



Role of per-operative milrinone on pulmonary hypertension having mitral valve replacement.

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ABSTRACT... Objective: To determine the role of perioperative milrinone on pulmonary hypertension in patients with mitral valve disease undergoing mitral valve replacement surgery. **Study Design:** Randomized Control Trial. **Setting:** Department of Cardiac Surgery, Faisalabad Institute of Cardiology, Faisalabad. **Period:** 10-10-2018 to 10-10-2019. **Material & Methods:** A total of 80 patients with mitral valve disease who underwent mitral valve replacement were included. The patients were divided into a control group of 40, who were not administered milrinone, and a study group of 40 who received milrinone perioperatively. TVPG, LVEF and NYHA class were recorded preoperatively and postoperatively and were compared. **Results:** In the study group, postoperative LVEFs and NYHA class were not statistically significant in both groups while postoperative TVPG was significantly lower in study group as compare to control group and is statistically significant ($P < 0.001$). **Conclusion:** Our study concludes that milrinone can be used as an effective therapy to reduce pulmonary pressure in patients with pulmonary hypertension undergoing mitral valve replacement surgery.

Key words: Left Ventricular Ejection Fraction, Mitral Valve Disease, Mitral Valve Replacement, Pulmonary Hypertension, Right Ventricular Failure.

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INTRODUCTION

Pulmonary hypertension (PH) is characterized by increase in pulmonary vascular resistance leading to right ventricular failure.¹ The most common cause of pulmonary hypertension worldwide is left heart disease² amongst which valvular heart disease is the leading cause of secondary pulmonary hypertension.³ Patients with symptomatic mitral valve disease are severely affected by pulmonary hypertension and upto 65% of patients with symptomatic mitral stenosis^{4,5} have increased risk of morbidity and mortality during mitral valve replacement (MVR).⁶ Mitral stenosis results in increase in left atrial pressures causing reversible increase in pulmonary arterial pressures⁷ Immediately after MVR, pulmonary arterial pressure does not usually regress completely and persist in about 75% of patients having pre-operation severe pulmonary hypertension⁸ Milrinone is a phosphodiesterase inhibitor which is commonly used in such patients during weaning from cardiopulmonary bypass,

to reduce the pulmonary vascular resistance⁹ Milrinone reduces biventricular filling pressures and afterload by systemic and pulmonary vasodilation.^{10,11,12} with no significant effect on patients heart rate¹³ The aim of this study is to determine the effect of perioperative milrinone on postoperative pulmonary hypertension after mitral valve replacement surgery.

MATERIAL & METHODS

This Randomized control trial was conducted at Cardiac Surgery Department, Faisalabad Institute of Cardiology for One year from October 2018 to October 2019.

The sample size was calculated By using WHO sample size calculator

$$n = \frac{Z\sigma^2 (Z_{1-\alpha/2} + Z_{1-\beta})^2}{(\mu_1 - \mu_2)^2}$$

$$\mu_1 = 41.25$$
$$\mu_2 = 44$$

$\alpha = 5\%$

$1-\beta = 80\%$

$\sigma = 4.24$

Sample size $n = 80$ (40 in each group)

SAMPLE SELECTION

Inclusion Criteria

- Patients of both gender and age.
- Patient with isolated mitral stenosis.
- Rheumatic mixed lesion with predominant mitral stenosis.
- Patients with moderate to severe pulmonary hypertension ($>30\text{mmHg}$).

Exclusion Criteria

- Patients with Right heart failure.
- Patients with moribund preoperative state.
- Patients having endocarditis and concomitant aortic valve disease.
- Patients with coronary artery disease, $\text{EF} < 45\%$.
- Patients with previous cardiac surgery.
- Patients with preoperative multi-organ disease.

After institutional ethical review committee approval informed consent was taken. 80 patients were enrolled who were scheduled for mitral valve replacement with severe pulmonary hypertension having tricuspid valve pressure gradient greater than 30 mm of hg on preoperative transthoracic echo were admitted through out-patient department. Clinical examination was done to confirm the diagnosis. Preoperative investigation was carried out in the ward. Two groups were formed depending upon milrinone administration. 40 patients who received milrinone were included in study group while 40 patients who did not were in control group. Postoperative TVPG, LVEF and NYHA class were recorded.

SURGICAL TECHNIQUE

Mitral valve replacement was done through median sternotomy. After aortic and bicaval venous cannulation cardiopulmonary bypass was established. Cold cardioplegia administered for myocardial protection and heart to stop. After left atrial atriotomy mitral valve excised

with or without preservation of posterior mitral leaflet and is replaced with mechanical or tissue valve according to patient's condition. 40 patients received milrinone during weaning from cardiopulmonary bypass with loading dose of $25 \mu\text{g/kg}$. Maintenance dose was administered at dose of $0.25 \mu\text{g/kg/min}$ for 24 hours postoperatively. Statistical analysis was done using IBM SPSS Statistics Version 26.

RESULTS

Mean age in control group was 39.50 ± 10.806 while in study group 41.38 ± 13.511 . Male ratio in control group were 18 (45%) in study group there were 11 (27.5%) (Table-I). We noticed no significant difference between LVEF and TVPG preoperatively in both groups (Table-III). Post-operative data showed that TVPG was significantly lower in study group (28.55 ± 8.470) than in control group (43.35 ± 15.019) and this difference was highly statistically significant ($p\text{-value} < .0001$) (Table-IV). There was no significant difference between two groups in terms of LVEF and NYHA class. However, 31 (77.5%) patients in study group were having NYHA class I postoperatively while in control group there were 28 (70%) (Table-II).

Variable	Control Group	Study Group	P-Value
Age (MEAN \pm SD) Years	39.5 ± 10.806	41.38 ± 13.511	0.513
Male Number (%)	18 (45%)	11 (27.5%)	0.151
NYHA II	24 (60%)	25 (62.5%)	0.818
NYHA III	16 (40%)	15 (37.5%)	

Table-I. Preoperative Data

Variable	Control Group	Study Group	P-Value
NYHA I	28 (70%)	31 (77.5%)	0.446
NYHA II	12 (30%)	09 (22.5%)	

Table-II. Postoperative NYHA Class

Variable	Control Group	Study Group	P-Value
LVEF	58 ± 5.038	58.38 ± 5.705	0.756
TVPG	51.80 ± 17.775	49.08 ± 18.798	0.507

Table-III. Preoperative ECHO Data

Variable	Control Group	Study Group	P-Value
LVEF	59±3.616	59.25 ± 2.667	0.726
TVPG	43.35±15.019	28.55 ± 8.470	0.0001

Table-IV. Postoperative ECHO Data

DISCUSSION

This study demonstrated that perioperative milrinone usage in patients having pulmonary hypertension reduces postoperative tricuspid valve pressure gradient and improves NYHA class after mitral valve replacement.

Mitral valve disease commonly results in pulmonary hypertension, which is associated with poor prognosis during mitral valve replacement.^{14,15}

Mitral valve disease cause increase in left atrial pressures because of increase in pulmonary vascular resistance which in turn causes alveolar stress and remodeling of pulmonary vasculature.¹⁶ As there are selective drugs for pulmonary vasculature, treatment of pulmonary hypertension has not been fully established. Different class of drugs, such as vasodilators, beta agonist or phosphodiesterase inhibitors were administered to reduce PH during cardiac surgery.¹⁷ However, arrhythmias and increased demand of myocardial oxygen may occur because of these drugs which results in ischemia and renal failure.¹⁸

Milrinone is a phosphodiesterase-III inhibitor which increases the cAMP levels in cells by decreasing its degradation and activates protein kinase A3. Therefore, its cardiac effects are positive inotropy and improved diastolic relaxation. The effect of milrinone which is a potent vasodilator also causes reduction in preload, afterload, and pulmonary vascular resistance which helps in weaning from cardiopulmonary bypass.¹⁹ Milrinone is also widely used in patients with heart failure as well as in congenital heart surgery.^{20,21}

Some of the studies demonstrated the use of milrinone in patients with pulmonary hypertension undergoing mitral valve replacement. Ahmet et al reported that with the use of milrinone perioperatively, systolic pulmonary artery

pressure and low cardiac output syndrome significantly reduces.⁹ Wang et al showed the reduction in mean pulmonary artery pressure and pulmonary vascular resistance with the use of milrinone.²² Some studies reported that by perioperative administration of milrinone which significantly reduces right and left ventricles filling pressures, causes reduction in pulmonary hypertension.¹⁹ In our study NYHA class and pulmonary hypertension improves with the use of milrinone in patients undergoing mitral valve replacement.

CONCLUSION

Perioperative administration of milrinone significantly reduces pulmonary hypertension and improves NYHA class after mitral valve replacement surgery.

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Fear is a **reaction**. Courage is a **decision**.

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“Sir Winston Churchill”

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Shahbaz Ahmad Khilji	Chief surgeon, Proof reading, Supervision of whole process.	
2	Shuja Tahir	Author surgeon, Literature review, Data collector, Statistical work.	
3	Shahid Abbas	Author physician, Proof reading, Collection of references.	