

Original Research Article

Levosimendan: a remedy for treating the patients of decompensated heart failure

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Received: 14 March 2020

Revised: 23 June 2020

Accepted: 30 June 2020

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ABSTRACT

Background: Levosimendan is a new-fangled calcium based sensitizer which is used to treat the patients with congestive or decompensated heart failure. The empirical study reveals that it intensifies myocardial contractility and expands coronary and peripheral vessels without affecting the diastolic function adversely. Levosimendan also performs as an opener of ATP-based K channels in vascular smooth muscle. The empirical research study shows the benefits of usage of levosimendan over other drugs in the treatment of decompensated and congestive heart failure.

Methods: Levosimendan has been administered to patients with decompensated heart failure conditions. Infusion of levosimendan started with a dose of 0.1 µg/kg/min and titrated to 0.2 µg/kg/min. The systolic BP has been monitored after the administration of levosimendan to maintain stability in the patient's BP for the initial 2-3 hours. The suggested duration of infusion of levosimendan in critical heart failure is twenty-four hours. Initially levosimendan is infused in the patients with systolic BP is more than hundred mmHg and diastolic BP is more than sixty mmHg.

Results: The outcomes of the usage of Levosimendan have been studied on 80 patients with decompensated heart problems and the comparative study has also been made with other inotropes, respectively. We have also performed a trial on two groups of people named as LIVO and NON-LIVO groups. The research study proves that the usage of levosimendan is better than other inotropes. Levosimendan can be recommended in the standard treatment of patients with acute heart conditions.

Conclusions: Levosimendan is offering an effective remedy to treat the patients with decompensated heart failure. In comparison to other inotropes available for the treatment of patients suffering from congestive heart ailments, levosimendan can be considered to be a safe and efficient sensitizer.

Keywords: Calcium based sensitizer, Decompensated heart failure, Inotropes, Levosimendan

INTRODUCTION

Heart dysfunction is a kind of critical clinical disease and the outcome of heart failures (HF) may cause numerous disorders such as pericardium, heart valves, endocardium, myocardium, and metabolic abnormalities.¹⁻³ The count of patients with chronic heart failure is keep on rising year by year due to bad life styles, consumption of drugs, obesity, other ailments such as diabetes, high blood

pressure and inactive routine.^{4,5} However, with the advent of new medicines and research in this area, the chances for survival have been improved over the last decade but still cardiovascular disease is the most prevalent reason behind the hospitalization of adults in 21st century, with an estimation of 27 million people around with world are suffering from heart diseases. However, there are great numbers of people suffer from cardiovascular diseases but still people with acute heart failure (AHF) are

relatively low.⁶ The patients with AHF conditions face considerable complications due to deterioration of heart health, frequent visit to hospitals, and high mortality rate.^{7,8} AHF condition is a major challenge for patients, doctors, and healthcare systems. The AHF patients experience deterioration in the quality of their lives due to frequent hospitalizations, expensive treatments and prolonged stay at hospitals.⁹

Though strict obedience is mandatory against the recommended treatment of patients with AHF to shape their life back to normal and to recover from the lethal AHF condition but there is no assurance whether the patient with AHF may bear the currently available treatments and therapies due to hypotension and comorbidities.¹⁰

The current standard of medical immersions prescribed for AHF includes the full range of established therapies such as diuretics, angiotensin-II receptor blockers (Azilsartan, Candesartan, Losartan (Cozaar), Olmesartan (Benicar), Telmisartan (Micardis), Eprosartan, Irbesartan (Avapro), Valsartan), ACE inhibitors, Nephilysin inhibitors, mineralocorticoid-receptor antagonists, Beta blockers, and Corlanor. The usage of traditional adrenergic inotropes has been considered unsatisfactory with respect to mortality rate and it has not exhibited any strong effects on hospitalization, except a few positive impacts on symptomatic and haemodynamics improvements in some research studies.

In the last decade, a new aspect on the treatment of decompensated HF has been proposed by introducing levosimendan which is a 'Ca' sensitizer and 'K' channel opener.^{11,12} This drug combines positive inotropic, vasodilation, and cardio-protective effects, without increasing the demand for oxygen.^{13,14}

Levosimendan is one of the most researched inotrope. The outcomes of the treatment of decompensated HF using levosimendan are far better than other conventional inotropes in terms of mortality and myocardial oxygen demand.¹⁵ Levosimendan promotes inotropy through non-adrenergic approaches; it may provide a way to comprehend the potential advantages of inotropic support in decompensated HF with minor adverse effects.¹⁶ The alternating usage of levosimendan for the long-term indicative improvements in patients with AHF is gaining popularity.¹⁷ Levosimendan yields a variety of cardiovascular impacts including arterio-ventricular recoupling, de-congestion, and cardiac protection from reoxygenation injury.

METHODS

The attributes mentioned in Table 1 have been considered for the research study on the patients suffering from decompensated HF. In Table 1, the description of each attribute is provided for the better understanding of readers.

Table 1: Attributes considered for the research study of patients with AHF.

Attributes	Description
Patient Id	Provides information about the patient
Diagnosis	It provides detail in the ailment like Coronary artery disease (CAD), Triple vessel disease(TVD), Hypertension, Acute inferior wall myocardial infarction (IWNI), Severe aortic regurgitation(AR) etc.
Surgery	Provides details on the surgical procedure performed such as coronary artery bypass grafting surgery, Aortic valve replacement + interpositional grafting.
Systolic BP	Provides reading on blood pressure
Urine output	Adequate or 75 to 100 ml
Other inotropes	Apart from Levosimendan if similar drugs have been infused
IABP requirement	Provides details whether intra-aortic balloon pump is required
Heart failure treatments	Provides the details on drugs used in the heart treatment
Diastolic BP	Provides reading on blood pressure
BPM	Depicts beats per minute
Other inotropes	The attributes provides details on other inotropes used in addition to levosimendan
Diuretics used	This attribute provides information whether the diuretics are used or not post procedure
ICU stay	This attribute provides information on the stay of the patient in ICU
Levosimendan given	This attribute tells whether levosimendan was added in the treatment of AHF patients or not. If yes, then the quantity of dosage

Authors have conducted research study on two groups named LIVO and NON-LIVO with 40 patients each. Levosimendan is infused to the patients belong to LIVO group and levosimendan is not used along with other inotropes for the patients belong to NON-LIVO group. We are describing below the parameters used for research study.

Diagnosis

The patients who have been diagnosed with AHF conditions such as Coronary artery disease (CAD), Triple vessel disease (TAD), Acute inferior wall myocardial infarction (AIWMI), Severe aortic regurgitation (SAR), Severe Aortic stenosis with aortic regurgitation (SASAR), Acute myocardial infarction (AMI), Peripheral vascular disease (PVD), Hypertension, Dyspnea on

exertion. Many patients were found with combination of these diseases during diagnosis.

Treatment

The corrective surgeries have been performed on the patients such as Coronary artery bypass surgery (CABG), Aortic Valve Replacement Surgery (AVRS), and Aortic valve replacement plus inter positional graft.

Levosimendan dosage

Inotropes such as levosimendan are required in acute heart conditions of patients when there is a low cardiac output. Infusion of levosimendan inotrope has been started with a dose of 0.1 $\mu\text{g}/\text{kg}/\text{min}$ to the patients post-surgery and titrated to 0.2 $\mu\text{g}/\text{kg}/\text{min}$ in our research study. Levosimendan is infused in the AHF patients with systolic BP is more than hundred mmHg and diastolic BP is more than sixty mmHg. The recommended duration of infusion of levosimendan in critical heart failure is twenty four hours. The systolic BP has been monitored after the infusion of levosimendan dosage to observe the impact of levosimendan on patient and to maintain stability in the blood pressure of the patient.

Other inotropes

All inotropes are considered to enhance the contractility of human heart. There are many inotropes available to ensure that the treatment to a patient of AHD is appropriate. Inotropes increase cardiac output, eventually increasing MAP (mean arterial pressure) and maintain oxygen supply to vital organs and tissues. The inotropes given to the patients in our research study along with dosage of levosimendan are noradrenaline, adrenaline and dobutamine. Inotropes were tapered for 2, 3 or 4 days with respect to the condition of a patient.

IABP requirement

IABP stands for an intra-aortic balloon pump which facilitates patient's heart in pumping more blood. The patient suffering from decompensated HF needs IABP if his heart is not able to pump enough blood to his body. Apart from inotropes, a few patients also needed IABP in our research study.

Blood pressure

The systolic and diastolic blood pressures are also considerable attributes in AHF patients. Patients have been monitored after the administration of levosimendan to maintain stability in the patient's blood pressure. The suggested duration of infusion of levosimendan in critical heart failure is 24 hours. Initially levosimendan is infused in the patients with systolic blood pressure more than hundred mmHg and diastolic blood pressure more than sixty mmHg.

Heart rate

The heart rate of patients has also monitored and it is observed especially after the infusion of levosimendan in LIVO group patients and after the infusion of other inotropes in NON-LIVO group of patients.

Diuretics usage

The diuretic doses were used in a few patients where the urine output of the patient was not sufficient as per the physiological standards.

ICU stay

The duration of ICU stay was from 3 to 6 days.

RESULTS

The cardiac healthcare centres aim for reduction in stay at hospitalization and reduction in mortality rate in the treatment of AHF patients. The methods we have used to conduct medical research have turned out to be very subtle endpoint in trials. Sometimes there exist confounding factors impacting the reliable measurements and ideal endpoints to test the effectiveness of the treatment.

Authors are concluding this research study with the results obtained from the trial on 80 patients which have been divided into two groups named LIVO and NON-LIVO. In a trial of LIVO group, levosimendan is infused along with other inotropes mentioned the previous section and in NON-LIVO group, levosimendan has not been administered along with other inotropes.

Authors have aggregated the results of each group to provide concrete analysis on the trials. The first parameter is IABP which is mechanical equipment that upsurges myocardial O_2 perfusion and also improves cardiac output but it is needed when the human heart is not capable enough to supply the sufficient blood to the body. We have compared the usage of IABP to the patients of LIVO and NON-LIVO group and results have been presented in Figure 1.

The second parameter considered for evaluation is 'ICU stay'. The number of patients stayed in ICU after the corrective surgeries as mentioned in previous section.

The third parameter for study is blood pressure. We have observed blood pressure of patients in both the groups post-surgery. It is noted that patients from LIVO group have shown systolic blood pressures (SBP) and diastolic blood pressures (DBP) as per physiological standards by the fourth day of post-surgery whereas patients of NON-LIVO group have shown high rise than the standard levels of SBP and DBP. We have aggregated the readings of SBP and DBP to represent the average readings post-

surgery from day 1 to day 5 for both the groups LIVO and NON-LIVO as shown in Figure 3.

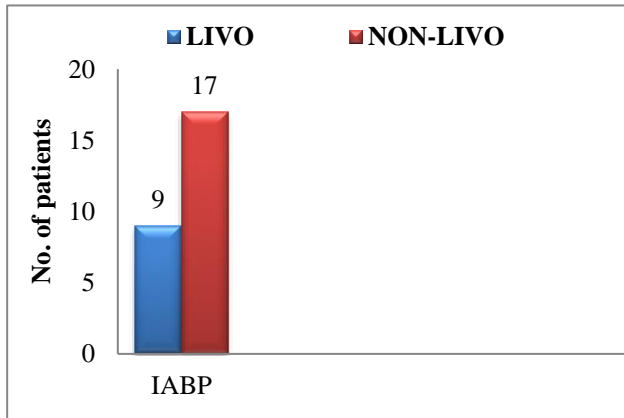


Figure 1: Representing patients from both groups who required IABP with inotropes.

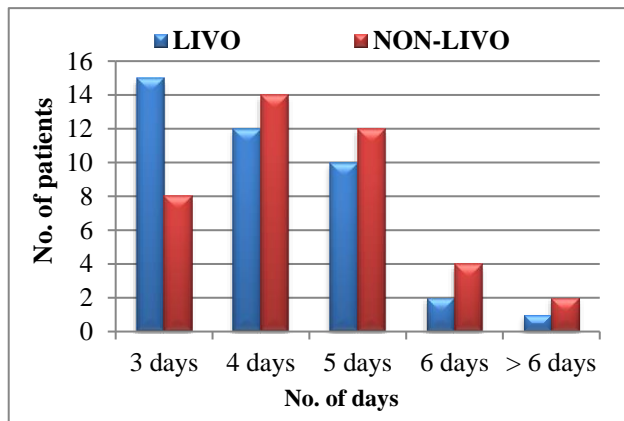


Figure 2: Depicting ICU stay of patients from both the groups.

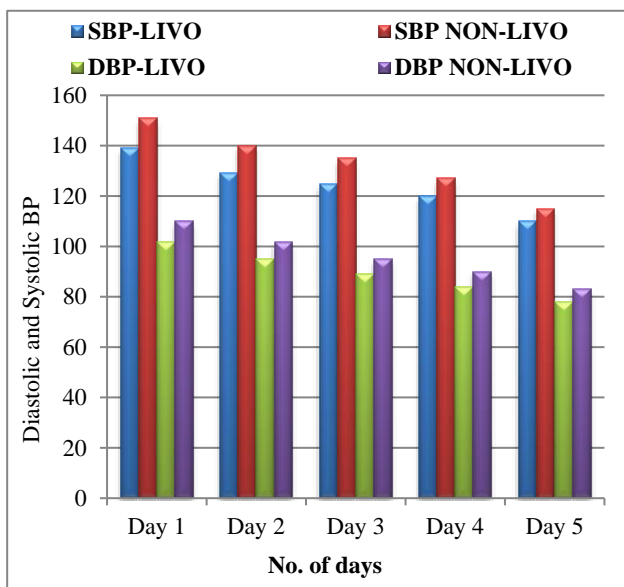


Figure 3: Representing SBP and DBP post-surgery from day 1 to day 5.

The next parameter considered for the study is BPM (Heartbeat rate per minute). We have observed the patients post-surgery from day 1 to day 5. The patients of LIVO group have HR less than 90 BPM post-surgery and infusion of levosimendan inotrope, whereas patients from NON-LIVO group were observed with HR more than 90 BPM. The average rate of BPM is displayed in Figure 4.

The next parameter considered for study is “Diuretic” doses. The diuretic doses were given to 10% patients of LIVO group and 25% patients of NON-LIVO group. Post-surgery follow-ups of patients in LIVO group are 5% lesser than those belong to NON-LIVO group.

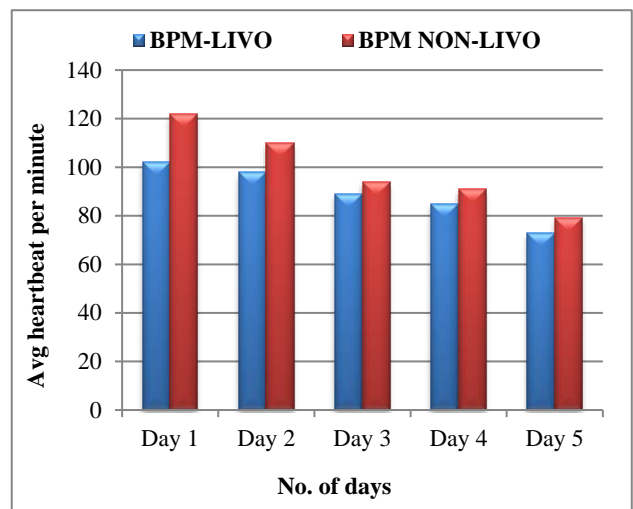


Figure 4: Representing BPM post-surgery from day 1 to day 5.

DISCUSSION

A composite result of reduction in mortality rate and re-hospitalisations could ensure the extensive acceptance of drugs such as levosimendan. However, with the usage of levosimendan inotrope only a proportion of the patients participating in the trial contribute to the end results. We have observed that the patients with similar ailment and similar surgeries were administrated with levosimendan along with other inotropes in LIVO group. It is observed that patients from LIVO have shown lesser stay at ICU, more stability in heart rate, controlled systolic and diastolic BP as compare to patients from NON-LIVO group. Subsequent effects are also accountable such as follow-up duration after hospital discharge, sampling size of patient population, and we may add these factors in our future research work.

There are other exiting approaches mentioned in where experimental study has been conducted with administration of levosimendan in comparison with other inotropes.¹⁸⁻¹⁹ The authors have concluded that Levosimendan is better than dobutamine inotrope for treating patients with chronic heart diseases, those patients who are on beta-blocker therapy or the patients who are hospitalized with severe decompensations.¹⁸ The

authors specify that Levosimendan plays a significant role in the management of acute heart problems (AHP); it produces greater relief to the heart failure symptoms and producing a number of beneficial effects on hemodynamic, neurohormonal and functional parameters.¹⁹ Spasmodic or repeated courses of levosimendan are associated with lesser need for AHP related hospitalizations. The survival advantages of levosimendan in comparison with traditional inotropes have also been reported. The authors have emphasized over maintaining good quality of life for patients with AHP.²⁰ The use of levosimendan certainly helps in achieving good quality of life as the patients respond to heart failure treatment in a better manner. The need for intermittent therapy is also reduced.

There are many research studies available in the literature that states the benefits of using levosimendan over other inotropes. We have attempted to prove the hypothesis of benefit of usage of levosimendan over other inotropes on 80 patients where two groups have been formed and 50% patients have been administrated with levosimendan and 50% are administrated with other inotropes. The result section of this paper shows advantage of using levosimendan with respect to ICU stay, IABP, blood pressure measures, diuretic doses and heart rate.

ACKNOWLEDGEMENTS

We acknowledge that the research studies (LIVO and NON-LIVO group patients) have been carried out at CTVS-ICU, Fortis Healthcare, Mohali, India. We are also thankful to the doctors and healthcare staff members who have contributed directly or indirectly in conducting this research study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Dhaliwal VS, Gill MS, Monica. Levosimendan: a remedy for treating the patients of decompensated heart failure. *Int J Adv Med* 2020;7:1280-5.