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Research Article

**PERCUTANEOUS TRANSMITRAL COMMISSUROTOMY IN
CHILDREN: INTERMEDIATE TERM RESULTS WITH
SPECIAL REFERENCE TO PULMONARY HYPERTENSION**Prof. Najma Patel^{1*}, Dr. Mubashir Kolachi² and Dr. Hussain bakhsh Korejo³¹FCPS, FSCAI, FACC Professor Paediatric Cardiology National Institute of Cardiovascular Disease, Karachi, Pakistan²MD cardiology, Liaquat University of Medical and Health Sciences Hyderabad³FCPS Post Fellow Paediatric cardiology NICVD Karachi**Abstract:****Objective:** To know the long-term results of percutaneous transmitral commissurotomy (PTMC) and fate of pulmonary hypertension in children who have undergone PTMC.**Material:** During the last 11 years 138 children, aged 10.48 ± 2.24 years (range 3.5 -16) had PTMC. Indications were echocardiographic evidence of moderate to severe mitral stenosis (MS) plus pulmonary hypertension (PH) more than 50 mmHg and/or FC III-IV**Result:** Pre PTMC, mean pressure gradient (MPG) across the mitral valve (MV) was $18.6 \text{ mmHg} \pm 3.4$ which decreased to $7.6 \text{ mmHg} \pm 2.21$. Mitral valve area (MVA) was $0.62 \text{ cm}^2 \pm 0.12$ which increased to $1.6 \text{ cm}^2 \pm 0.3$. Systolic Pulmonary artery pressure (SPAP) was $83 \text{ mmHg} \pm 13$ decreased to $50 \text{ mmHg} \pm 14.5$. Three procedures were unsuccessful. There were 2 deaths, one within half an hour in patient with SPAP of 100 mmHg and left ventricle (LV) dysfunction, had no mitral regurgitation (MR), arrhythmias or tamponade after PTMC. Another had thromboembolism of left anterior descending coronary artery during procedure; he revived and had successful PTMC but died after 24 hours. One had tamponade which was drained and had a successful PTMC after 1 week. There was no change in Mitral Regurgitation in 50 pts. After a mean follow-up period of $44.3 \text{ months} \pm 30.6$ of 110 pts (10 months to 10 years), 8 needed repeat PTMC after $5.37 \pm 2.3 \text{ yrs}$ (0.5–8 years), and 2 had mitral valve replacement (MVR) after 1 and 7 years. SPAP was $83 \text{ mmHg} \pm 13$ pre procedures which decreased to $50 \text{ mmHg} \pm 14.5$ immediately after and to $42 \text{ mmHg} \pm 13$ after 6 months. Immediately after PTMC, 54 pts had SPAP more than 50 mmHg and after 6 months only 24 pts. Out of these 2 died: one had severe PH despite adequate relief of MV, died after 3 years; another had mild MS and +2 MR with persistent severe PAH, had MVR after 1 year. PAP did not decline after surgery and he died two years after PTMC. Both had initial SPAP of more than 100 mmHg.**Conclusion:** PTMC is effective in relieving stenosis, however initial high PAP is predictor of persistent pulmonary hypertension.**Corresponding Author:****Prof. Najma Patel,**Professor, Paediatric, Cardiology,
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INTRODUCTION:

The incidence of rheumatic fever has decreased dramatically in developed nations [1,2] but is still a common problem in developing countries like Pakistan with a prevalence rate of 22/1,000 population. This high prevalence rate put Pakistan among the highest in the world [3]. The usual presentation of Rheumatic fever is arthritis, chorea and carditis; however carditis is the commonest presentation. Endocardium is mostly affected, the common of which is the mitral valve involvement [4], which predominately affects 2/3 of the female having rheumatic carditis [5,6]. In mitral valve, stenotic lesions are more common in females and regurgitant lesions are more common in males.

ECG, X-ray chest can be helpful for assessing the severity, however echocardiogram being the most important diagnostic modality for evaluating the severity of mitral stenosis [7,8]. The mitral valve severity is assessed by left atrium (LA) size, mitral valve area, mitral valve gradient, and pulmonary artery pressure [9]. Normal mitral valve area is 4–6 cm². Stenosis is mild when the area is more than 1.6 cm²; it is moderate when the area is between 1.0–1.6 cm² and it is severe when the area is less than 1.0 cm² [10]. Normal valve gradient is 0–4 mm Hg, it is mild when it is less than 5, moderate when it is 5–10 and severe when more than 10 mm Hg [10, 11]. Normal pulmonary artery pressure is between systolic is 15–25 mm Hg. PH is mild when below 30, moderate when between 30 and 50, and severe above 50 mm Hg [12]. Pulmonary artery hypertension is well established complication of long standing MS. According to the ACC/AHA Valvular Heart Disease guidelines of 2006 [13], absence or the presence of PH with the mitral valve stenosis is the key component for deciding the management. Mostly moderate to severe mitral stenosis is linked with variable degree of PH. Pathophysiology of PH in MS involves structural variation of pulmonary vascular bed mediated through potent vasoconstrictor endothelin-1 (ET-1). ET-1 levels are three times higher in cases having severe MS as compared to healthy cases [14]. In a group of patients who underwent PTMC or MVR due to severe MS, the baseline concentration of ET-1 was found to be an independent predictor of decreases in PCWP at the 6 months following mitral valve intervention.

According to ACC/AHA valvular Heart Disease guidelines, PTMC is class I indication in symptomatic patients with functional class II–IV with severe MS and a in asymptomatic patients with PH (SPAP greater than 50mmHg at rest or greater than 60 mmHg with exercise), and class II b indication in patients with severe MS and new onset of atrial fibrillation, in symptomatic patients with MVA >1.5 cm² if there is evidence of hemodynamically significant MS during exercise (PAP > 60 mm Hg, PA wedge pressure ≥ 25 mm Hg or MVMPG ≥ greater than 15 mm Hg during exercise provided morphology is favorable, MR less than moderate and no clot in LA (13)

METHODOLOGY:

158 children suffering from severe mitral stenosis and functional class III to IV and/or SPAP more than 50 mmHg who had PTMC during the period of 2000 to 2012 were studied. Routine ECG was done to ascertain the normal sinus rhythm. None of the patient was in atrial fibrillation. Routine 2D echocardiography was done to assess the valve area by planimetry and to assess the valve morphology for suitability. Wilkinson score was 4-14 (8). Doppler studies were carried out to calculate the pressure gradient across mitral valve, measurement of valve area by pressure half time method, and to evaluate concomitant mitral regurgitation and grading of MR and to assess the other valves. Any possibility of left atrial appendage thrombus was excluded. LA size and LV function measured. RV function was also assessed.

Mitral valve Annulus was measured in 4 chamber apical and long parasternal view both in systole and diastole to select the size of balloon. Systolic function was assessed both pre-PTMC and post PTMC by calculating EF.

Blood tests for ESR and ASOT was done in each case to rule out acute rheumatic. CBC, Blood sugar levels, serum urea, creatinine levels and serum electrolytes in each case to find out any abnormality. X-ray chest in PA view helped us in the assessment of pulmonary edema and to detect any lung pathology like lung infection or infarction



Fig 1: Measurement of Annulus in Apical 4 chamber and Parasternal long axis view

ECG was done to assess any arrhythmias, evidence of PH in the form of large R wave in lead V1. Patients were followed up for the period of up to 46 months ± 30.6 (10 months to 10 years) by clinical assessment of symptoms and repeat echo studies.

Percutaneous mitral commissurotomy

Patients had procedure under local anaesthesia with heavy sedation. Those who were symptomatic and those who had severe PH had procedure under general anaesthesia. All patients who were planned for PTMC had haemodynamic measurements like RA, RV and PA pressure and also PA wedge by using Berman wedge pressure anterogradely. Aortic pressure and LV systolic and end diastolic pressures (LVEDP) were taken retrogradely by pigtail catheter during cardiac catheterization and had LV angiogram.

Trans septal puncture were done anterogradely by using standard method. LA pressure measured directly.

MV crossed with Berman wedge pressure catheter in all patients, then wire stabilized either in LV or in Aorta.

PTMC done with Inoue balloon in first 16 cases and in the rest with multitrack double balloon over the wire and in few small children with single balloon. Balloon size which is 70% of the annulus was selected.

All haemodynamic measurements and LV angiogram were done after dilatation and if indicated balloon upsized.

In some cases echocardiogram done during procedure in cath lab to assess for pericardial effusion and also

Post-procedure echocardiogram done to assess LV function, MPG across MV, MR and to assess PH within 24 hours and then in the follow up.

Statistical analysis

SPSS version 20 was used for data analysis. Normal distribution was calculated by the Shapiro Wilk test.¹⁷ Student's t-test was applied for paired data to determine the significance before and after PTMC. For relationship b/w variables in groups, Pearson correlation was applied. P-value < 0.05 was considered as significant.

RESULTS:

Total 158 children suffering from Mitral Stenosis with pulmonary artery hypertension and/ FC III to IV were registered in NICVD Karachi from year 2000 to 2012 and subjected to PTMC. Age of patients in Years were 10.48 ± 2.24 (3.5-16). Body surface area (BSA/m^2) was 1.03 ± 0.19 (. 7-1.5). Weight in kg was 27.24 ± 7.66 (9-48).

Table 1: Demographic data of 158 patients who underwent PTMC

Age(years)	10.48 ± 2.24 (3.5-16)
BSA(m^2)	1.03 ± 0.19 (0. 7-1.5)
Weight (kg)	27.24 ± 7.66 (9-48)

PTMC was considered successful when MVA increased to 1.5cm^2 or 50% increase in MVA. Out of total 158 cases, 3 cases had unsuccessful PTMC.

Pre dilatation Mitral valve area (MVA) was $0.62\text{cm}^2 \pm 0.12$ which increased to $1.6\text{cm}^2 \pm 0.3$ post dilatation so there was increase in MVA to 144% .Fig 2.

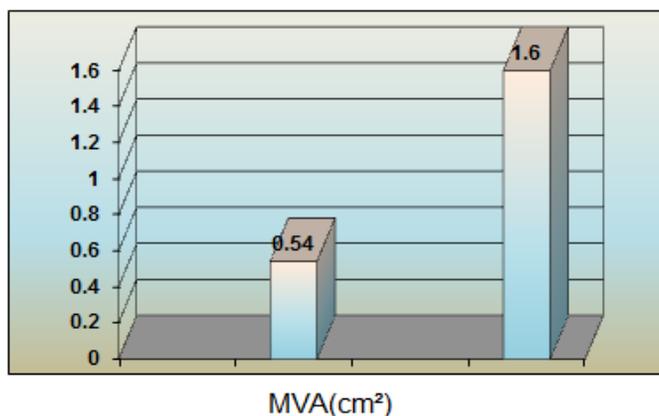


Fig 2: Increase in Mitral valve area after PTMC

Pre-dilatation mean pressure gradient (MPG) was 18.6 ± 3.4 mmHg which decreased to 7.6 ± 2.21 mmHg. So there is reduction of 69% in MPG (Fig4). Pre-dilatation SPAP was 83 ± 13 mmHg which decreased to 50 ± 14.5 mmHg post dilatation so there was reduction 43% in SPAP. (FIG:3 and 4)

In 12 patients the LV EF before PTMC was 30-45% which increased to normal in all except one after PTMC.

In 16 patients LVEDP was 16-25mmHg which decreased Post PTMC to 10-16mmHg immediately after PTMC.

In 3 patients LVEDP increased from 10- 12 mmHG to 20-25mmHg with increase in mean LA pressure with increase in a wave without any MR, this may be due to sudden increase in flow, this decreased to near pre PTMC level in half hour

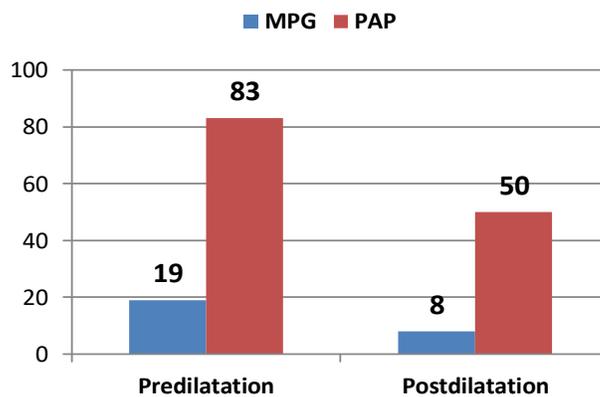


Fig 3: Decrease in MPG and PAP after PTMC. MPG –mean pressure gradient across mitral valve during diastole. PAP – systolic pulmonary artery pressure

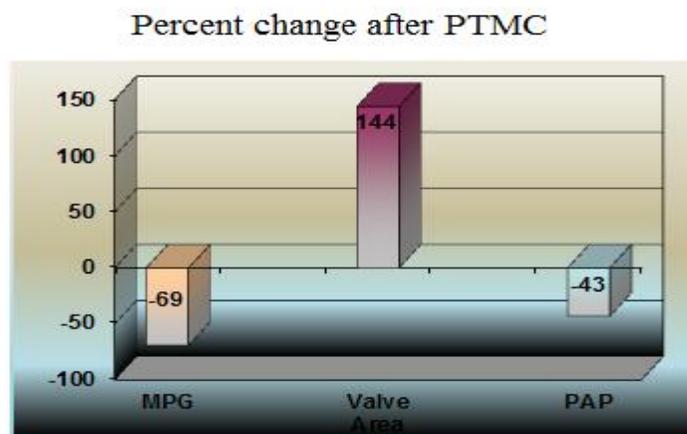


Fig 4: Percent change in MPG, MVA and PAP after PTMC. MPG –mean pressure gradient. MVA mitral valve area, PAP, systolic pulmonary artery pressure

Complications: 2 deaths occurred after the procedure. One 10 years old child had thromboembolism embolism of LAD, echo showed sever dysfunction, Inj Streptokinase was given intracoronary, revived, LVEF and blood pressure

normalized and successful PTMC was but died after 24 hours as had cerebral insult during the procedure. Second 11 years old child died after about half hour of PTMC, had sever PH and LV dysfunction preprocedure. Did not have any complications of procedure like MR, arrhythmias or tamponade. Cause of death is not ascertained.

One patient had Tamponade which was drained and patient had successful PTMC after one week.

Out of total 158 patients, there was no change in the severity of MR after the procedure in 57 patients (36%) , while in 88 pts (56%) it increased to +1(majority had trivial MR), in 10 pts (6%) +2 and 3 pts (2%) developed +3 MR

However in 10 patients with +1MR there was no MR on echocardiography next day, in one patient with +2 MR there was no MR and the severity of MR was less in all patients with +2 and +3 MR

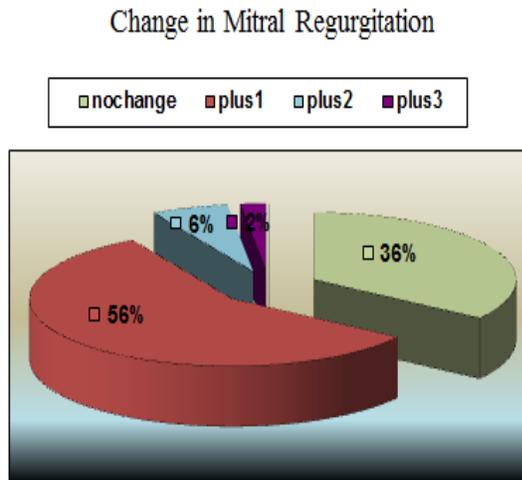


Fig 5: Change in Mitral regurgitation as assessed by pre and post PTMC left ventricular angiogram

Effect of PTMC on Pulmonary artery pressure:

Pre-PTMC SPAP was < 50mmHg only in 4 patients, in 48 patients it ranged between 51-75mmHg, in 98 patients it was 76-100 mmHg and in 8 patients it was > 100mmHg

Immediately after PTMC, SPAP in 110 patients was <50 mmHG, in 36 patients it was 51-75mmHG and in 12 patients it was 76-100. There was not a single patient having PAP > 100 after PTMC.

At 6 month follow up, 135 patients had SPAP less than 50mmHg, in 21 patients it ranged between 51-

75mmHg, and in only 3 patients had PAP was 76-100mmHg. (Figure 6)

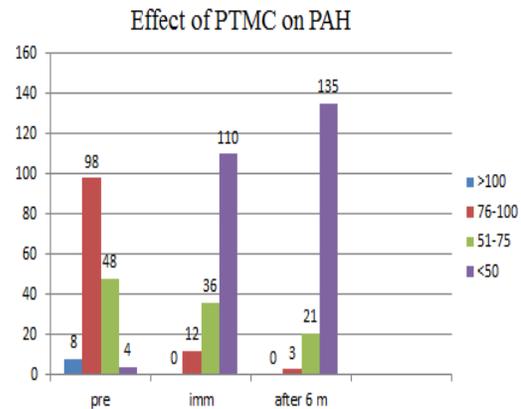


Fig 6: Change in pulmonary artery pressure, immediately, after 1 and 6 months follow up .

LONG TERM FOLLOW UP RESULTS:

130 patients had follow up for 46 months \pm 30.6 (10months to 10years) .Out of them 12 had redo PTMC after 5.37 ± 2.3 (6 monhs-8 years). 2 pts had PTMC three times. 2 had MVR, one after I year and another after 7years.

Persistent PH (>50mmHg) was noted in 24 pts, one had severe PAH despite adequate relief of MV stenosis without MR, died after 3 years of PTMC. Another had mild (MPG 7mmHg.MVA 1.5cm²) MS and +2 MR with persistent sever PH, had MVR after 1year; PAP did not decline after surgery and died after two years of PTMC. 22 have elevated PH but mild to moderate (40-60mmHg).

DISCUSSION:

PTMC is an effective and safe method of relieving MS. The successful PTMC in our study was defined as $MVA \geq 1.5\text{cm}^2$ and $MR \leq 2/4$. Since MS patients with $MVA \geq 1.5\text{cm}^2$ are generally considered to have mild stenosis and are relatively asymptomatic, this value was chosen as the threshold for procedural success.¹⁸Using this definition, the PTMC procedural success rate in our study was > 90%. Other studies, using the same definition, reported success rates to be ranging from 70 to 90% [19,20].

In our study patients ages are less than other studies ,youngest patient was 3.5 years old ,he had redo PTMC after 9months another patient was 5 years old .Out of 158 patients 25 patients i-e 15.8% were younger than 10years of age.

PH is the common complication of the rheumatic mitral valve disease [20,21]. It has a well-established relation with the rheumatic MR and the MS [22] disease natural history and prognosis after intervention [23]. PH in MS is usually due to passive transmission of LA pressure. In patients of MS with PH, the pulmonary veins of patients show development of muscular media. Hypertrophy moderate to marked is stated to occur in pulmonary arteries in medium sized branches. Tandon et al [24] and Chopra et al [25], stated that in their autopsy studies the plexiform lesion was found in 4%. PH frequently regresses after successful PTMC, but it may not regress in a significant number of patients [26-30]. Mainly determined through clinical and hemodynamic characteristics as; advanced age, upper Wilkin's echocardiographic score, small MVA, and at baseline greater mean of PAP [29].

In our study the patients having PH were relatively older in age, suggesting longstanding disease which may have contributed to development of PH as they also had higher systolic and mean PAP, both these factors contributing to pulmonary vascular disease and PH.

In the study of Fawzy et al [20], it is reported that PAP normalized in several cases having optimal findings after PTMC and our results are in partial agreement to these finding. It is reported in a study by Krishnamoorthy et al [26], that increase in MVA was not con was not constantly predictive of decreases in PAP, suggesting that some other factors might be contributing to persistent PH like occurrence or worsening of MR following PTMC, MR increases the LA pressure which in turn increases the PAP, leading to gradual increase in PVR which leads to non-regression of PH following PTMC and eventually ultimately to PPAH. However in our study SPAP decreased to normal level (25-30 mmHg) only in 12 patients though there was decrease from pre PTMC level and it may be due to initially very high PAP. In 4 out of 21 patients with post PTMC PAP between 51-75mmHg there was MR of +2 and in 3 patients suboptimal results. Two out of three patients with post PTMC PAP of 76-100mmHg died, one had no gradient and MVA was 1.7 cm²

and no MR died after 3years, another had mild MS (MPG 7mmHg.MVA 1.5cm²) and +2 MR with persistent sever PH, had MVR after 1year; PAP did not decline after surgery and died after two years of PTMC.

Another feature that may contribute to PPAH is shunting of the blood from the left to right atrium by iatrogenic ASD developed during the PTMC, but number of cases with recognizable ASD by color Doppler echo on follow-up in both in our study was insignificant.

Studies have shown a number of patients develop restenosis and return of PAP to pre-PTMC level, need redo or are switched over to surgery³¹. In our study 12 patients had redo PTMC, 2 patients were done thrice while 2 patients underwent MVR. Majority of these patients were having very high PAP at their baseline.

The ACC-AHA recommendation for percutaneous mitral valvotomy includes PAP as a criterion for selecting the patients. PAP > 50 mmHg at rest or > 60 mmHg post exercise is an indication to perform PTMC even moderate to severe MS in asymptomatic cases [31]. In our population patients first presentation was with sever PH. This is due to lack of early diagnosis. Our study shows that regression of PAP depends on initial PAP. PAP failed to fall to normal levels in patients with higher pre procedure PH. However now the 2014 AHA/ACC valvular Heart diseases guideline recommends PTMC for asymptomatic patient with sever MS and PAP greater than 30 mmHg. This will result in normalization of PAP in patients with severe MS after PTMC.(32)

CONCLUSION:

PTMC is safe and effective procedure in children provides good long term palliation and saves the child from the complication of thoracotomy and multiple surgeries. Operator must be very careful to avoid sever MR as in a small child valve replacement is difficult with unfavorable long term consequences. Redo PTMC is also safe. However regression of pulmonary artery pressure depends on initial PAP therefore it is very crucial to diagnose such cases at early stages.

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