

## A Review On: “The Study of Milrinone in the Treatment of Chronic Heart Failure”

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### ABSTRACT:

Chronic Heart Failure is one of the most common and life-threatening cardiovascular condition affecting nearly 64.3 million people in worldwide. Almost half of the patient with CHF will die within a Year, Hospitalization is common in this patient and associated with poor prognosis, in this situation after 3 to 6 months from discharge they had need for readmission. The percentage range of the readmission is 30 % to 50%. Congestive Heart Failure (CHF) is a clinical syndrome in which the heart is unable to pump blood at the pace required by the metabolizing tissues, or can only do so with an increase in filling pressure. Insufficient or defective cardiac filling, as well as poor contraction and emptying, may cause the heart to be unable to pump enough blood to satisfy the needs of the body's tissues. To sustain the heart's pumping function and produce a redistribution of blood flow, compensatory mechanisms increase blood volume, cardiac filling pressure, heart rate, and cardiac muscle mass. Despite these compensating measures, the heart's ability to contract and relax weakens over time, leading to heart failure (HF). **Milrinone** which is phosphodiesterase inhibitors and commonly used inotropic agent that used for short term intravenous treatment for exacerbation of CHF and it helps to relieve symptoms of CHF and improve the hemodynamic in patients, it having both inotropic and vasodilation property.

**Keywords:** Milrinone, Congestive, Exacerbation, Inotropic, Phosphodiesterase, Vasodilator

### I. INTRODUCTION:

Congestive Heart Failure

- CHF refers to clinical syndrome caused by inherited, abnormalities of Heart Structure and the function causing symptoms and signs that leads decrease quality and quantity of life.

- Important to understand CHF is a type of Heart Failure (HF) not totally distinct: -
  - The failure at left half cause different signs and symptoms causes LHF.
  - The failure at right half causes distinct set of features that called as RHF.
  - The combination of the two (RHF&LHF) known as CHF.

### ➤ SYMPTOMS:

In the CHF following are the signs and symptoms

- Shortness of breath, Dizziness or lightheaded and weight gain.
- Unusual swelling in legs, hands, feet and abdomen
- Persistent cough or Chest congestion, Dyspnea, falling O<sub>2</sub> Saturation and weak pulse rate.

### Milrinone:

It commonly known and marketed as the brand name 'Primacor'. and mostly used as pulmonary vasodilator. Works against to increase heart contractility and decrease pulmonary resistance and helps to improving pumping action of heart. Milrinone helps the heart's ventricular function by reducing cAMP breakdown and increasing phosphorylation levels.

Milrinone use following cardiac surgery under some debate in postoperative atriaarrhythmias. In the critically ill patients with evidence of cardiac dysfunction was good that deal to recommend use. It has inotropic and vasodilating Which helps to increase cardiac output reduce, the pulmonary capillary wedge and systemic vascular resistance (SVR). Hemodynamic effect without any changes in heart rate and myocardial O<sub>2</sub> consumption. and this important because coronary artery disease and CHF exist this due to intravenous agent (e.g.: Milrinone, Dobutamine)

## II. METHODOLOGY:

All the study has been soaughted by the Outcomes of Prospective Trial of Intravenous MilrinoneExacerbation of CHF (OPTIME-CHF) for the further evaluate strategyfor short term use of Milrinone in addition to standard therapy. After observing the pain in CHF patients has been hospitalized for observation more than 48 hrs. after approval of each site of review and written information obtained from patients were randomly assigned for a treatment of an intravenous infusion of Milrinone.

### Physical, Chemical and Pharmacokinetic Data:



Structure of Milrinone:

IUPAC Name: 2-Methyl-6-oxo-1,6-dihydro-3,4'-bipyridine-5-carbonitrile.

Formula:  $C_{12}H_9NO$

Melting point :  $315^{\circ}C$

Route of administration: IV Only

Bioavailability : 100% (as IV bolus infusion)

Protein binding : 70 to 80 %

Excretion : Urine (85% as unchanged drug within 24Hrs)

### INTRAVENOUS ADMINISTRATION:

- Loading dose 25 to 50 mcg/kg (loading dose given over 10 min)
- Rate of infusion between 0.375 to 0.75 mcg/kg/min.
- Pediatric infusion rate range 0.3mcg/kg/min to 1 mcg/kg/min.

### INHALATION ADMINISTRATION:

- Not an FDA approved use, there is no consensus on dosing via this route.

## MECHANISM OF ACTION

- Milrinone is the phosphodiesterase inhibitors class in which that enzyme hydrolyzes cAMP and cGMP terminating their effect in various tissue. PDE 3 is present in cardiac sarcoplasmic reticulum, smooth muscle in arteries and vein. Milrinone having a selective low dose and nonselective high dose
- cAMP causes increasing activation of protein kinaseA (PKA). PKAis enzyme that phosphorylate contractile machinery of heart cell.
- PDE 3 which responsible for breakdown of cAMP, lower the level of cAMP in the cell they also lower the fraction of PKA within cell and reduce force contraction.
- It prevents the degradation of cAMP,with maintaining this level PKA will phosphorylate many components of cardiomyocyte such as  $Ca^{+}$  channel and myofilaments.
- Milrinone allow stimulation of cardiac function independently of  $\beta$ - adrenergic receptor which appears to be regulated in those with heart failure.

### ADVERSE EFFECT OF MILRINONE:

- Common adverse effects include Ventricular Arrhythmias.Supraventricular arrhythmias, hypotension and headache.
- Milrinone may causes ventricular tachyarrhythmiaswhich may lead cardiac ischemia or sudden cardiac death.
- Milrinone may also effectplatelets function and inflammatory pathways, it may block platelateaggregation which causes endothelial injury or attenuated proinflammatory effect.
- Nausea, vomiting, Thrombocytopenia.

### CLINICAL USE:

Commonly use in therapy severe Pulmonary Arterial Hypertension (PAH).

- Used as a rescue drug in Bronchial Asthmaor acute severe as list.
- Also use to prevent allergic Inflammation in HDM -driven model of allergic airway inflammation.

## III. CONCLUSION:

Milrinone is a bipyridine derivatives and Phosphodiesterase inhibitor that is often classed as an Inodiators. It works by inhibiting PDE 3 enzymes. Is functioning by improving cardiac contractility which called as inotropy and cardiac relaxation (Lucitropy) and inducing Vasodilation.

There is a synergistic effect of Milrinone and  $\beta$ - blockers in the heart failure patients. then we conclude that IV Milrinone and  $\beta$  – blockers are a new treatment option that may result in successful weaning from Milrinone in some cases.

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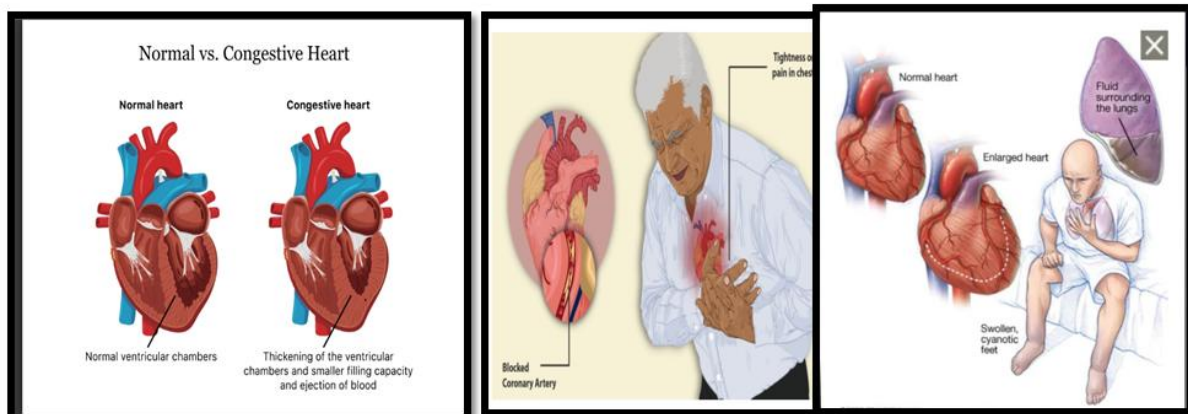


Figure1: Situation in Congestive Heart Failure

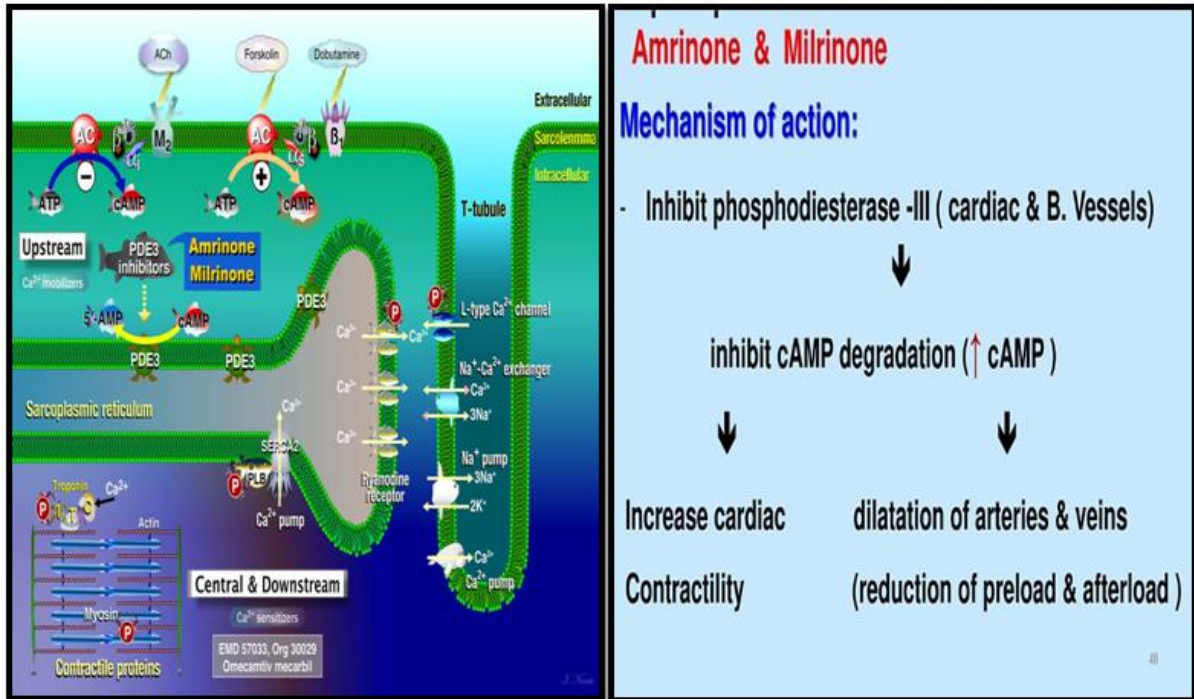


Figure2: Mechanism of action and degradation of milrinone