Original Research Paper

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Evolution of Pulmonary Arterial Hypertension in Severe Mitral Stenosis Following Successful PTMC

Medical Science

KEYWORDS : 1. Pulmonary Hypertension, 2. Mitral stenosis, 3. Echocardiography

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ABSTRACT

BACKGROUND:- *Pulmonary Hypertension (PH) frequently complicates mitral stenosis. Pulmonary hypertension significantly influences symptomatology and long-term prognosis. Pulmonary artery pressures also decrease following PTMC. The determinants of change and extent of reversibility in pulmonary hypertension among patients undergoing balloon valvuloplasty has not been studied extensively.*

OBJECTIVE:- *To identify the determinants of decrease in pulmonary arterial hypertension after percutaneous balloon mitral commissurotomy in Severe Mitral Stenosis.*

METHODOLOGY:- *Patients with severe mitral stenosis and pliable valve having no significant mitral regurgitation, aortic valve disease, or left atrial thrombus were selected for Percutaneous Trans venous Mitral Commissurotomy (PTMC). All patients underwent echocardiography, left and right heart catheterization before and after PTMC. Echocardiography was repeated at day 1, day 7, day 30, & day 90. Univariate and multivariate analysis was done to assess the relation of age, gender, left atrial size, right atrial size, gradient across mitral valve, valve area, and presence of Tricuspid Regurgitation (TR) on the decrease in pulmonary arterial pressure over a period of 3 months.*

RESULTS:- *Left atrial pressure, Right Ventricular systolic pressure(RVSP), peak and mean Mitral valve gradient and Pulmonary artery systolic pressure(PASP) decreases in younger aged group more commonly than in older aged patients. Mitral valve orifice area(MVOA) improves more earlier in <30 years than in older aged groups. linear correlation improving from negative to positive at 3 months indicating good prognosis.*

CONCLUSION:- *Patients with successful PTMC has marked reduction in pulmonary arterial pressure which is greatest after first 24 hours, but continues to declines up to 3 months. This reduction is more in younger and male patients.*

INTRODUCTION:-

Pure Mitral Stenosis (MS) develops in approximately 40% of all patients with Rheumatic heart disease.[1] After an episode of Rheumatic fever, the latency period is 10-20 years or more before the onset of symptoms.[2] Pulmonary Hypertension (PH) frequently complicates mitral stenosis. Pulmonary Arterial Hypertension (PAH) is defined as a sustained elevation of systolic pulmonary arterial pressure to more than 25 mmHg at rest or to more than 30 mmHg with exercise, with a mean pulmonary-capillary wedge pressure and left ventricular end-diastolic pressure of less than 15 mmHg.[3] At a stage when patient with mitral stenosis need intervention, 50% of the patients have moderate pulmonary hypertension while 25% of the patients have severe PAH.[4] Pulmonary hypertension significantly influences symptomatology and long-term prognosis.[2] Mitral valve replacement, surgical or percutaneous balloon mitral commissurotomy often result (PTMC), first described in 1984, had good short and intermediate-term results.[5] Its effectiveness and long-term results have now been well-documented.[6,7] Pulmonary artery pressures also decrease following PTMC.[8,9] PTMC is commonly performed by antegrade access to the mitral valve through trans septal puncture by one of the four techniques (Inuoe, double balloon, metallic commissurotome, single balloon and multitrack system) as described by Vahanian *et al.*[10,11] Because of its lower cost the double balloon techniques are mostly used.[12] The determinants of change and extent of reversibility in pulmonary hypertension among patients undergoing balloon valvuloplasty has not been studied extensively, though some authors have suggested predictive models about overall outcome of the patients following PTMC.[5,13] This study was done to determine the immediate and late effect of PTMC on pulmonary pressure. Such knowledge will help to identify patients of higher likelihood of benefiting from PTMC.

The objective of this study was to identify the determinants of decrease in pulmonary arterial hypertension after PTMC over a period of 3months.

METHODOLOGY:-

The study was conducted from Jan-2013 to Jan 2014 over a period of one year. 50 Patients with severe Rheumatic mitral-valve stenosis were assessed in the Sri Jayadeva Institute of Cardiovascular sciences and Research, Bangalore, and selected for PTMC. History was obtained from all patients, who also underwent physical examination, two-dimensional Echocardiography and Doppler study. Informed consent was obtained for the procedure and this study had the approval of our local Ethics committee. Patients not in sinus rhythm underwent a trans esophageal echocardiography before undergoing the procedure to rule out left atrial thrombus. All patients undergoing PTMC with pure mitral stenosis and pulmonary hypertension diagnosed on pre-procedure echocardiography were included in the study.

EXCLUSION CRITERIA:-Patients under 15 & more than 60 years of age, with significant aortic valve disease, greater than mild mitral regurgitation, failed PTMC or left atrial clot were excluded.

Procedure:- Cardiac catheterization was performed before and after the procedure. Pulmonary artery, right and left ventricular and left atrial pressures were recorded in all patients. After a single atrial trans septal puncture, an 8-French Mullins sheath was advanced to the left atrium.

A balloon floatation catheter was used to cross the mitral valve, after which one 0.035 inch (0.9 mm) extra stiff guidewire was placed in the apex of the left ventricle or advanced to the ascending aorta. A septostomy dilator was used to dilate the septum after which two valvuloplasty balloons, 5.5 cm long were inflated simultaneously across the mitral valve (ranging from 14mm to 20 mm). The therapeutic end point was nearly complete elimination of the mitral valve gradient without a substantial increase in mitral regurgitation. All patients underwent M-mode, two dimensional and Doppler echocardiography pre-procedure and then one day after the procedure. Mitral pressure gradient, mitral valve area and right ventricular systolic pressure were measured. All patients underwent right heart catheterization with measurement of hemodynamic variables before and after valvuloplasty. Data was collected on a pre-tested questionnaire. A verbal consent was taken from all patients before filling their information. Again they have been called for Echocardiographic assessment of Mitral valve area, Mitral valve-gradient, Mitral regurgitation, Tricuspid regurgitation & Pulmonary arterial systolic pressure on 7th day, 30thday & at 3months.

STATISTICAL METHODS:- Descriptive and inferential statistical analysis has been carried out in the present study. The following assumptions on data is made, **Assumptions: 1.**Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients , Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters.

RESULTS:- Study design: An observational clinical study.

Table 1: Complete Evaluation of peak MV GRADIENT (mm/Hg) at Pre PTMC, day1, day7, day30, 3 months according to age in years

peak MV GRADIENT (mm/Hg)	Pre-PMTC	Day 1	Day 7	Day 30	3 months
Age in years					
15-20	34.45±11.6	14.43±3.69	10.29±2.14	7.14±1.86	4.71±0.49
21-30	26.10±5.78	14.00±3.09	9.60±1.58	6.90±1.2	4.50±0.53
31-40	25.29±5.73	12.88±3.3	9.59±2.67	6.76±2.25	4.88±1.05
41-50	28.18±8.89	15.36±4.5	11.18±3.82	7.82±1.83	5.00±1.18
>50	25.40±6.54	12.00±2.45	9.60±1.67	6.40±1.14	4.60±0.55
P value	0.107	0.324	0.569	0.562	0.726

Table 2: Complete Evaluation of PASP (mmHg) at Pre PTMC, day1, day7, day30, 3 months according to age in years

PASP (mmHg)	Pre-PMTC	Day 1	Day 7	Day 30	3 months
Age in years					
15-20	82.29±21.48	50.57±10.86	36.43±5.09	31.29±2.75	28.57±3.26
21-30	68.50±20.6	44.90±10.24	34.30±4.85	30.00±3.23	27.20±1.93
31-40	74.06±24.69	47.29±15.64	36.35±7.06	31.53±4.12	27.24±1.86
41-50	72.45±23.62	45.64±16.22	36.45±7.87	30.73±5.44	27.18±2.4
>50	66.4±15.14	47.20±6.3	38.20±3.49	33.80±3.63	29.60±2.61
P value	0.725	0.932	0.841	0.547	0.209

Table 3: Pearson correlation of MVOA and PASP

Pearson correlation	Pre-PMTC	Day 1	Day 7	Day 30	3 months
MVOA vs PASP					
r value	-0.466	0.078	0.051	0.080	0.235
p value	0.001**	0.589	0.725	0.582	0.100

Total number of patients included in the study were 50. Most of the patients, that is 34(68%)were belongs to less than 40 years of age, female were 33 (66%), & were house wife (60%) in their occupation. Common complaints are breathlessness, cough, fatigue, palpitation and chest pain.

Poor nutrition status that is BMI less than 18.5 kg /m^2 seen in 11(22%) patients. Anemia seen in 14(28%) patients, atrial fibrillation in 13(26%) patients.

DISCUSSION:-

Pulmonary hypertension frequently complicates mitral stenosis. PAH contributes to symptoms of dyspnea in patients with mitral stenosis. The mechanisms believed to contrib-

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ute to the development of pulmonary hypertension in patients with mitral stenosis are multiple. There is a passive retrograde transmission of elevated left atrial and pulmonary venous pressures in to pulmonary vasculature; pulmonary venous hypertension leads to reactive pulmonary vasoconstriction and morphologic changes are induced in the pulmonary vasculature.[2] Immediately following PTMC, pulmonary hypertension decreases slightly with further substantial regression occurring over time.[9] The persistence of some pulmonary hypertension after PTMC relates to the residual mitral stenosis as well as permanent morphologic changes in the pulmonary vasculature. In this study, the immediate and late decrease in PAH after PTMC and determinants of decrease in pressure were determined.

In our study, Left atrial pressure immediately decreases on day1 in the younger age group of patients that is from 31.29 ± 5.38 to 15.86 ± 5.08. In male patients it decreases immediately on day1 compared to females that is from 31.71 ± 6.32 to 17.24 ± 5.19 .

RVSP decreases immediately on day1 in younger age group compared to older age that is from 71.57 ± 21.1 to 41.29 ± 10.75 in <20 years of age,where as in after 50 years of age it was from 57.40 ± 11.44 to 39.20 ± 4.32. RVSP also decreases immediately on day one compared to females that is from 66.76 ± 23.0 to 38.59 ± 10.48.

MOVA improves immediately on day 1 in <40 years of age compared to old age patients that is from 0.91 ± 0.11 to 1.76 ± 0.14.

Table 1 shows Peak and mean Mitral valve gradient decrease immediately on day1 in the younger age group that is <20 years of age compared to older age group where in they took 1-3 months that is from 0.84 ± 0.13 to 1.66 ± 0.2, in males it decrease more earlier than the females .

Table 2 shows PASP is decreased immediately on day1 in younger age patients compared to older age patients, that is from 82.29 ± 21.48 to 50.57 ± 10.86. where as in older age group that is after 30 years of age patients are taking more number of days, that is from 1-3 months to get decrease PASP to normal level. PASP will decrease immediately more commonly in male patients compared to female patients that is from 75.59 ± 25.11 to 47.06 ± 13.33.

Sub group Analysis :- Patients with severe PASP (>70 mmHg) shows that, severe PASP seen in older aged group of patients that is after 30 years of age in 17 patients, but it was only in 9 patients with <30 years of age. It decrease immediately on day1 in less than 30 years of age, but it takes more days to decrease PASP in older aged group that is after 30 years of age.

Table 3 indicates Pearson correlation of MVOA and PASP shows that r value is improving from 0.466 on pre PTMC to 0.235 at 3 months. Linear correlation improving from negative to positive at 3 months indicating good prognosis.

Ahmad Noor etal[21], reports that the Pulmonary Arterial Systolic Pressure(PASP) decreased by 29%, the mean left atrial pressure decreased by 48% and the left atrio ventricular gradient by 77%. Right ventricular systolic pressure and pulmonary artery systolic pressure decreased by 29%. In a study by Fawzy *et al,* the PASP fell from 48.6 ± 17.4mmHg before PTMC to 31 ± 10 mmHg.[14] Hannoush *et al*, reported 31% decrease in PASP immediately after PTMC.[15] Among these two studies, the patients were young as in the present study, while Gomez *et al,* Found no immediate decrease in PASP in older patients with a mean age of 52 years.[16] Age, mean left atrial pressure, and right ventricular size were independent predictors of decrease in systolic pulmonary pressure at post procedure in the regression analysis. Association of increasing age with more severe PAH and less reversible changes in pulmonary circulation is known previously as well. In the study by Moaquin *et al,* older patients had more severe pulmonary pressure while Hannoush *et al,* observed less decrease in PASP in older age group, aged more than 35years.[8,15]Ahmad Noor et al[21]study, showed that younger patients show more decrease in pressures post procedure. With each one year decrease in age, the systolic pulmonary pressures decreased more by 0.26mmHg. With increasing age, the pulmonary arteries are stiffer and their compliance explaining the lesser decrease in pulmonary pressure after PTMC. In a study by Shaw *et al,* increasing age was found to lead to less favourable results.[17] In that series advancing age was associated with higher echocardiographic score, more incidence of post procedure MR, and lesser increase in valve area. Fawzy *et al,* observed that their younger patients had lower echocardiographic scores, smaller valve areas, higher gradient across mitral valve and more mitral valve area.[18] These factors may be contributory to the lesser reduction in PAH with advancing age. In this study, decrease in PAH was seen more in patients with increasing left atrial mean pressure. As a consequence of the stenosis, an increase in left atrial pressure is required to maintain cardiac output. Ali *et al,* found left atrial size as a predictor for improved leaflet excursion after PTMC.[19] The increase in left atrial pressure causes an increase pulmonary venous pressures. But after PTMC, there is a decrease in left atrial pressure and with more pressures, there was more decrease in pulmonary PASP. After the PTMC, the PASP decreased by 4.059 mmHg for each decrease of 1 mmHg in left atrial pressure. Increase in pulmonary artery pressure leads to dilatation of right ventricular pressure and dilatation.[9] Right ventricular size was also an independent predictor of decrease in PASP (b=0.216; p=0.038: CI=0.25–0.871). Right ventricular enlargement is seen with worsening pulmonary hypertension. Right ventricular systolic and diastolic dysfunction has been described in patients with pure mitral stenosis and the diastolic dysfunction was found to be independent of pulmonary and left atrial pressures. This finding by Yildirim*et al,* suggests a possible rheumatological involvement of right ventricle as described for left ventricle.[20]

LIMITATION OF THE STUDY:-This study did not enrolled all consequitive patients who had undergone successful PTMC . The PASP after PTMC derived from TR jet gradient which has its own limitations.

CONCLUSION:-

Patients with successful PTMC had marked reduction in pulmonary arterial pressure which is greatest after first 24 hours, but continues to declines upto 3 months. This reduction is more in younger and male patients. No patients with severe PAH had marked improvement in PASP immediately.

REFERENCES:-

1. Zaman SK, Saghir T, Dadjan, Masood T, Tasneem H, Faruqui A.Percutaneous metallic mitral commissurotomy at NICVD.*Pak Heart J* 2001; **34**:2-7
2. Bano RO, Carabella BA, Chatterjee K, de Leon AC, Faxon DP,Freed MD, *et al.* AHA/ACC Guidelines 2006 for the managementof patients with valvular heart disease: a report of the AmericanCollege of Cardiology/American Heart Association task force onpractice guidelines (writing committee to revise the 1998guidelines for the management of Patients with valvular

heartdisease). *Circulation* 2006; **114**:450-527.

3. Farber HW, Loscalzo J. Pulmonary arterial hypertension.*N Engl J Med* 2004; **351**:1655-65.
4. Guerios EE, Bueno R, Nercolini D, Tarastchuk J, Andrade P,Pacheco A, *et al.* Mitral stenosis and percutaneous mitralvalvuloplasty (Part 1). *J InvasineCardiol*2005; **17**:382-6.
5. Fawzy ME, Hegazy H, Shoukri M, El-Shaer F, El-Dali A, Al-AmriM. Long-term clinical and echocardiographic results aftersuccessful mitral balloon valvotomy and predictors of long-termoutcome. *Eur Heart J* 2005; **26**:1647-52.
6. Carabello BA. Modern management of mitral stenosis.*Circulation*2005; **112**:432-7.
7. Song H, Kang DH, Kim JH, Park KM, Song JM, Coi KJ, *et al.*Percutaneous mitral valviloplasty versus surgical treatment inmitral stenosis with severe tricuspid regurgitation. *Circulation*2007; **116**:I246-50.
8. Moaqin S, Guoxiang H, Zhiyuan S, Luxiang C, Houyuan H,Liangyi S, *et al.* The clinical and hemodynamic results of mitralballoon valvuloplasty for patients with mitral stenosis complicated by severe pulmonary hypertension. *Eur J Intern Med*2005; **16**: 413-8.
9. Iung B, Nicoud-Houel A, Fondard O, Akoudad H, Haghighat T,Brochet E, *et al.* Temporal trends in percutaneous mitralcommissurotomy over a 15-year period. *Eur Heart J* 2004; **25**:701-7.
10. Vahanian A. Balloon valvuloplasty. *Heart* 2001; **85**:223-8.
11. Vahanian A, Palacios IF. Percutaneous approaches to valvulardiseases. *Circulation* 2004; **109**:1572-9.
12. Song JM, Kang DH, Song JK, Jeong YH, Lee CW, Hong MK,*et al.* Outcome of significant functional tricuspid regurgitationafter percutaneous mitral valvuloplasty. *Am Heart J* 2003; **145**:371-6.
13. Braunwald E. Valvular heart disease. In: Braunwald E. Heartdisease. 7th ed. Philadelphia: *WB Saunders,* 2008; 10047-11017.
14. Fawzy ME, Shoukri M, Al-Buraiki J, Hassan W, Widaal H,Kharabsheh S, *et al.* Seventeen years clinical andechocardiographic follow-up of mitral balloon valvoplasty in 520patients, and predictors of long-term outcome. *J Heart Valve Dis*2007; **16**:454-60.
15. Hannoush H, Fawzy ME, Stefadouros M, Moursi M, ChaudharyMA, Dunn B. Regression of significant tricuspid regurgitationafter mitral valvotomy for severe mitral stesnosis. *Am Heart J* 2004;**148**:865-70.
16. Gomez-Hospital JA, Cequier A, Romero PV, Canete C,Ugartemendia C, Esplugas E, *et al.* Persistence of lung functionabnormalities despite sustained success of percutaeous mitral volvotomy, the need for early indication. *Chest* 2005; **127**:40-6.
17. Shaw TRD, Sutaria N, Prendargast B. Clinical and hemodynamicprofile of young, middle aged and elderly patients withmitral stenosis undergoing mitral balloon valvotomy. *Heart* 2003;**89**:1430-6.
18. Fawzy ME, Stefadouros M, El-Amraoui S, Osman A, Ibrahim I,Nowayhed O, *et al.* Long-term (upto 18 years) clinical andechocardiographic results of mitral balloon valvuloplasty inchildren in comparison with adult population. *J Interv Cardio* 2008;**21**:252-9.
19. Ali H, Shams-Eddin H, Abd-Elsayed A, Maghraby MH.Echocardiographic assessment of mitral valve morphology afterpercutaneous transvenous mitral comissurotomy (PTMC).*Cardiovasc Ultrasound* 2007; **5**:48.
20. Yildirim N, Saricam E, Ozbakir C, Bozboga S, Ocal A.Assessment of the relationship between functional capacity andright ventricular ultrasound tissue characterization by integratedback-setter in patients with isolated mitral stenosis. *Int Heart J* 2007; **48**:87-96.
21. Ahmad Noor et al Determinants of Decrease in Pulmonary Hypertension Following Percutaneous Transvenous Mitral Commissurotomy JCPSP 2009, 19 (2): 81-85