Effect of Milrinone on Short Term Outcome of Patients with Myocardial Dysfunction Undergoing Off-Pump Coronary Artery Bypass Graft: A Randomized Clinical Trial

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Abstract- Myocardial dysfunction is a major complication in cardiac surgery that needs inotropic support. This study evaluates the effect of milrinone on patients with low ventricular ejection fraction undergoing off-pump coronary artery bypass graft (OPCAB). The present study is designed to evaluate the effect of milrinone on myocardial dysfunction. Eighty patients with low ventricular ejection fraction (<35%), candidate for elective OPCAB, were enrolled in this study. They were randomly assigned to two groups. One group received milrinone (50 μg/kg) intravenously and another group received a saline as placebo followed by 24 hours infusion of each agent (0.5 μg/kg/min). Short outcome of patients such as hemodynamic parameters and left ventricular ejection fraction were variables evaluated. Serum levels of creatine phosphokinase, the MB isoenzyme of creatine kinase, occurrence of arrhythmias and mean duration of mechanical ventilation were significantly lower in milrinone group (P<0.05). The mean post operative left ventricular ejection fraction was significantly higher in milrinone group (P=0.031). There were no statistical significant differences between the two groups in terms of intra-aortic balloon pump, inotropic support requirement, myocardial ischemia, myocardial infarction, duration of inotropic support, duration of intensive care unit stay, mortality and morbidity rate. Administration of milrinone in patients undergoing OPCAB with low ventricular ejection fraction is useful and effective.

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Keywords: Low ventricular ejection fraction; Milrinone; Myocardial dysfunction; Off-pump coronary artery bypass graft

Introduction

Off-pump coronary artery bypass graft (OPCAB) is a universal procedure safe for treatment of ischemic heart disease that has reduced complications in comparison to on pump coronary artery bypass graft (CABG). One of the complications in cardiac surgery is myocardial dysfunction that needs inotropic support (1-4). Low output syndrome (LOS) is a major complication of CABG that leads to serious hemodynamic changes such as ventricular dysfunction due to heart pressure during OPCAB (5,6). Both right and left ventricular dysfunctions are common complications in echocardiography findings after CABG which is more common in hemodynamically unstable patients (7). LOS involves about 30% of patients undergoing CABG (5,8). It leads to more hospital stay and cost, more intensive care unit (ICU) stay, long days of recovery and organ failure (9,10). In patients with ventricular dysfunction, LOS or right ventricular diastolic dysfunction can increase risk of mortality post CABG (5).

Preventing from LOS or right ventricular diastolic dysfunction needs to improve myocardial dysfunction with inotropic and vosoactive drug support (11). One of

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these drugs is milrinone. Milrinone is a phosphodiesterase III inhibitor that consumes myocardial Oxygen less than other drugs like it (12-14). It increases cardiac output with positive and vasodilative effects and increases blood flow of internal mammary arteries in CABG. Also, it improves hemodynamic profile and prevents decreased mixed venous oxygen saturation in OPCAB (15-17). Milrinone is an effective drug in patients with beta-receptor down-regulation; for instance, those who have congestive heart failure. It improves diastolic performance in these patients (18,19). However, there are studies that are in contrast with this effect of milrinone (20,21). Previous studies in patients with ventricular dysfunction show that milrinone improves function of ventricle, and also improves hemodynamic components (22,23). There are no studies about outcomes of patients in OPCAB who take milrinone. The present study is designed to evaluate effect of milrinone on myocardial dysfunction and to test the hypothesis that milrinone can decrease myocardial ischemia and myocardial infarct in patients undergoing off-pump CABG.

Materials and Methods

Our randomized, double-blind, placebo controlled clinical trial study was approved by the regional ethical committee of Shahid Sadoughi University of Medical Science. We received the written consent form patients, who participated voluntarily in off-pump CABG surgery in Afshar Cardiovascular Center of Yazd. Eighty patients with severe myocardium dysfunction (left ventricular ejection fraction [LVEF] lower than 35%) (24) were enrolled in this study. Patients who underwent emergency CABG, those with myocardial infarction (MI) or ventricular arrhythmias within 72 hours before the operation, and those requiring inotropic support prior to the surgery were excluded. Concomitant valvular heart disease and left bundle branch block were other exclusion criteria. Eighty eligible patients were randomly divided into two groups. One group (n=40) took 50 µg/kg milrinone and another group (n=40) received placebo intravenously immediately after surgery and continued as an infusion (0.5 µg/kg/min) for 24 hours later. Ejection fraction (EF) of all patients was measured 24 hours before and after surgery with transthoracic echocardiography by a single expert cardiologist who was blind to the study. All of the operations were performed by the same senior surgeons. Creatine phosphokinase (CPK), creatine kinase MB (CK-MB) and troponin (TP) were measured immediately after surgery and 24 hours later. Demographic data, pre-and post-LVEF, CPK and CK-MB level, CK-MB/CPK, the need for intra aortic balloon pump (IABP), duration of inotropic support, length of ICU stay, duration of mechanical ventilation and appearance of ventricular or atrial arrhythmia were recorded for each patient. Also, evidence of myocardial ischemia and myocardial infarct (MI) were recorded. The characteristics for diagnosing of myocardial ischemia were new ST depression (at least 0.1 mV) or new ST elevation (at least 0.2 mV). Evidence of MI was by elevating CPK, CK-MB or CK-MB/CPK ratio more than 6% or TP concomitant with changing in electrocardiography (new Q wave or conductive abnormality); evidence of ischemia in echocardiography (new wall motion abnormality) was also recorded. Our data were analyzed by SPSS 16.5 software. ANOVA, Chi-square, Fisher's exact test and T-test were used for quantitative and qualitative variables. A P-value < 0.05 was considered statistical significant.

Results

Eighty patients candidate for off-pump CABG were enrolled in this study. The mean age of patients was 62.45±10.12 (standard deviation). Of 80 patients, 57 patients (71.2%) were male and 23 patients (28.8%), female. There were no statistical significant differences between the two study groups regarding sex and age distribution. The demographic characteristics of our patients are shown in table 1. The number of involved vessels is also recorded in table 1.

The mean preoperative EF was lower in the control group but there was no statistical significant difference between the two groups (P=0.74). There was statistical significant difference in post operative EF between the two groups (P=0.031). Three patients (7.5%) in milrinone group and 7 patients (17.5%) in the control group required IABP (P=0.17). Evidence of myocardial ischemia was found in 5 patients (12.5%) in milrinone group and 11 patients (27.5%) in the control group (P=0.09). Evidence of MI was found after surgery in 4 patients (10.0%) in milrinone group and 9 patients (22.5%) in the control group (P=0.13). There was no statistical significant difference between the two groups regarding myocardial ischemia and MI; however, the rates of myocardial ischemia and MI were lower in milrinone group.

Table1. Comparison of baseline and demographic data of patients between the two groups.

Data	Milrinone (n=40)	Control (n=40)	*P*-value
Age	61.90±10.71	63.00±9.60	0.63
Sex (male/female)	31/9	26/14	0.21
Diabetes mellitus (%)	35	40	0.64
Hypertension (%)	40	32.5	0.48
Hyperlipidemia (%)	45	40	0.65
Prior myocardial infarction (%)	50	40	0.36
Single vessel CAD (%)	2.5	5	0.17
Two vessels CAD (%)	25	37	0.17
Three vessels CAD (%)	57	55	0.17
LMCAD (%)	15	2.5	0.17
Pre-operative LVEF (%)	29.02±5.46	28.62±5.65	0.74
Post-operative LVEF (%)	29.75±5.76	26.95±5.66	0.031

Data presented as mean±standard deviation; CAD: coronary artery disease; LMCAD: left main coronary artery disease; LVEF: left ventricular ejection fraction

Table 2. Comparison of post-operative parameters between the two groups.

Data	Milrinone (n=40)	Control (n=40)	*P*-value
Need for IABP (n (%))	3 (7.5%)	7 (17.5%)	0.17
Myocardial Ischemia (n (%))	5 (12.5%)	11 (27.5%)	0.09
Myocardial Infarction (n (%))	4 (10%)	9 (22.5%)	0.13
Duration of inotropic support (h)	8.02±9.61	12.47±13.54	0.09
ICU stay (days)	2.35±0.53	2.50±0.59	0.24
Duration of mechanical ventilation (h)	10.32±4.65	14.30±9.57	0.021
Arrhythmia (n (%))	5 (12.5%)	14 (35%)	0.017
Mortality (n (%))	1 (2.5%)	1 (2.5%)	1.00
Morbidity (n (%))	3 (7.5%)	4 (10%)	0.69

Data presented as mean±standard deviation; IABP: intra aortic balloon pump; ICU: intensive care unit

Nineteen patients (47.5%) in milrinone group and 21 patients (52.5%) in the control group needed inotropic support (*P*=0.65).

Duration of inotropic support was longer in the control group than milrinone group, but there was no significant difference between two groups (*P*=0.09). The mean ICU stay was 2.3 days in milrinone group and 2.5 days in the control group (*P*=0.24).

The values of CPK immediately after surgery was higher in the control group than milrinone group; therefore, there was a statistical significant difference between the two groups in CPK values (*P*=0.00). Also, there was significant difference in CK-MB values immediately and 24 hours later after surgery between the two groups (*P*=0.00; *P*=0.032). It was higher in the control group than milrinone group in both conditions. There was a statistical significant difference in CK-MB/CPK, 24 hours later after surgery (*P*=0.031). There was no significant difference in TP between the two groups.

Duration of mechanical ventilation was longer in the control group than milrinone group. There was a statistical significant difference in duration of mechanical ventilation between the two groups (*P*=0.021).

The rate of mortality was one (2.5%) in both groups. The cause of mortality in both groups was cardiac shock. The rate of morbidity was 3 (7.5%) in milrinone group and 4 (10%) in the control group. These morbidities were bleeding, renal failure and cerebrovascular accident (CVA). The most common morbidity was renal failure that occurred in 4 patients (5%); 1 patient (2.5%) in milrinone group and 3 patients (7.5%) in the control group. There was no statistical significant difference in mortality and morbidity between the two groups (*P*=1.00; *P*=0.69). Comparison of post-operative parameters between the two groups is presented in table 2.

There was a statistical significant difference in arrhythmias between the two groups (*P*=0.017). There were 5 patients (12.5%) with arrhythmia in milrinone group and 14 patients (35%) with arrhythmia in the control group.

Table 3. Comparison of types of arrhythmias between the two groups.

Type of Arrhythmias	Milrinone (n=40)	Control (n=40)
PVC (n (%))	2 (5%)	5 (12.5%)
AF (n (%))	2 (5%)	3 (7.5%)
Ventricular tachycardia (n (%))	0	3 (7.5%)
AF + PVC (n (%))	1 (2.5%)	2 (5%)

PVC: premature ventricular contraction; AF: atrial fibrillation

There were three types of arrhythmias: atrial fibrillation (AF), ventricular tachycardia (V-Tach) and premature ventricular contraction (PVC). The most common arrhythmia among the patients was PVC (8.8%). These kinds of arrhythmias are presented in table 3.

Discussion

The result of this study disclosed that utilization of milrinone in patients with ventricular or myocardial dysfunction undergoing off-pump CABG can reduce the level of CPK, CK-MB and CK-MB/CPK ratio in these patients. Also, these results showed that administration of milrinone in these patients can decrease duration of mechanical ventilation, rate of arrhythmias and improve post operative EF in these patients.

Previous study was shown that milrinone maintains plasma concentrations at the verge of therapeutic consequences (24). Studies showed that administration of milrinone has safety and efficacy in treatment of LOS (18,25). Bailey *et al.* (24) showed that administration of milrinone can reduce myocardial ischemia in patients undergoing elective CABG. The results of present study also observed high rate of myocardial ischemia and myocardial infarct in the control group. However, there was no significant difference between the two groups regarding myocardial ischemia and MI.

Previous studies done by Kikura *et al.,* Oztekin *et al.* and Yamaguchi *et al*. indicated that milrinone can decrease inotropic support after surgery (26-28). Results of the present study showed that there was no statistical significant difference regarding inotropic support between the two groups. However, the duration of inotropic requirement was lower in milrinone group, making this result almost in accordance with the result of the study done by Levy *et al.* (29).

Previous studies done by Konstam *et al*., George *et al.* and Conture *et al*. showed that milrinone can increase left ventricular systolic performance, cardiac output and correct low EF (30-32). In the present study, there was statistical significant difference regarding post operative EF between the two groups. It was higher in milrinone group than in the control group. A study done by Konstam *et al.* (30) showed no significant difference in using IABP. The present study also had no statistical difference in using of IABP between both groups.

A study conducted by Jebeli *et al.* (33) reported statistical significant differences regarding myocardial ischemia, myocardial infarction and duration of inotropic support. In the present study, there was no statistical significant difference in myocardial Ischemia, MI and duration of inotropic support. Similar to previous study (33), the present study had statistical significant difference in CPK, CK-MB between the two groups.

A study done by Gorodeski *et al.* (34) showed that there was no significant difference regarding mortality in patients administered with milrinone. In the present study, there was no statistical significant difference in mortality and morbidity between the two groups. However, this result is in contrast with the study of Zangrillo *et al.* (35), who reported that milrinone may increase mortality in patients undergoing cardiac surgery. Jo *et al.* (36) reported that administration of milrinone has a beneficial effect on cardiac output in patients undergoing OPCAB. In the present study, there was a statistical significant difference regarding cardiac output between the two groups. Cardiac output had been improved in milrinone group. Fleming *et al.* (37) reported that milrinone is an independent risk factor for postoperative atrial fibrillation after elective cardiac surgery. The result of present study was different from that. This study had lower arrhythmias such as AF, in milrinone group. There was a statistical significant difference regarding arrhythmias between the two groups. Two studies done by Feneck (18,38) showed that milrinone may be effective and safe in the treatment and improvement of low cardiac out in patients undergoing cardiac surgery. The present study showed that milrinone can increase cardiac output following cardiac surgery.

This study had some limitations. There was no data on Swan-Gans measurements of cardiac function. Also,

this study had no data on cardiac index. It was a short follow-up, which can be another limitation of this study.

The present study shows that administration of milrinone in patients undergoing off-pump CABG with low LVEF, has no effect on myocardial infarct and myocardial ischemia but, it has effect on other conditions. It may reduce duration of mechanical ventilation and arrhythmias. Also, it may make better LVEF after surgery.

References

1. Heringlake M, Wernerus M, Grunefeld J, Klaus S, Heinze H, Bechtel M, Bahlmann L, Poeling J, Schön J. The metabolic and renal effects of adrenaline and milrinone in patients with myocardial dysfunction after coronary artery bypass grafting. Crit Care 2007;11(2):R51.
2. Hart JC, Spooner TH, Pym J, Flavin TF, Edgerton JR, Mack MJ, Jansen EW. A review of 1,582 consecutive Octopus off-pump coronary bypass patients. Ann Thorac Surg 2000;70(3):1017-20.
3. Porat E, Sharony R, Ivry S, Ozaki S, Meyns BP, Flameng WJ, Uretzky G. Hemodynamic changes and right heart support during vertical displacement of the beating heart. Ann Thorac Surg 2000;69(4):1188-91.
4. Abu-Omar Y, Taggart DP. The present status of off-pump coronary artery bypass grafting. Eur J Cardiothorac Surg 2009;36(2):312-21.
5. Jeon Y, Ryu JH, Lim YJ, Kim CS, Bahk JH, Yoon SZ, Choi JY. Comparative hemodynamic effects of vasopressin and norepinephrine after milrinone-induced hypotension in off-pump coronary artery bypass surgical patients. Eur J Cardiothorac Surg 2006;29(6):952–6.
6. Nierich AP, Diephuis J, Jansen EW, Borst C, Knape JT. Heart displacement during off-pump CABG: how well is it tolerated? Ann Thorac Surg 2000;70(2):466-72.
7. Costachescu T, Denault A, Guimond JG, Couture P, Carignan S, Sheridan P, Hellou G, Blair L, Normandin L, Babin D, Allard M, Harel F, Buithieu J. The hemodynamically unstable patient in the intensive care unit: hemodynamic vs. transesophageal echocardiographic monitoring. Crit Care Med 2002;30(6):1214–23.
8. Bernard F, Denault A, Babin D, Goyer C, Couture P, Couturier A, Buithieu J. Diastolic dysfunction is predictive of difficult weaning from cardiopulmonary bypass. Anesth Analg 2001;92(2):291–8.
9. Avery GJ 2nd, Ley SJ, Hill JD, Hershon JJ, Dick SE. Cardiac surgery in the octogenarian: Evaluation of risk, cost, and outcome. Ann Thorac Surg 2001;7(2)1:591–6.
10. Liu J, Tanaka N, Murata K, Ueda K, Wada Y, Oyama R, Matsuzaki M. Prognostic value of pseudonormal and restrictive filling patterns on left ventricular remodeling and cardiac events after coronary artery bypass grafting. Am J Cardiol 2003;91(5):550–4.
11. Liu LL, Gropper MA. Respiratory and hemodynamic management after cardiac surgery. Curr Treat Options Cardiovasc Med 2002;4(2):161–9.
12. Feneck RO, Sherry KM, Withington PS, Oduro-Dominah A. European Milrinone Multicenter Trials Group. Comparison of the hemodynamic effects of milrinone with dobutamine in patients after cardiac surgery. J Cardiothorac Vasc Anesth 2001;15(3):306–15.
13. Kikura M, Levy JH, Michelsen LG, Shanewise JS, Bailey JM, Sadel SM, Szlam F. The effect of milrinone on hemodynamics and left ventricular function after emergence from cardiopulmonary bypass. Anesth Analg 1997;85(1):16-22.
14. Monrad ES, Baim DS, Smith HS, Lanoue AS. Milrinone, dobutamine, and nitroprusside: comparative effects on hemodynamics and myocardial energetics in patients with severe congestive heart failure. Circulation 1986;73(3 Pt 1):III 168-74.
15. Lobato EB, Gravenstein N, Martin TD. Milrinone, not epinephrine, improves left ventricular compliance after cardiopulmonary bypass. J Cardiothorac Vasc Anesth 2000;14(4):374–7.
16. Solina A, Papp D, Ginsberg S, Krause T, Grubb W, Scholz P, Pena LL, Cody R. A comparison of inhaled nitric oxide and milrinone for the treatment of pulmonary hypertension in adult cardiac surgery patients. J Cardiothorac Vasc Anesth 2000; 14(1):12–7.
17. Kwak YL, Oh YJ, Shinn HK, Yoo KJ, Kim SH, Hong YW. Haemodynamic effects of a milrinone infusion without a bolus in patients undergoing off-pump coronary artery bypass graft surgery. Anaesthesia 2004;59(4):324-31.
18. Feneck RO. Effect of variable dose milrinone in patients with low cardiac output after cardiac surgery. European Multicenter Trial Group. Am Heart J 1991;121(6 Pt 2):1995-9.
19. Monrad ES, McKay RG, Baim DS, Colucci WS, Fifer MA, Heller GV, Royal HD, Grossman W. Improvement in indexes of diastolic performance in patients with congestive heart failure treated with milrinone. Circulation 1984;70(6):1030–7.
20. Maslow AD, Regan MM, Schwartz C, Bert A, Singh A. Inotropes improve right heart function in patients undergoing aortic valve replacement for aortic stenosis. Anesth Analg 2004;98(4):891–902.

21. Lobato EB, Willert JL, Looke TD, Thomas J, Urdaneta F. Effects of milrinone versus epinephrine on left ventricular relaxation after cardiopulmonary bypass following myocardial revascularization: assessment by color m-mode and tissue Doppler. J Cardiothorac Vasc Anesth 2005;19(3):334–9.
22. Kikura M, Levy JH, Bailey JM, Shanewise JS, Michelsen LG, Sadel SM. A bolus dose of 1.5 mg/kg amrinone effectively improves low cardiac output state following separation from cardiopulmonary bypass in cardiac surgical patients. Acta Anaesthesiol Scand 1998;42(7):825–33.
23. Rathmell JP, Prielipp RC, Butterworth JF, Williams E, Villamaria F, Testa L, Viscomi C, Ittleman FP, Baisden CE, Royster RL. A multicenter, randomized, blind comparison of amrinone with milrinone after elective cardiac surgery. Anesth Analg 1998;86(4):683–90.
24. Bailey JM, Levy JH, Kikura M, Szlam F, Hug CC Jr. Pharmacokinetics of intravenous milrinone in patients undergoing cardiac surgery. Anesthesiology 1994;81(3):616–22.
25. Wright EM, Sherry KM. Clinical and haemodynamic effects of milrinone in the treatment of low cardiac output after cardiac surgery. Br J Anaesth 1991;67(5):585–90.
26. Kikura M, Levy JH, Michelsen LG, Shanewise JS, Bailey JM, Sadel SM, Szlam F. The effect of milrinone on hemodynamics and left ventricular function after emergence from cardiopulmonary bypass. Anesth Analg 1997;85(1):16–22.
27. Oztekin I, Yazici S, Oztekin DS, Goksel O, Issever H, Canik S. Effects of low-dose milrinone on weaning from cardiopulmonary bypass and after in patients withmitral stenosis and pulmonary hypertension. Yakugaku Zasshi 2007;127(2):375-83.
28. Yamaguchi A, Tanaka M, Naito K, Kimura C, Kobinata T, Okamura H, The efficacy of intravenous milrinone in left ventricular restoration. Ann Thorac Cardiovasc Surg 2009;15(4):233-8.
29. Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. Ann Thorac Surg 2002;73(1):325-30.
30. Konstam MA, Cody RJ. Short-term use of intravenous milrinone for heart failure. Am J Cardiol 1995;75(12):822–6.
31. George M, Lehot JJ, Estanove S. Haemodynamic and biological effects of intravenous milrinone in patients with a low cardiac output syndrome following cardiac surgery: multicentre study. Eur J Anaesthesiol 1992;5:31–4.
32. Couture P, Denault AY, Pellerin M, Tardif JC. Milrinone enhances systolic, but not diastolic function during coronary artery bypass grafting surgery. Can J Anaesth 2007;54(7):509-22.
33. Jebeli M, Ghazinoor M, Mandegar MH, Rasouli MR, Eghtesadi-Araghi P, Goodarzynejad H, Mohammadzadeh R, Darehzereshki A, Dianat S. Effect of milrinone on shortterm outcome of patients with myocardial dysfunction undergoing coronary artery bypass graft: A randomized controlled trial. Cardiol J 2010;17(1):73-8.
34. Gorodeski EZ, Chu EC, Reese JR, Shishehbor MH, Hsich E, Starling RC. Prognosis on chronic dobutamine or milrinone infusions for stage D heart failure. Circ Heart Fail 2009;2:320-4.
35. Zangrillo A, Biondi-Zoccai G, Ponschab M, Greco M, Corno L, Covello RD, Cabrini L, Bignami E, Melisurgo G, Landoni G. Milrinone and mortality in adult cardiac surgery: a meta-analysis. J Cardiothorac Vasc Anesth 2012;26(1):70-7.
36. Jo HR, Lee WK, Kim YH, Min JH, Chae YK, Choi IG, Kim YS, Lee YK. The effect of milrinone infusion on right ventricular function during coronary anastomosis andearly outcomes in patients undergoing off-pump coronary artery bypass surgery. Korean J Anesthesiol 2010;59:92-8.
37. Fleming GA, Murray KT, Yu C, Byrne JG, Greelish JP, Petracek MR, Hoff SJ, Ball SK, Brown NJ, Pretorius M. Milrinone use is associated with postoperative atrial fibrillation after cardiac surgery. Circulation 2008; 118(16):1619-25.
38. Feneck RO. Intravenous milrinone following cardiac surgery: I. Effects of bolus infusion followed by variabledose maintenance infusion. The European Milrinone Multicentre Trial Group. J Cardiothorac Vasc Anesth 1992;6(5):554-62.