassium channel opener that is effective in the prevention and treatment of low cardiac output syndrome (LCOS) after cardiac surgery. The purpose of this study was to investigate the need for inotrope during ICU admission, the incidence of myocardial infarction within 3 days after surgery, the need for insertion of intra-aortic balloon pump within 3 days after surgery, and examining the time of extubation of the endotracheal tube and the time of discharge from the ICU. Levosimendan have recently been used in more than 60 countries to prevent and treat low cardiac output syndrome (LCOS) (7.9). But so far, the effect of levosimendan on patients undergoing off-pump open heart surgery has not been examined. In this study, we investigated the effect of use of prophylactic levosimendan in the prevention of low cardiac output syndrome and other important complications on patients with low cardiac output syndrome who were candidates for off pump open heart surgery. The use of prophylactic levosimendan started at the same time as surgery started and lasted up to 24 hours after surgery.

Methods

In this randomized clinical trial, 60 patients with mean age of 65 years with left ventricular ejection fraction (% 30 ≥) (LVEF), who were candidates of off pump coronary artery bypass graft surgery were examined to investigate the effect of use of prophylactic levosimendan. The criteria for inclusion of the subjects were off pump CABG surgery and ejection fraction less than 40 percent. The criteria for exclusion of the subjects were moderate to severe kidney failure, advanced liver failure, systolic blood pressure less than 80 mmHg, left bundle branch block in echocardiography, and ventricular arrhythmias in the form of Torsade de point in the patientب electrocardiography. Patients were screened for 20 days before surgery, and those with renal insufficiency or liver failure as well as those who simultaneously needed to use inotropic or vasopressor drugs or were candidates for cardiac surgery using a cardiopulmonary pump were excluded. Patients were randomly divided into experimental and control groups. After insertion of the arterial catheter and simultaneously with the skin incision in the experimental group, intravenous prophylactic levosimendan (0.1 g / kg / min) was used from the start of surgery to 24 hours after surgery. The control group did not receive any inotrope. An electrocardiogram was recorded on the base and after surgery, it was recorded on days 0, 1, 2, 3. This study aimed to investigate the need for inotrope during ICU admission, the incidence of myocardial infarction within 3 days after surgery, the need for insertion of intra-aortic balloon pump within 3 days after surgery, and examining the time of extubation of the endotracheal tube and the time of discharge from the ICU. For statistical analysis of data U Mann-Whitney test and Chi-square test were used (P< 0.05).

Results

Table 1 Indicates the characteristics of patients under study (Table 1). The results of U Mann-Whitney test showed that there was no significant difference between the mean time of extubation of the endotracheal tube in the control group (18.20 ه 12.35) and the levosimendangroup (9.20 ه 14.70) (p = 0.336). Therefore, it can be concluded that the use of levosimendanhas no significant effect on the time of discharge from the ICU of patients with left ventricular dysfunction during off pump coronary artery bypass graft surgery.

The findings also showed that there was no significant difference between the mean discharge time of ICU in control group (3.46 ± 0.89) and levosimendan group (3.22 ± 0.62) (p = 0.292). Therefore, it can be concluded that the use of levosimendan had no significant effect on the time of extubation and discharge of ICU in patients with left ventricular dysfunction during off pump coronary artery bypass graft surgery (Table 2). Analysis of chi-square test showed that 16 subjects, i.e., 53.33% of the control group contracted myocardial infarction three days after the surgery, while in levosimendan groupnone of the patients gotinvolved with myocardial infarction, and given the significant level obtained from the chi-square test,the use of levosimendan had a significant effect on myocardial infarction three days after the surgery and reduced it (p<0.001). Also, the use of levosimendan had a significant effect on the need for the insertion of intra-aortic balloon pump (IABP) (0.038). Four people (i.e., 13.33%) of the control group needed intra-aortic balloon pump within three days after operation, but none of the people in the levosimendan group needed the insertion of intra-aortic balloon pump (IABP) (Table 3).

Table 1. Characteristics of patients in the study

Groups Variable	Experimental group (Levosimendan) (N=30)	Control group (No Drug) (N=30)
Average Age (Year)	65	65
Gender		
Male	16	15
Female	14	15
Hypertension (%)	80	80.2
Diabetes mellitus (%)	55	54.8
Chronic lung disease (%)	30	26.6
Myocardial infarction (%)	54	52
Heart Failure (%)	80.6	81
Stroke (%)	14	12
Heart condition before surgery		
Heart Rate(beats/min)	70	71
Systolic Pressure Mean(mmHg)	130	128
LVEF Mean (%)	25	26
Preoperative medications		
Aspirin (%)	75	76
Beta blocker (%)	82	81

Table 2. U Mann-Whitney test to compare the time variables of extubation of the endotracheal tube and discharge from the ICU in the research groups

Variable	Group	Mean± SD	Z	P
Extubation of the Endotracheal Tube	Control	18.20±12.35	-0.96	0.33
	Levosimendan	14.70±9.20		
Discharge from the ICU	Control	3.46±0.89	-1.05	0.29
	Levosimendan	3.23±0.62		

Table 3. Chi-square Test for Comparison of Myocardial Infarction Variables and Intra-Aortic Balloon Pump (IABP) in the Study Groups

Variable	Group	Frequency and Percentage		df	X^2	P
Myocardial infarction		Having Myocardial Infarction	Lacking Myocardial Infarction	1	18.25	0.001
	Control	(%53.33) 16	(%46.66) 14			
	levosimendan	(% 0) 0	(%100) 30			
IABP		Having IABP	Lacking IABP	1	4.28	0.03
	Control	(%13.33) 4	(%86.66) 26			
	levosimendan	(% 0) 0	(%100) 30			

Discussion

Levosimendan is a calcium sensitizer that increases myocardial function. This increase in function is caused by more energy production through more effective myocardial contraction than is induced by adrenergic stimulation with catecholamines, therefore, potentially levosimendan is a useful alternative to standard drugs for the prevention of low cardiac output syndrome after open heart surgery. The limitations of this study was that this drug is relatively new and produced by foreign companies and we faced problems to provide it, and that open coronary artery bypass grafts are mostly operated under the heart-lung pump and there is a case limitation to collect data in the off-pump operation with low cardiac output. It can be concluded that the use of levosimendan has no significant effect on the time of extubation of the endotracheal tube and the discharge of the ICU of patients with left ventricular dysfunction in off-pump coronary artery bypass graft surgery. However, it reduces the incidence of myocardial infarction and reduces the percentage of the need for insertion of intra-aortic balloon pump in patients with left ventricular dysfunction undergoing off-pump coronary artery bypass graft surgery.

Conclusion

The use of levosimendan has no significant effect on the time of extubation of the endotracheal tube and discharge from the ICU of patients with left ventricular dysfunction during off pump coronary artery bypass graft surgery. But it reduces the incidence of myocardial infarction and reduces the percentage of need for insertion of intra-aortic balloon pump in patients with left ventricular dysfunction under off pump coronary artery bypass graft surgery.Therefore, it is recommended to use levosimendan to reduce the incidence of myocardial infarction and reduce the need for insertion of intra-aortic balloon pump in patients with left ventricular dysfunction in off pump coronary artery bypass graft surgery.

Ethical issues

Not applicable.

Authors' contributions

All authors equally contributed to the writing and revision of this paper.

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