A STUDY ON BENEFICIAL EFFECTS OF METOPROLOL IN CONGESTIVE HEART FAILURE

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ABSTRACT

BACKGROUND

Metoprolol has beneficial effects in congestive heart failure, it binds with beta adrenergic receptors of brain, heart, kidney there by it will reduce sympathetic neurotransmitters release, decreases heart rate, force of contraction and cardiac output, decreases renin hormone release from the kidneys. By these three actions it will reduces pre load and after load on heart. It directly opens specific L-type of membrane calcium channels in heart and also glycogenolysis which leads to increase in pumping capacity of left ventricle, there by heart will meet various metabolic demands of the body.

Aim- To provide Safe and effective management for congestive heart failure patients by adding metoprolol (selectiveβ1 blocker).

MATERIALS AND METHODS

6 minutes walking test, chest X-Rays, ECG, 2 D-Echo and other required investigations are conducted for validation of beneficial effects of metoprolol in improving ejection fraction at base line and also at follow up by using various study materials in four months duration. Over 2.4 million patients who are hospitalized have HF as a primary or secondary diagnosis, and nearly 300,000 deaths per annum are directly attributable to HF.

Statistical Analysis- Data was articulated in percentage.

Design **-** A concurrent interventional cohort study.

RESULTS

A total of 70 patients were recruited; among that, 50 patients were test and 20 patients were standard. Exercise capacity and ejection fraction of test group patients and standard group patients was estimated and improvement in ejection fraction, exercise capacity was observed in test group compared to standard group at first (0.92%), (0.72 min) and final follow up (3.74%), (3.24 min) respectively. Statistically significant difference was observed in ejection fraction (< 0.05) and exercise capacity (< 0.05) test group, but not in standard group (E.F.- 0.067, E.C.- 0.079). Also found improvement in chest X-ray, ECG at base line Vs final follow up.

CONCLUSION

Metoprolol use in congestive heart failure- increases left ventricle ejection fraction, exercise capacity, anti-remodeling effect by decreasing myocardial apoptosis and also reduces cardiac disability frequencies, prevents long term complications, reduces morbidity and mortality. For providing better patient care to CHF patients there is a need to add metoprolol.

KEYWORDS

Congestive Heart Failure, Ejection Fraction, Exercise Capacity, Electrocardiogram, Chest X Ray, 2D-Echo, ß-blockers, Metoprolol.

HOW TO CITE THIS ARTICLE: Reddy MS, Ramana PV, Reshma S, et al. A study on beneficial effects of metoprolol in congestive heart failure. J. Evid. Based Med. Healthc. 2018; 5(13), 1179-1183. DOI:10.18410/jebmh/2018/244

Financial or Other, Competing Interest: None.
Submission 05-03-2018, Peer Review 10-03-2018,
Acceptance 19-03-2018, Published 23-03-2018.
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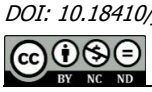
DOI: 10.18410/jebmh/2018/244



BACKGROUND

Heart failure is define as "a complex clinical syndrome that can result from any structural or functional cardiac disorder that interfere with the ability of the ventricle to fill or eject blood." which eventually leads to deceased perfusion to all parts of the body and impairs their functional capacities.[1,2,3] With reduction in cardiac output, a decrease in baroreflex-mediated inhibition of the vasomotor centre activates renal vasoconstrictor nerves and the RAAS system, causing sodium and water retention. Incomplete ventricular emptying (systolic heart failure) or inadequate ventricular relaxation (diastolic

heart failure) both leads to an elevation of ventricular diastolic pressure.[4] If the impairment of cardiac function primarily involves the right ventricle, pressures in the systemic veins and capillaries rise, augmenting the transudation of fluid into the interstitial space and enhancing the likelihood of peripheral oedema.[5] Over 2.4 million patients who are hospitalized have HF as a primary or secondary diagnosis, and nearly 300,000 deaths per annum are directly attributable to HF.[6] From the 1970s to 1990s, a remarkable increase in the prevalence of HF.[7,8] The ejection fraction (EF) compares the amount of blood in the heart to the amount of blood pumping out. It is an essential measurement in determining how well the heart is pumping blood out and in diagnosing and tracking heart failure. In normal EF 50-70% is pumped out during each contraction, in Border line EF 41-49% blood is pumped out during each contraction, the symptoms become noticeable only during physical activities.[9,10] In reduced EF≤40% blood is pumped out during each contraction an evidence of heart failure. Whereas in case of reduced EF, the symptoms noticeable even during rest. This leads to symptoms like increased fatigue.[11,12,13] Recent research studies have given conclusion in congestive heart failure metoprolol along with standard therapy will improves left ventricular function.[14,15] Current available therapy includes Diuretics, ACE inhibitors, ARBs, Positive inotropic agents, Digoxin,nitrates and hydralazine,β-blockers.[16,17] Metoprolol has beneficial effects in congestive heart failure, it binds with beta adrenergic receptors of brain, heart, kidney there by it will reduces sympathetic neuro transmitters release, decreases heart rate, force of contraction and cardiac output of heart, decreases renin hormone release from kidneys. By these three actions it will reduces pre load and after load on heart.[18,19,20] Metoprolol also stimulates G- protein couple receptors in myocytes leads to activation of adenylyl cyclase results in intracellular accumulation of secondary messengers (CAMP) and also reduces degradation of CAMP by inhibiting phosphodiesterase enzyme, These increase in cyclic AMP levels directly opens specific L-type of membrane calcium channels in heart and also induces glycogenolysis which leads to increase in left ventricular ejection fraction of heart there by heart will meet various metabolic demands of the body.[21,22,23]

Aims and Objectives

1. To provide Safe and effective management for congestive heart failure patients by adding metoprolol (selectiveβ1 blocker).
2. To identify the congestive heart failure patients by using their subjective and objective evidence.
3. To categorize the selected patients in to two groups i.e., test group and standard group.
4. To give the metoprolol to test group and other than metoprolol therapy to standard group.
5. To asses and compare the outcomes in both groups.
6. To study the benefits of metoprolol.

MATERIALS AND METHODS

This concurrent interventional cohort study performed for a period of 6 months in general medicine department Rajiv Gandhi Institute of Medical sciences, a south Indian tertiary care teaching Government hospital Kadapa. This study got ethical approval from the IEC of RIMS, Kadapa. A total of 70 study populations were taken and patients were enrolled based on inclusion and exclusion criteria by using study materials like specially designed patient data collection form, informed consent form and specially designed laboratory investigation and interpretation form. Both males and females of age group between 20 to 70 years diagnosed as congestive heart failure evaluated by reduced ejection fraction <40 %, CHF patients with other co morbidities (HTN, CAD, LVD, COPD, C.A, Type 2 DM), patients who are willing to participate in this study are under inclusion criteria. Exclusion criteria includes patients are excluded if they are contraindicated to beta blockers, heart failure patients < 20 years were excluded and heart failure patients without decreased ejection fraction. In first two months of study period patients were recruited based on inclusion criteria (i.e., based on symptoms of CHF, other required investigations like chest X-Ray, ECG, ECHO-ejection fraction ≤40% and other investigations). After selection of patients, they are categorized into two groups' i.e. test group and standard group, later standard group of patients was treated with other than metoprolol therapy for CHF and test group of patients were treated with metoprolol (25 mg/per day/per oral) along with other drugs therapy. Both group of patients were followed for next four months of period including monthly checkups for any improvements or other problems in their health, at the end of study period we conducted 6 minutes walking test, chest X-Rays, ECG, ECHO (ejection fraction) and other required investigations, finally we compared the initial condition (both symptomatically and ejection fraction wise) and final condition of both group of patients and also we estimated the benefits of metoprolol in congestive heart failure patients.

Statistical Analysis

A total of 70 congestive heart failure patients was selected. Ejection fraction data and 6 minutes walking test data analysed by using Student Paired t – test. The ejection fraction of patients during at the time of recruitment and at first follow – up, second follow – up, third follow – up, and fourth follow – up respectively, was compared. All the statistical data analysis was determined by using IBM SPSS Statistics Software, Version 24.

RESULTS

A total 70 patients were categorized with respect to their age groups, majority between the age group of 60 to 70 years, in that 70 patients 43 were male patients 13 (18.5%) were only with CHF, 30 (42%) with co morbid condition, and 27 were female patients in that 11 (15.7%) were only with CHF and 16 (22%) with co morbid condition (includes HTN, Anaemia, MI, COPD, Type 2 DM) which was showed in (Figure 1). Out of 70 patients

majority (35.7%) with ejection fraction 35-37% and 41-43%, 20(28.5%) with ejection fraction 38-40%. which was showed in (Figure 2). By the usage of metoprolol 50(71.4%) patients were used metoprolol (considered as test group) and 20(28.4%) patients were not used metoprolol (considered as standard group) which was represented in (Figure 3). Overall average results of ejection fraction and 6 minutes walking test during baseline period and final follow – up period in test group and standard group of patients was showed in (Figure 4) and (Figure 5).

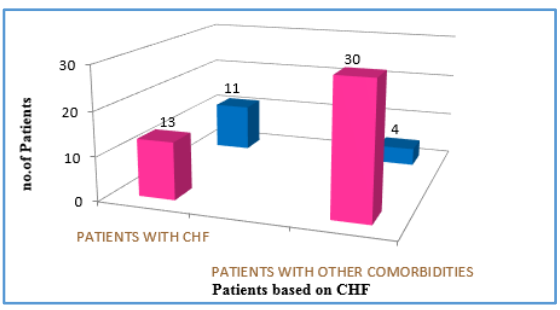


Figure 1. Patient's Distribution based on CHF and other Co Morbid Conditions

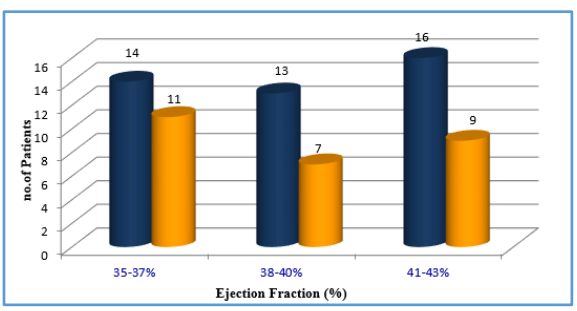


Figure 2. Patient's Distribution based on Ejection Fraction

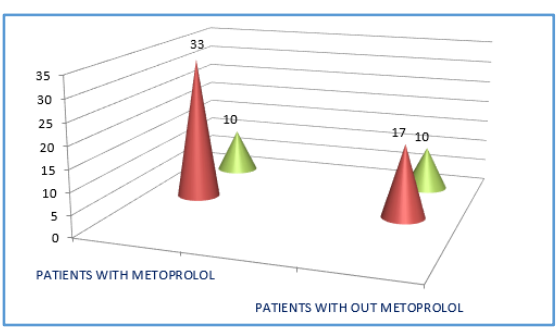


Figure 3. Patient's Distribution based on Metoprolol Use

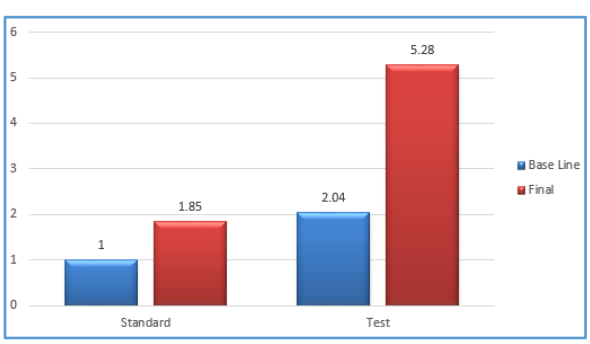


Figure 4. Comparison results of average 6 minute walking test during baseline period and final follow-up period in standard and test group of patients

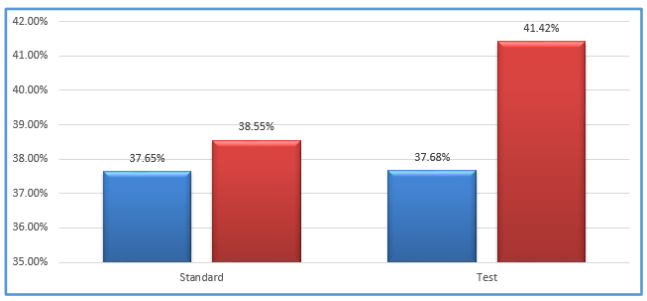


Figure 5. Comparison results of average ejection fraction during baseline period and final follow-up period in standard and test group of patients

DISCUSSION

In the present study we have recruited CHF patients (70 patients) based on inclusion criteria (i.e., based on symptoms of CHF and other required investigations like chest X-Ray, ECG, ECHO-ejection fraction ≤40% and other investigations) and exclusion criteria. 43(62%) patients' males and female subjects were 27(38%). The average age of patient test group is (61.78) years and average age of standard group is (47.4) years. In patient group more than 50 of patients were in the age group of 50-70 years. Generally these age group people are more prone for chronic disease and congestive heart failure occurs in aged groups (>50 years) we have also found 34% patients between 30-40 years. This indicates the occurrence of congestive heart failure in middle age group is rising. We found that around 53% of patients had risk factor of CHF. In that most of the patients were having alcoholism and smoking, very few with both risk factors. This indicates social habits are the major risk factor for congestive heart failure. We also found that around 55% of patients had disease history of 1-3 years and 24% of patients had disease history of <1 year, 20% of patients had disease history of in between 4-5 years[21]. We also found that around 35% of patients had only CHF and 65% of patients had CHF with other co morbidities. In that 65% of patients had CHF with other cardiovascular co morbidities like HTN+M.I+U.A.P+C.A etc. 30.2% of patients had other than cardiovascular diseases as co morbidities like ANEMIA+COPD+D.M[22]. We have estimated ejection fraction of study population including test group patients and standard group patients by using 2- dimensional Echo cardiogram. At base line average ejection fraction of test group Vs standard group is found to be 37.68% and 37.65% respectively, almost both the values are equal and we found that both groups ejection fraction is <40%, this indicates they are in dangerous stage (symptoms may become noticeable even during rest) We have estimated ejection fraction of test group at each follow up i.e., at first follow up (38.6%), second follow up (39.3%), third follow up (40.46%) and fourth follow up (41.42%) respectively, which has been observed in 4 months duration, extremely statistical significance difference observed between base line Vs first follow up ($P<0.00083$), second follow up ($P<0.000093$), third follow up ($P<0.0000018$), fourth follow up ($P<0.00000012$) respectively.

We have estimated ejection fraction of standard group at each follow up i.e., at first follow up (37.7%), second follow up (37.85%), third follow up (38.25%) and fourth follow up (38.55%) respectively, which has been observed in 4 months duration, no statistical significance difference observed between base line Vs first follow up (P = 0.330), second follow up (P = 0.312), third follow up (P = 0.085) and fourth follow up (P = 0.067) respectively. We have compared ejection fraction of test group of patients and standard group of patients at each follow up and we found improvement of ejection fraction in test group at first and final follow up i.e. (0.92%) and(3.74%) respectively. We have estimated exercise capacity of test group at base line (2.04 mints.), at each follow up i.e., at first follow up (2.76 mints.), second follow up (3.74 mints.), third follow up (4.46 mints.) and fourth follow up (5.28 mints.) respectively, which has been observed in 4 months duration, extremely statistical significance difference observed between base line Vs first follow up (P **<**0.0008), second follow up (P **<**0.00057), third follow up (P **<**0.00068) and fourth follow up (P <0.00004) respectively. We have estimated exercise capacity of standard group at baseline period (1 mint) at each follow up i.e., at first follow up (1.05 mints.), second follow up (1.3 mints.), third follow up (1.65 mints.) and fourth follow up (1.85 mints.) respectively, which has been observed in 4 months duration, no statistical significance difference observed between base line Vs first follow up (P = 0.330), second follow up (P = 0.255), third follow up (P = 0.147) and fourth follow up (P = 0.079) respectively.

We have compared exercise capacity of test group of patients and standard group of patients at each follow up and we found improvement in exercise capacity in test group of patients at first and final follow up i.e. (0.72 mints.) and (3.24 mints.) respectively. We have observed statistical difference in ejection fraction of standard Vs test group, 6 minutes walking test standard Vs test group. We have also found there is improvement in Chest X ray and ECG at base line Vs final follow up. This indicates improvement in cardiovascular function.

CONCLUSION

Our study found that use of metoprolol in congestive heart failure will increases left ventricle ejection fraction, exercise capacity, anti-remodeling effect by decreasing myocardial apoptosis. Our study also found that use of metoprolol in congestive heart failure patients increases ejection fraction range from 0.92% – 3.74%.

We concluded that for safe and effective management of CHF patients, for reducing cardiac disability frequencies, for preventing long term complications, for reducing morbidity and mortality, for better patient care, there is a need to add on metoprolol in congestive heart failure.

Recommendations

- Heart failure is an upcoming cardiovascular disease affects nearly 16 million peoples worldwide; it is the leading cause of hospitalization in people older than age 65.
- For preventing mortality associated with CHF early diagnosis and proper management is necessary.
- Digitalis derivatives, Dilators, Diuretics, Dopamine, Di-esterase enzyme inhibitors are the available treatment for CHF with minimal influence on Ejection fraction.
- Addition of metoprolol to above treatment regimen will improves left ventricular ejection fraction, increases working capacity, decreases hospital admissions, decreases mortality rate.

Limitations

1. Failure of the randomization to achieve identical patients.
2. Standard Sample size is very less. (20 patients)
3. Limited study period (6 months)
4. Lack of sophisticated diagnostic procedures like 3-D Echo, angiographic left ventriculography and Radionuclide ventriculography.

ACKNOWLEDGEMENT

We would like to thank all the participants who provided their valuable inputs for completion of this study.

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