Original Research Paper

Volume-9 | Issue-7 | July - 2019 | PRINT ISSN No. 2249 - 555X

Pharma

EFFECTS OF CARVEDILOL IN LEFT VENTRICULAR DYSFUNCTION IN PATIENTS WITH HEART FAILURE

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ABSTRACT

Background: we conducted single center single drug study designed to establish the efficacy and safety of Carvedilol, a beta blocker of third generation which have vasodilator properties, in chronic heart failure.

Methods: 50 patients with heart failure were treated with Carvedilol, and echocardiographic evaluation was performed at the start and after 6 months.

Results: Ejection fraction, blood pressure, pulse rate were improved in patients after 6 months treatment compared to before start of treatment with carvedilol. we found significant differences in :systolic blood pressure(p value 0.0479);diastolic blood pressure (p value 0.2455);ejection fraction(p value 0.2691); pulse rate(p value 0.2192).

Conclusion: From this study we conclude that Carvedilol have proved to have good efficacy on the ejection fraction in patients with left ventricular dysfunction despite of few limitations like small sample size. Therapy of several months is required for improvement of ejection fraction, as these changes do not occur in the short term.

KEYWORDS : Carvedilol, Ejection fraction, Left ventricular dysfunction, Heart failure, Blood Pressure, Pulse rate.

INTRODUCTION

Heart failure is a progressive syndrome resulting from the heart's inability to adequately perfuse and oxygenase peripheral tissues. This syndrome is manifested by fatigue dyspnea, and congestion (1, 2). Heart failure is associated with patholgic ventricular remodeling and worsening ventricular dysfunction, resulting in adverse hemodynamic changes (3). Activation of the sympathetic nervous system is known to be associated with progressive deterioration of cardiac function and clinical condition and increased mortality in patients with heart failure (4-10). Beta adrenergic blocking agents, because of their ability to inhibit sympathoadrenergic drive, are therefore useful for the long-term treatment of this syndrome (11, 12).Carvedilol is a new beta blocker devoid of intrinsic sympathomimetic activity with associated vasodilators effects mediated by alpha$_1$-receptor antagonism (10, 13, 14).Carvedilol is a third generation β-blocker with vasodilatory and antioxidant actions, which has been established as an effective drug for mild to severe CHF (15). Heart failure is associated with an increase in adrenergic activity and in that of rennin angiotensin-aldosterone system (16,17).beta blockers are one of the main stays of treatment due to their ability to reverse neuro humoral effects of sympathetic nervous system with ensuing symptomatic benefits (18,19,20). Carvedilol has significant anti oxidant properties (21, 22). It inhibits oxygen free radicals generation and prevents LDL (low density lipoprotein) oxidation, in turn LDL uptake in to coronary vasculature is reduced. This anti oxidant property contributes to Carvedilol's cardio protective effects (23).Carvedilol produce less “inverse agonism” than most other beta blockers. Thus, carvedilol produces relatively fewer negative chronotropic and ionotropic effects than other beta blockers (24). In this study, we investigated the effects of Carvedilol on parameters of ejection fraction, systolic blood pressure, diastolic blood pressure and pulse rate in heart failure patients with left ventricular dysfunction. Carvedilol is a beta blocker and have more anti adrenergic activity than others because of its unselective blockade of beta1 and beta2, alpha blockade and has anti oxidant properties, which provides a greater reduction of cardiac adrenergic drive and work (25). The aim of the study is to assess the Carvedilol efficacy on ejection fraction of heart failure patients with left ventricular dysfunction.

MATERIALAND METHODS

It is a prospective, observational single drug study conducted in patients of “MGM hospital”. Patients were explained about the study &informed consent were seeked by explaining them in their local language.

Inclusion criteria

Males and females of 25-80years diagnosed with left ventricular dysfunction will be included in our study

Exclusion criteria

Age above 80 years , patients with bradycardia, uncontrolled diabetes mellitus, asthma, unstable angina, resting angina, severe liver impairment, grade II or III atrio ventricular block, hyperthyroidism, pregnant women, corpulmonale, valvular heart disease, life threatening arrhythmia, cardiogenic shock, hypertrophic obstructive cardio myopathy. Patients were also excluded if myocardial infarction or coronary artery bypass grafting had occurred within the preceeding 3 months .

Study design

It is a prospective, observational, single centered, single drug study design performed for a period of 6 months and the patients included are on beta blocker therapy with Carvedilol. The goal was to achieve improvement in ejection fraction, blood pressure, pulse rate with adds on therapy of Carvedilol.

Institutional Human Ethical Committee Endorsement was obtained after submission of protocol and IHEC number is MGM/ VCOP/ PHARM/ D/V/05/2018.

Clinical response assessment

The efficacy of Carvedilol was assessed by measuring the change in the Ejection fraction, systolic blood pressure, diastolic blood pressure, pulse rate after 6 months of treatment. Primary end point was change in ejection fraction after 6 months treatment as compared to the baseline levels. The secondary end point was change in blood pressure, pulse rate which were measured after 6 months treatment as compared to baseline levels.

Statistical analysis

All parameters were expressed as mean±SD. Data analysis was performed using the EXCEL sheet 2007 .Paired t test was used to assess significant differences between values obtained before and 6 months after the addition of Carvedilol (**Figure 1**).

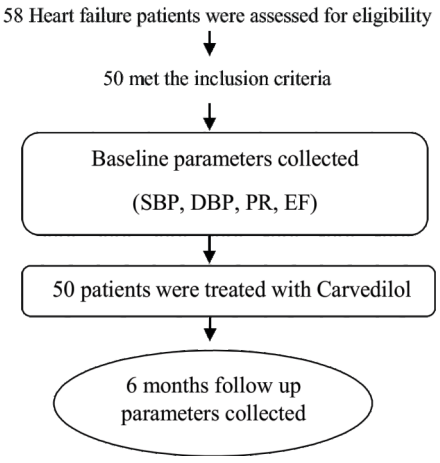


Figure 1: Total number of patients completed the study.

RESULTS

Ejection fraction (Figure 2)

Alteration in ejection fraction could lead to devastating conditions. This study includes measuring ejection fraction at the baseline and after 6 months Carvedilol therapy. Mean change in Ejection fraction of baseline was 32.02±9.87.Mean change in Ejection fraction after 6 months of treatment was 34.16±9.38.

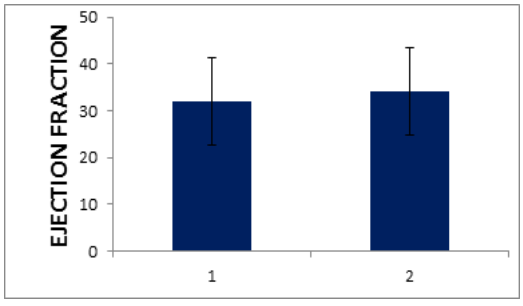


Figure 2.Mean change in Ejection fraction of Baseline (1) , Carvedilol treated (2) .

Systolic Blood Pressure (Figure 3)

Systolic blood pressure elevation could be a risk factor for cardio vascular disease. This study includes measuring SBP at the baseline and after 6 months Carvedilol therapy. Mean change in Systolic blood pressure of baseline was 133.8±19.78Mean change in systolic blood pressure after 6 months of treatment was 127±13.59

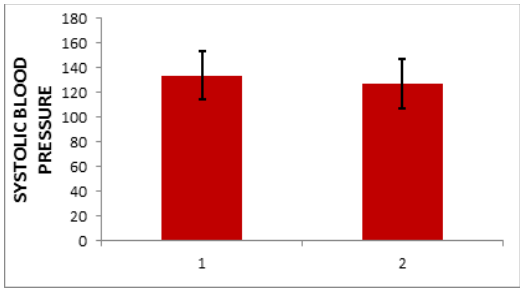


Figure 3.Mean change in Systolic blood pressure of baseline (1), Carvedilol treated (2) .

Diastolic blood pressure (figure 4)

DBP is the pressure in arteries when the heart rests between beats .High DBP is a sign that blood vessels have become less elastic, hardened and scarred.This study includes measuring DBP at the baseline and after 6 months Carvedilol therapy .Mean change in Diastolic blood pressure of baseline was 84.4±10.33Mean change in Diastolic blood pressure after 6 months of treatment was 82.2±8.40

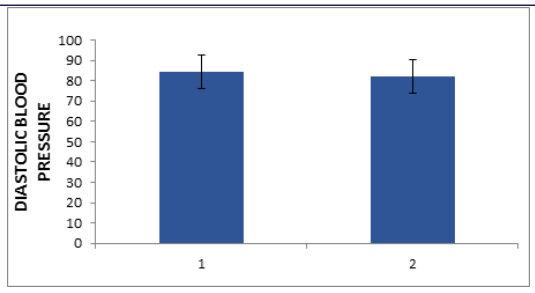


Figure 4. Mean change in Diastolic blood pressure of baseline (1), Carvedilol treated (2) .

Pulse rate (figure 5)

Pulse rate is the number of heart beats per minute.If pulse rate is left untreated can lead to potentially serious health complications . This study includes measuring Pulse rate at the baseline and after 6 months Carvedilol therapy. Mean change in Pulse rate of baseline was 85.66±12.33Mean change in Pulse rate after 6 months of treatments was 83.1±7.89

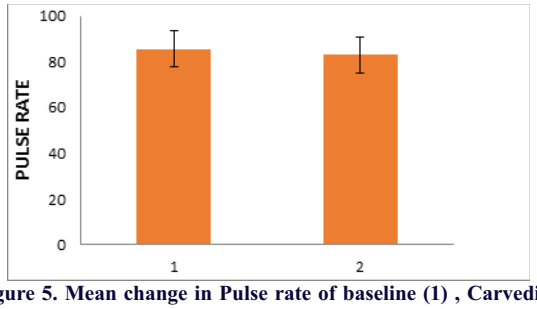


Figure 5. Mean change in Pulse rate of baseline (1) , Carvedilol treated (2) .

DISCUSSION

Efficacy study of Carvedilol was done on left ventricular dysfunction patients with heart failure the following changes in parameters like Systolic blood pressure, Diastolic blood pressure, Pulse rate and Ejection fraction were observed.

The main finding of this study is significant improvement in Ejection fraction,Systolic blood pressure,Diastolic blood pressure,Pulse rate from the baseline and 6 months after treatment with carvedilol. Ejection fraction was improved significantly from 32.02 to 34.16 (mean value), p value 0.2691.Systolic blood pressure has decreased significantly from 133.8 to 127 (mean value), p value 0.0479.Diastolic blood pressure has decreased significantly from 84.4 to 82.2 (mean value), p value 0.2455.Pulse rate has decreased significantly from 85.66 to 83.1 (mean value), p value 0.2192.These changes occurred in subjects in a stable clinical condition .Results were also seen in similar studies regarding ejection fraction conducted by Masatsugu et al., "Low doses of carvedilol improves left ventricular function and reduces cardiovascular hospitalization in Japanese patients with chronic heart failure: the multicentre carvedilol heart failure dose assessment (MUCHA) trial" .

A study undertaken by Micheal et al., which was "carvedilol produces dose related improvements in left ventricular function and survival in subjects withchronic heart failure" has concluded that in subjects with mild to moderate heart failure from systolic dysfunction carvedilol produced dose related improvements in LV function and dose related reduction in mortality and hospitalization rate".

CONCLUSION

From this study we conclude that Carvedilol proved to have good efficacy on ejection fraction. Hence, we conclude that Carvedilol is an efficacious drug for management of left ventricular dysfunction patients with heart failure by improving ejection fraction and lowering Systolic blood pressure, Diastolic blood pressure and Pulse rate.

Our study, using the sample size of 50 with carvedilol therapy for 6 months, was safe and tolerable for patients with heart failure and showed an improvement in ejection fraction (32.02±9.87 to 34.16±9.38.),systolic blood pressure(133.8±19.78 to 127±13.59),diastolic blood pressure (84.4±10.33 to 82.2±8.40) and pulse rate (85.66±12.33 to 83.1±7.89).

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