



## Outcome of preoperative oral sildenafil in patients with pulmonary hypertension after mitral valve replacement.

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**ABSTRACT... Objective:** To determine the role of preoperative administration of sildenafil on outcome of patients having pulmonary hypertension 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:** June 2018 to June 2020. **Material & Methods:** A total of 310 patients with mitral valve disease who underwent mitral valve replacement were included. The patients were divided into a control group of 155, who were not administered oral sildenafil, and a study group of 155 who received oral sildenafil preoperatively. TVPG, LVEF and NYHA class were recorded preoperatively and postoperatively to compare outcome. **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 oral administration of sildenafil preoperatively can be used as an effective treatment module to reduce pulmonary artery pressure in patients with pulmonary hypertension undergoing mitral valve replacement surgery and hence improves post-operative outcome.

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

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## INTRODUCTION

Increase in pulmonary vascular resistance due to mitral valve disease with pulmonary hypertension leads to right ventricular failure and mortality.<sup>1,2</sup> Pulmonary hypertension is defined as an increase of the mean pulmonary arterial pressure more than 25mmHg at rest.<sup>3,4</sup> Pulmonary hypertension affects all patients having mitral valve disease.<sup>5</sup> Mitral valve disease increases left atrial pressures leading to potentially reversible increase in pulmonary pressures which in turn causes vascular injury along with remodeling of vessels results in right ventricular dysfunction.<sup>6</sup> Pulmonary vascular resistance can be lowered by enhancing cyclic adenosine monophosphate (cAMP) using Beta agonist or phosphodiesterase inhibitors.<sup>2,7</sup> In preoperative management of pulmonary hypertension, oral sildenafil is found very effective as it is a selective inhibitor of isoform 5 phosphodiesterase enzyme which increases in cyclic guanosine monophosphate

(cGMP) levels.<sup>8,9</sup> Sildenafil can also be used to manage secondary pulmonary hypertension in perioperative period in patients undergoing open heart surgeries.<sup>10</sup> There are fewer studies on the use of oral sildenafil regarding preoperative management of pulmonary hypertension with mitral valve disease.<sup>11</sup> This study was planned to evaluate the efficacy of preoperative oral sildenafil on post-operative pulmonary hypertension after mitral valve replacement surgery.

## MATERIAL & METHODS

This Randomized control trial was conducted at Department of Cardiac Surgery, Faisalabad Institute of Cardiology for two years from June 2018 to June 2020. The sample size was 310 patients (155 in each group).

## SAMPLE SELECTION

### Inclusion Criteria

- Patients of both gender and age ranging from

15-65 years.

- Patients with isolated mitral stenosis
- Rheumatic mixed lesions with predominant mitral stenosis
- Patients with moderate to severe pulmonary hypertension (Mean PAP  $\geq$ 40mmHg)

### 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, EF <45%
- Patients with previous cardiac surgery
- Patients with preoperative multiorgan disease

After institutional ethical review committee approval, informed consent was taken. Three hundred and ten patients were enrolled who were scheduled for mitral valve replacement with moderate to severe pulmonary hypertension having tricuspid valve pressure gradient (TVPG) greater than 40 mm of Hg on preoperative transthoracic echo and were admitted through out-patient department. Clinical examination done in each case along with echocardiography, X-ray chest, ECG and routine laboratory investigation. Two groups were formed depending upon preoperative oral sildenafil administration. Study group consisted of 155 patients who received oral sildenafil (25mg thrice a day for two days preoperatively) and control group comprised of 155 patients who did not. Postoperative TVPG, LVEF and NYHA class were recorded.

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. Statistical analysis was done using IBM SPSS Statistics Version 26.

### RESULTS

Mean age in control group was  $39.68 \pm 10.347$  while in study group  $41.03 \pm 13.047$ . Male patients in control group were 69 (44%) while in study group there were 60 (38.7%) (Table-I). We noticed no statistically significant difference between LVEF and TVPG preoperatively in both groups (Table-III). Post-operative data showed significantly lower TVPG in study group ( $32.54 \pm 9.038$ ) than in control group ( $43.08 \pm 14.608$ ) which was highly statistically significant (p-value <.0001) (Table-IV). There was no significant difference between two groups in terms of LVEF and NYHA class. However, 119(76.8%) patients in study group were having NYHA class I postoperatively while in control group there were 110(71%) (Table-II).

### DISCUSSION

This study showed that administration of preoperative oral sildenafil reduces postoperative tricuspid valve pressure gradient and improves NYHA class after mitral valve replacement.

Variable	Control Group	Study Group	P-Value
AGE (MEAN $\pm$ SD) Years	$39.68 \pm 10.347$	$41.03 \pm 13.047$	0.314
MALE SEX NUMER (%)	69 (44%)	60 (38.7%)	0.357
NYHA II	91 (58.7%)	99 (63.9%)	0.414
NYHA III	64 (41.3%)	56 (36.1%)	

Table-I. Preoperative Data

Variable	Control Group	Study Group	P-Value
NYHA I	110 (71%)	119 (76.8%)	0.301
NYHA II	45 (29%)	36 (23.2%)	

Table-II. Postoperative NYHA CLASS

Variable	Control Group	Study Group	P-Value
LVEF	58.13 ± 4.940	58.32 ± 5.734	0.750
TVPG	51.57 ± 17.345	48.86 ± 18.471	0.183

Table-III. Preoperative ECHO DATA

Variable	Control Group	Study Group	P-Value
LVEF	59.10 ± 3.488	59.23 ± 2.681	0.715
TVPG	43.08 ± 14.608	32.54 ± 9.038	0.0001

Table-IV. Postoperative ECHO DATA

Mitral valve disease is common cause of pulmonary hypertension which is associated with poor prognosis after mitral valve surgery.<sup>12,13</sup> Increased pulmonary hypertension give rise to increase in left atrial pressure causing low cardiac output.<sup>14,15</sup> As there are selective drugs for pulmonary vasculature, treatment of pulmonary hypertension has not been fully established.<sup>16,17</sup> 5-phosphodiesterase inhibitors have proven clinical efficacy in management of pulmonary hypertension.<sup>18,19</sup> Randomized controlled trials, by Shim et al<sup>10</sup> and the other by Gandhi et al<sup>20</sup> showed reduction in pulmonary hypertension and also systolic and mean arterial pressures. However, shim et al treated with single dose of sildenafil while Gandhi et al used 3 doses for 24 hour preoperatively. In a study by Ram et al, sildenafil demonstrates a favorable decreasing effect on pulmonary vascular pressure without systemic hypotension and ventilation-perfusion mismatch.<sup>21</sup> With a dose as low as 25mg, hemodynamical effects of sildenafil on pulmonary circulation could be achieved as demonstrated by Wilkens et al.<sup>22</sup> In order to reduce pulmonary hypertension and to improve RV function before surgery we used oral sildenafil 25mg thrice a day over 24h. In our study NYHA class and pulmonary hypertension improves with the use of oral sildenafil in patients undergoing mitral valve replacement.

## CONCLUSION

Preoperative administration of oral sildenafil in patients with pulmonary hypertension effectively reduces pulmonary hypertension and improves NYHA class after mitral valve replacement surgery.

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**AUTHORSHIP AND CONTRIBUTION DECLARATION**

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3	Shuja Tahir	Author surgeon, Literature review, Data collector, Statistical work.	