RESPONSE TO SYMPTOMATIC TREATMENT IN MITRAL VALVE PROLAPSE, AN EXPERIENCE AT KHYBER PAKHTOONKHWA

Imran Khan[1], Shah Zeb[2], Hidayatullah[2], Muhammad Ishaq khan[2], Muhammad Waleed[2], Muhammad Salman[3]

[1]Cardiology Department, Lady Reading Hospital, Peshawar
[2]Department of Cardiology, Peshawar Institute of Cardiology Peshawar
[3]Fellow, Department of Cardiology, MTI Hayatabad Medical Complex Peshawar

ABSTRACT

Objectives: *To determine the subjective response to treatment in mitral valve prolapse patients.*

Materials and Methods: *This was a cross-sectional observational study was conducted in department of Cardiology LRH Peshawar, from 21 November 2019 to 30 April 2020. All consecutive patients having Prolapse of mitral valve fulfilling the inclusion criteria were studied. Their subjective response to treatment were studied. Statistical Analysis was done with SPSS version 18.0 software. Percentages & Frequency were used for categorical variables like ender, mitral regurgitation and response to treatment. While mean and standard deviation was used for quantitative variables like age were calculated.*

Results: *A total No of 142 patients have documented evidence of echocardiographic mitral valve prolapse were included. They all were and treated with Beta blockers and selective serotonin reuptake inhibitors (SSRI). Mean age were 19.45±7.32 years. Females were 89(62.7%). Out of total study population 128(90%) have palpitation, 111(78%) have chest pain, 102(72%) have dizziness, 93(65%) have Apprehension & Pre-syncope in 85(60%). Of the total, 32(22.53%) patients were also taking ACI/ARB and 42(29.5%) were on benzodiazepine. Their 04 month's subjective response to treatment was documented. Of all the patients 16 patients have lost to follow up. In the remaining 126 patients, response to medications were excellent in 21(16.67%), good in 29(23.01%), satisfactory/Fair in 41(32.53%). No response to symptoms was documented in 23(18.25%) patients and 12(9.5%) have worsening of symptoms.*

Conclusion: *Symptomatic patients have echocardiographic documented prolapse of Mitral valve fairly respond to SSRIs and beta blockers.*

Key words: *Mitral valve prolapse (MVP), Mitral regurgitation(MR)*

INTRODUCTION

Mitral valve prolapse (MVP) syndrome is also known as Barlow syndrome, systolic click-murmur syndrome and Syndrome of redundant cusp[1,2].This is a unique clinical syndrome having diverse pathological mechanisms of one or more mitral valve portion i.e. mitral leaflets, apparatus, annulus, chordae tendineae and papillary muscle.1Most majority of MVP patients are asymptomatic and have no issues throughout their lives. But Some patients complains of Presyncope, palpitations, Syncope, chest discomfort and Low cardiac output symptoms, chest discomfort sometimes confused with typical angina but in most occasion it is atypical and prolonged, no association with exertion and usually punctuated by small brief episodes of severe stabbing chest pain at the apex. This discomfort sometimes may be explained by abnormal tension on papillary muscles. These Patients may present with symptomatic

Correspondence:
Shah Zeb
Associate professor, Department of Cardiology,
Peshawar Institute of Cardiology Peshawar
Cell: +923339859640
Email: drshahzeb.mohmand@yahoo.com

arrhythmias.[1]

The estimated prevalence of MVP is reported between 0.4% - 35% in different studies.[2-5]A frequent MVP diagnosis and its emphasis on possible complications may have mental, physical, and socioeconomic effects in this younger population.

Usually patients with MVP are treated with beta blockers and low dose anxiolytic and SSRIs. There is no local data available to show clear-cut benefit of these patients in term of symptomatic improvement. But conventionally these patients with symptoms of anxiety are treated with beta blockers and SSRIs. We are have conducted this observational study to know the subjective response to treatment in our local population.

MATERIALS AND METHODS

This Cross-sectional study was conducted in cardiology department, Lady Reading Hospital Peshawar started from 21 November 2019 and continued till 30 April 2020. Because of estimated 30% attrition rate the study population was increased to 142 from the original 73 at 5% prevalence. . All patients of both gender having documented echocardiographic proven prolapse of mitral valve and eligible for treatment with beta blockers and SSRIs were included in the study. 2 D echocardiography was performed by echocardiographer having atleast 05 years of echocardiography experience for diagnosis of MVP. MVP was defined according to current standard guidelines as single or bi-leaflet prolapse at least 2 mm beyond the long axis annular plane, with or without leaflet thickening in the long-axis parasternal view. All patients with more than moderate Mitral regurgitation, other valvular lesion, rheumatic heart disease, structural heart diseases and rhythm disturbances were excluded from the study. All patients with secondary causes of various symptoms (palpitation, lightheadedness, pre-syncope, chest pain and shortness of breath) and patients who were not candidates for SSRI and beta blockers treatment were excluded. All the consecutive MVP patient's eligible for treatment with beta blockers and SSRI were included. All the baseline (demographic, clinical, echocardiographic variable) and outcome variable (subjective response to treatment) were entered via a specially designed proforma. All the study population who were eligible for treatment with beta blockers and SSRIs were given citalopram 5 to 10 mg and bisoprolol of 2.5 to 5 mg dose. The Subjective response to treatment was documented after 04 months of treatment. Subjective response to treatment were classified as:

1. Excellent (improvement of all symptoms),
2. Good (improvement of most of symptoms),
3. Fair (improvement in few symptoms),
4. No effect
5. Increased symptoms with treatment.

Statistical Analysis was done with SPSS version 18.0 software. Percentages & Frequency were used for categorical variables like ender, mitral regurgitation and response to treatment. While mean and standard deviation was used for quantitative variables like age were calculated.

RESULT

A total No of 142 patients have documented evidence of echocardiographic mitral valve prolapse were included. They all were and treated with Beta blockers and selective serotonin reuptake inhibitors (SSRI). Mean age were 19.45±7.32 years. Females were 89(62.7%). Out of total study population 128(90%) have palpitation, 111(78%) have chest pain, 102(72%) have dizziness. The details of symptoms is given in table 1 below. Some patients were also using concurrent medication, which are

Table 1: Baseline and clinical characteristics of patients with MVP

Variable	Total number	Percentage
Males	53	37.30%
Females	89	62.70%
Mean Age(years)	19.45±7.32	
Mean systolic Blood pressure(mm of Hg)	101.34±14.32	
Mean Diastolic Blood pressure(mm of Hg)	60.24±15.87	
Mean pulse rate(Heart beats/min)	82.46±18.74	
Palpitation	128	90.14%
Chest pain	111	78.16%
Dizziness/ vertigo	103	72.34%
Apprehension	93	65.5%
Presyncope	85	59.85%
Midsystolic ejection click	79	55.63%

Table 2: Treatment given to patients of MVP

Drugs	Numbers	Percentages
SSRIs	142	100%
Beta blockers	142	100%
ACI/ARB	32	22.53%
Benzodiazepine	42	29.57%

Table 3: Subjective response to treatment

Response	Number	Percentage (%)
Excellent	21	16.67
Good	29	23.01
Fair/Satisfactory	41	32.53
No response	23	18.25
Increase symptoms/ New symptoms	12	9.5

summarized in table 2. Their 04 month's subjective response to treatment was documented. Of all the patients 16 patients have lost to follow up. In the remaining 126 patients, response to medications were excellent in 21(16.67%), good in 29(23.01%), satisfactory/Fair in 41(32.53%). No response to symptoms was documented in 23(18.25%) patients and 12(9.5%) have worsening of symptoms. These results are summarized in table 3 below.

DISCUSSION

This study as per our knowledge is first study on this subject in our local population i.e. to know the response to conventional symptomatic treatment of mitral valve prolapse. Most of these patients came for cardiologist consultation to outpatient department regarding their symptoms associated with MVP. The estimated prevalence of prolapse of mitral valve in various studies is 5- 15% or more.[6,7,8] Recently anatomy of mitral valve is more clear on the 3-D echocardiography which resulted in impoved accuracy of diagnosis of true prevalence of prolapse of mitral valve. And some recent studies showed that estimated true frequency is 2-3% nowadays.[2] Some patients complains of Presyncope, palpitations, Syncope, chest discomfort and Low cardiac output symptoms, chest discomfort sometimes confused with typical angina but in most occasion it is atypical and prolonged, no association with exertion and usually punctuated by small brief episodes of severe stabbing chest pain at the apex. This discomfort sometimes may be explained by abnormal tension on papillary muscles.[2] More than three fourth of our study population is having palpitation, chest pain, dizziness, Apprehension and Presyncope. This finding is supported by Terechtchenko L et al, they have observed various tachy and bradyarrhythmias in MVP more than general population.[9]

Filho AS et al found in their study that MVP is associated with mental disorders including anxiety and depression.[10] Some other studies also reported higher prevalence of anxiety symptoms MVP patients as compared to healthy population and that these symptoms also responded to medication or psychotherapy.[11,12]

We have also documented in our study that more than 60% of the patients have subjective improvement in symptoms. Beta blockers has been quiet effectively used in treatment of these atypical symptoms in most of the studies. O'Rourke RA found that beta blocker is quiet effective in symptomatic treatment of MVP[13].

Nowadays there are vague statement regarding the effectiveness of SSRIs in Symptomatic treatment of Mitral valve prolapse. Also in some studies it has been questions the association of Anxiety disorder with Mitral valve prolapse.[10] But as still most of the cardiologist give treatment with low dose SSRI to MVP patients who have presented with anxiety symptoms. Although there is some dout between association of MVP and and psychological problems, it was observed in some studies that anxiety is more intense in MVP patients compared with general population so its medical treatment will be beneficial.[11] Psychological stress also result in rhythm disturbances[14]. It is evident from previous studies that anxiety aggravate symptoms of MVP and hence it treatment will improves symptoms.[10-12,15-18] SSRIs are treatment of choice for anxiety and depressive disorders.[19] SSRI administration have no adverse outcome in valvular diseases.[20] One of study on rodents also claims improvement in symptoms after co-administration of β-blockers, SSRI and benzodiazepine.[21]

So this observational study was just to elucidate the subjective response to various symptoms with conventional treatment in our part of the world. It is current routine of most of the cardiologist that they treat the mild axiety symptoms with low dose of SSRI. If patient have more symptoms of anxiety and they are getting worse despite low dose SSRI, they are referred to psychiatrist for detail assessment and

treatment. In our observational study the citalopram dose used was from 2.5 to 10 mg. Most of the patients have quiet good tolerability with these drugs. But it is still very important that about 10% of patients have no response to conventional treatment and about 10% got worse. No response and worsening of symptoms may be due to adverse effect of the drugs or interaction with drug. As one of the study which compare the fluoxetine combination with beta blockers and beta-blockers alone showed that the combination regime slightly increased the symptoms as compare to better tolerability of the beta blockers alone.[22] The same phenomenon may exist here in those patient whose symptoms worsen. Other causes of psychiatric symptoms, palpitation, chest pain, syncope should be excluded before starting patient on beta blockers and SSRI. Also patients with moderate to severe mitral regurgitation should be properly assessed. We are treating patients of mitral prolapse first with volume expansion. When patients not respond to volume expansion they are treated conventionally with beta blockers and SSRIs.

About one third of them have subjective evidence of improvement in the symptomatology while in rest of the patient the response was fair or no improvement in their symptoms.

It was previously shown that adrenergic receptor is upregulated in MVP, so it may respond to treatment with B-blockers.[14,23,24] This antiadrenergic be sympathetic tone may be responsible for symptomatic treatment with B-blokers.[25] SSRIs were also shown to be more efficacious in treatment of non- Cardiac chest pain so symptomatic improvement with SSRI in MVP may be the reason as in MVP chest pain is usually non cardiac.[26,27] The tachycardia associated with SSRIs is blunted by B-Blockers so its co-administration is more beneficial.[28,29]

Other studies may get different results because of using different criteria for symptomatic improvement. Also, we relied on participant's reports which may use other medication or inaccurate answers because of possible life events prior to each of their visits. In order to compensate for these bias, we suggest a common questionnaires for further studies.

CONCLUSION

Most of the atypical symptoms of the mitral valve prolapse which are not associated with structural heart disease or secondary causes fairly respond to SSRIs and beta blockers. In-ordered to probe this area of symptomatic response, randomized control trails are warranted.

LIMITATION

We used only 2 D transthoracic echocardiography and color Doppler for diagnosis of mitral valve prolapse. We have not used the three dimensional echocardiography which is more specific and reliable for studying mitral valve anatomy.

REFERENCES

1. Otto CM, Bonow R. Valvular Heart Disease. In: Bonow RO, mann DL, Zipes DP, Libby P, et al., editors. Braunwald's Heart Disease A Textbook of Cardiovascular medicine. 9Th ed. St. Louis: Saunders Elsevier; 2011. P. 1510-14.
2. Hayek E, Gring CN, Griffin BP. Mitral valve prolapse. Lancet 2005; 365 (9458): 507
3. Rizzon P, Biasco G, Brindicci G, Mauro F. Familial syndrome of midsystolic click and late systolic murmur. Br Heart J 1973;35:245-59.
4. Warth DC, King ME, Cohen JM, Tesoriero VL, Marcus E, Weyman AE. Prevalence of mitral valve prolapse in normal children. J Am CollCardiol 1985;5:1173-7.
5. Hepner AD, Morrell H, Greaves S, Greaves J, Movahed MR. Prevalence of mitral valvar prolapse in young athletes. Cardiol Young 2008;18:402-4.
6. Playford, David; Weyman, Arthur (2001). "Mitral valve prolapse: time for a fresh look". Reviews in Cardiovascular Medicine2 (2): 73–81.
7. Levy D, Savage D. Prevalence and clinical features of mitral valve prolapse. Am Heart J.1987;113(5):1281–90.
8. Warth DC, King ME, Cohen JM, Tesoriero VL, Marcus E, Weyman AE. Prevalence of mitral valve prolapse in normal children. Journal of the American College of Cardiology.1985;5 (5):1173–7.
9. Terechtchenko L, Doronina SA, Pochinok EM, Riftine A. Autonomic tone in patients with supraventricular arrhythmia associated with mitral valve prolapse in young men. Pacing ClinElectrophysiol.2003;26 (1 Pt 2):444–6.
10. Filho AS, Maciel BC, Romano MM, Lascala TF, Trzesniak C, Freitas-Ferrari MC, et al. Mitral valve prolapse and anxiety disorders. Br J Psychiatry. 2011;199(3):247–8. doi: 10.1192/bjp.bp.111.091934.
11. Zinchenko YP, Pervichko EI, Martynov AI. Psychological underpinning of personalized approaches in modern medicine: syndrome analysis of mitral valve prolapsed patients. Psychol Russ State Art. 2013;6(2):89–102. doi: 10.11621/pir.2013.0208.

12. Zinchenko YP, Pervichko EI. Qualitative Characteristics of Emotion Regulation Process in Adolescents with Mitral Valve Prolapse. Procedia - Soc Behav Sci. 2014;146:76–82. doi: 10.1016/j.sbspro.2014.08.089.

13. O'Rourke RA. Mitral valve prolapse syndrome. In: Alexander RW, Schlant RC, Fuster V, et al., eds. Hurst's The heart, arteries and veins. New York, N.Y.: McGraw-Hill, 1998:1821–31.

14. Combs RL, Shah PM, Klorman RS, Klorman R. Effects of induced psychological stress on click and rhythm in mitral valve prolapse. Am Heart J. 1980;99(6):714–21. doi: 10.1016/0002-8703(80)90620-1.

15. Hu X, Zhao Q. Autonomic dysregulation as a novel underlying cause of mitral valve prolapse: A hypothesis. Med Sci Monit. 2011;17(9):27–31. doi: 10.12659/msm.881918.

16. Lung FW, Cheng CT, Chang WT, Shu BC. Anxiety and mood disorder in young males with mitral valve prolapse. J Multidiscip Healthc. 2008;1:89–92.

17. Pervichko E, Zinchenko Y, Martynov A. EPA-0581 - Long-term integrative psychotherapy of anxiety disorders in mitral valve prolapse patients: the factors of mental health improvement. Eur Psychiatry. 2014;29(1):1. doi: 10.1016/S0924-9338(14)77970-2.

18. Pervichko EI, Zinchenko YP, Martynov AI. 2865 – Assesment of quality of life at mitral valve prolapse patients suffering anxiety disorders. Eur Psychiatry. 2013;28(1):1. doi: 10.1016/S0924-9338(13)77444-3.

19. Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol. 2014;28(5):403–39. doi: 10.1177/0269881114525674.

20. Maréchaux S, Jeu A, Jobic Y, Ederhy S, Donal E, Réant P, et al. Impact of selective serotonin reuptake inhibitor therapy on heart valves in patients exposed to benfluorex: A multicentre study. Arch Cardiovasc Dis. 2013;106(6–7):349–56. doi: 10.1016/j.acvd.2013.04.006.

21. Shahzad N, Ahmad J, Khan W, Al-Ghamdi SS, Ain MR, Ibrahim IAA, et al. Interactions of atenolol with alprazolam/escitalopram on anxiety, depression and oxidative stress. Pharmacol Biochem Behav. 2014;117:79–84. doi: 10.1016/j.pbb.2013.12.015.

22. Esfehani RJ, Kamranian H, Jalalyazdi M. Effect of Fluoxetine Administration on Clinical and Echocardiographic Findings in Patients with Mitral Valve Prolapse and Generalized Anxiety Disorder: Randomized Clinical Trial. Electron Physician. 2017 Jan; 9(1): 3483–3491.

23. Hu X, Wang HZ, Liu J, Chen AQ, Ye XF, Zhao Q. A novel role of sympathetic activity in regulating mitral valve prolapse. Circ J. 2014;78(6):1486–93.

24. Steenen SA, van Wijk AJ, van der Heijden GJ, van Westrhenen R, de Lange J, de Jongh A. Propranolol for the treatment of anxiety disorders: Systematic review and meta-analysis. J Psychopharmacol. 2016;30(2):128–39. doi: 10.1177/0269881115612236.

25. Theofilogiannakos EK, Boudoulas KD, Gawronski BE, Langaee TY, Dardas PS, Ninios V, et al. Floppy mitral valve/mitral valve prolapse syndrome: Beta-adrenergic receptor polymorphism may contribute to the pathogenesis of symptoms. J Cardiol. 2015;65(5):434–8. doi: 10.1016/j.jjcc.2014.07.020.

26. George N, Abdallah J, Maradey-Romero C, Gerson L, Fass R. Review article: the current treatment of non-cardiac chest pain. Aliment Pharmacol Ther. 2016;43(2):213–39. doi: 10.1111/apt.13458.

27. Varia I, Logue E, O'connor C, Newby K, Wagner HR, Davenport C, et al. Randomized trial of sertraline in patients with unexplained chest pain of noncardiac origin. Am Heart J. 2000;140(3):367–72. doi: 10.1067/mhj.2000.108514.

28. Conner R, Sheikh M, Grubb B. Postural orthostatic tachycardia syndrome (POTS): Evaluation and management. Br J Med Pract. 2012;5(4):540. 29. Gollan JK, Fava M, Kurian B, Wisniewski SR, Rush AJ, Daly E, et al. What are the clinical implications of new onset or worsening anxiety during the first two weeks of SSRI treatment for depression? Depress Anxiety. 2012;29(2):94–101.