

Rational Use of AEG Inhibitors in Congestive Heart Failure

Khawaja Tahir Mahmood, Maryam Zaka, Zainab safder, Amna Khan
Lahore College for Women University, Lahore.

Abstract:

Congestive heart failure is inability to pump enough blood to the body organs causing congestion in the tissues. ACE inhibitor is use as first line of therapy. The therapeutic objective of ACE inhibition in congestive heart failure is to prevent cardiac remodeling so as to delay or arrest progression of heart failure and death. The aim was to observe the rational use of ACE inhibitor for the purpose of achieving best therapeutic outcome. A retrospective study was done in Services institute of medical sciences and Punjab institute of cardiology Lahore 21/7/10 to 21/9/10 40 patients were observed who were suffering from CHF & are receiving ACE therapy. Data gathered based on history, clinical examination and laboratory methods. 90% of the patients suffer no side effects after taking ACE inhibitors. Only 10% of the patients have side effects like mild hypotension at the start of therapy which can be coping up with dose adjustment & some face mild cough or hyperkalemia very rarely. The most commonly ACE I use was lisinopril& captopril with 60% & 32.5% respectively so the improvement in outcome is a class effect. We concluded that Dose management & therapeutic drug monitoring is very much important in ACEI therapy. It is carried out during hospitalizations but no proper compliance is done after discharge. Serum electrolytes, blood urea creatinine & blood pressure should be monitored regularly. There should be clinical pharmacist in every hospital as pharmacist should be a part of health care team to achieve optimal outcomes of drug therapy.

Key Words: ACEI (angiotensin converting enzyme inhibitor), CHF (congestive heart failure), hyperkalemia, hypotension.

INTRODUCTION:

Heart failure is a complex of symptoms fatigue, shortness of breath, and congestion that are related to the inadequate perfusion of tissue during exertion and often to the retention of fluid. Its primary cause is an impairment of the heart's ability to fill or empty the left ventricle properly [1].

The most common causes are coronary heart disease (CHD) and primary heart muscle diseases (cardiomyopathies), with heart valve disease less common. [2] .The contributing factors that lead to the development of HF are considered the precursor to the vicious cycle of events that cause the remodeling of the heart muscle. These events include uncontrolled hypertension, myocardial infarction, and valvular disease [3]

For diagnosis, no single test can be used to establish the clinical diagnosis of heart failure. Instead, history and physical examination findings showing signs and symptoms of congestion and/or end-organ hypoperfusion are used to make the diagnosis. Imaging studies documenting systolic or diastolic dysfunction and biomarkers are helpful adjuncts. Physical

examination is not helpful in discriminating between systolic and diastolic heart failure [4]

Drug therapy includes the use of time-tested medications, such as diuretics and digitalis, and the addition of newer agents, such as angiotensin-converting enzyme (ACE) Inhibitors, angiotensin II receptor blockers, β -blockers and spironolactone. The cornerstone of medical management of CHF is the ACE Inhibitor class of drugs. When used with conventional therapy (diuretics and digoxin), ACE Inhibitors have been clearly shown in randomized trials to improve survival among symptomatic patients who have documented left ventricular dysfunction [5]. In the last decade, angiotensin-converting enzyme (ACE) Inhibitors has been added as an important treatment option. These agents counteract the overstimulation effects of diuretics on the renin-angiotensin-aldosterone system. In addition, it is indicated that ACE Inhibitors may improve symptoms and survival. Recent evidence suggested that in patients with mild to moderate CHF, ACE Inhibitor and a diuretic should be administered with or without digitalis to achieve the maximum clinical benefit [6]

Current therapy for CHF can maintain function, improve quality of life, and prolong survival. Diuretics, angiotensin-converting enzyme inhibitors (ACE), and digoxin remain in standards of therapy. Documentation of the clinical benefit of ACE inhibitors represented the most important advance in therapeutics for CHF in the last decade. [7]

ACE inhibitors are given as first-line therapy in early presymptomatic CHF, the evidence is also good, based on the prevention arm of the Studies of Left Ventricular Dysfunction also suggested a role for ACE inhibitors as effective first-line monotherapy in early heart failure, acting on left ventricular function to avoid or lessen unfavorable remodeling [8]

(ACE) inhibitors, such as Captopril, Enalapril, and Quinapril, have been shown to improve hemodynamics, reduce symptoms of fatigue and dyspnea, increase exercise capacity, correct hyponatremia, reduce diuretic requirements and ventricular arrhythmias, and conserve potassium and magnesium. ACE inhibitors reduce circulating levels of angiotensin II and aldosterone and may reduce plasma norepinephrine and vasopressin levels. They are equally effective in patients with mild to moderate heart failure and in patients with severe cardiac impairment. ACE Inhibitors improve prognosis in patients with severe heart failure and in patients with hyponatremia [9]

Angiotensin converting enzyme inhibitors (ACE-I) competitively inhibit the angiotensin converting enzyme. ACE is a non-specific enzyme involved in the metabolism of many small peptides, including the conversion of angiotensin I, an inactive octapeptide, into angiotensin II. Kininase, an enzyme that catalyses the degradation of bradykinin and other potent vasodilator peptides, is also competitively inhibited by ACE-I [10]

There are some contraindications or cautions for the use of ACE Inhibitors in CHF, such as preexisting hypotension, high-renin states such as bilateral renal artery stenosis with hypertensive heart failure, aortic stenosis combined with CHF, overdiuresis with excess sodium depletion, and significant preexisting renal failure. ACE Inhibition therapy may have

deleterious effects on renal function in heart failure, for example, by decreasing the glomerular filtration [11]. The most common adverse effects of ACE Inhibitors are headaches, dizziness, fatigue, diarrhea, coughing, and hypotension. The most frequent of these adverse effects is coughing. Patients describe their cough as dry and nagging, which is reversible once the drug has been discontinued. If the side effects can be tolerated the patient should be encouraged to stay on the ACE Inhibitor, as its benefits outweigh the adverse effects [12]

For an individual congestive heart failure (CHF) patient to gain maximum benefit from their angiotensin converting enzyme (ACE) inhibitor treatment, it is important for him or her to adhere fully with treatment. Since ACE inhibitors reduce mortality, it is self evident that non-adherence will increase mortality. In the case of adherence with an ACE Inhibitor, a unique opportunity presents itself—that is, to use serum ACE measurements to assess adherence [13]

Outcomes in heart failure can be improved with a clinical pharmacist as a member of the multidisciplinary heart failure team. This observation may be due to higher doses of angiotensin-converting enzyme inhibitors and/or closer follow-up [14].

A pharmacist intervention for outpatients with heart failure can improve adherence to cardiovascular medications and decrease health care use and costs, but the benefit probably requires constant intervention because the effect dissipates when the intervention ceases [15]

The aim of the retrospective study was to evaluate the rational use of ACE inhibitors in congestive heart failure.

MATERIAL AND METHODS:

A hospital based retrospective study was carried out in services institute of medical sciences and Punjab institute of cardiology Lahore. The data was collected from 21/7/10 to 21/9/10. A group of 40 patients was observed. Patients observed were suffering from congestive heart failure and are receiving ACE inhibitor therapy, patients under 18yr's age are excluded from the study.

The data collected was analyzed manually and presented in the form of tables and graphs. A questionnaire was designed to take the complete patient complaints, history of patient, diagnosis, risk factors, side effects and compliance. Treatment given to CHF patients was observed. ACE inhibitors given to these patients were observed keenly and its rational use is checked. Data from the questionnaire was analyzed. The result were calculated and presented in form of graphs. The study was approved by Department of Pharmacy, LCWU and respective hospitals.

The data collection form was prepared. Both genders were considered. Complete patient profile was taken. Patient's past and presenting complaints were noted. Detailed medical history was noted. Questions regarding risk factors and side effects were asked. Recommended ACE inhibitors with dose frequency and brand are noted exclusively other medications were also keenly observed. We also made great emphasis on patient's life style modifications.

All the patients were observed keenly. Mainly the labs carried out were ECHO, ECG, chest x-ray, serum electrolytes, blood urea nitrogen, random blood sugar level, liver function test, blood count.

RESULTS:

We surveyed 40 patients admitted in hospitals for 60 days.

Figure 1 shows that more males were affected by congestive heart failure than females as there percentage was 60% and female percentage was 40%

Figure 2 shows most common symptoms of CHF patients which we observed SOB(75%), edema(62.5%),orthopenia(62.5%), PND(57.5%),cough(25%),lack of appetite(25%) and fatigue(27.5%).

Figure 3 shows risk factors leading to congestive heart failure in these patients were family history (50%), hypertension (47.5%), diabetes mellitus (37.5%), smoking (30%), and hyperlipidemia (5%)

Figure 4 shows diseases which were present in combination with CHF of which ischemic heart diseases (50%), hypertension (47.5%), diabetes mellitus (37.5%), myocardial infarction (32.5%) were most common

Figure 5 shows patients having any side effects due to ACE inhibitors therapy 90% patient show no side effects while only 10% shows side effects including mild hypotension and cough sometimesFigure 6 shows compliance of patients. Compliant patient out number with 80% and 20% of patients were noncompliant.

Figure 7 explains the life style modifications acquired by our patients like 80% of patient change diet, 22.5% of them do exercise, 12.5% reduce stress activities and 10% quit smoking.

Figure 8 indicates the most common generics of ACE inhibitors use in these hospitals most commonly lisinopril is used with 60% captopril is used 32.5% and enalapril used in 7.5%.

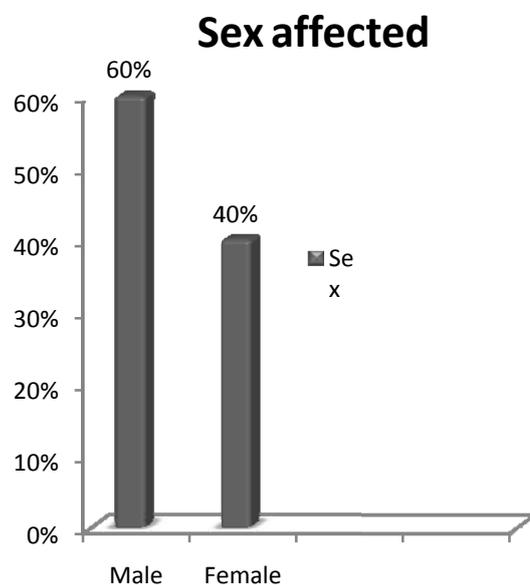


Figure 1 shows % age of sex affect

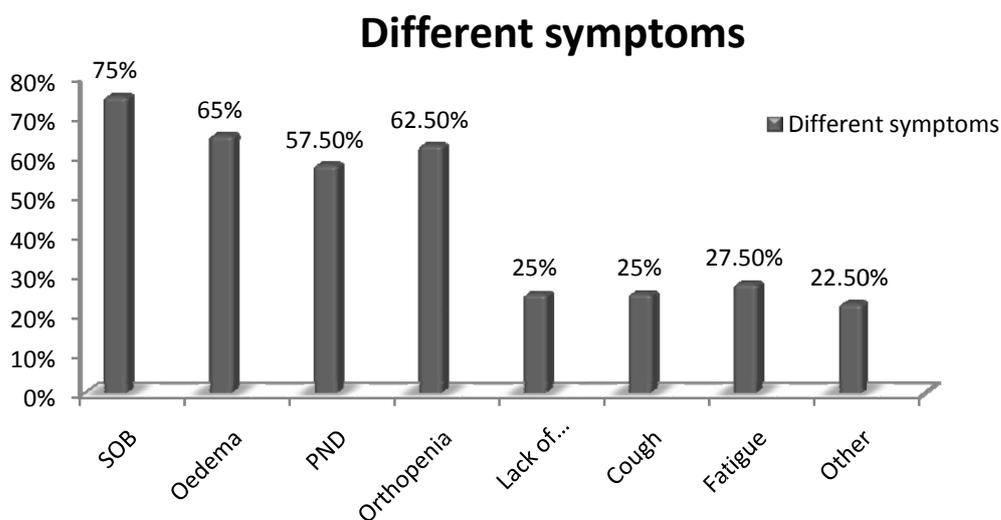


Figure 2 shows %age of different symptoms of patients

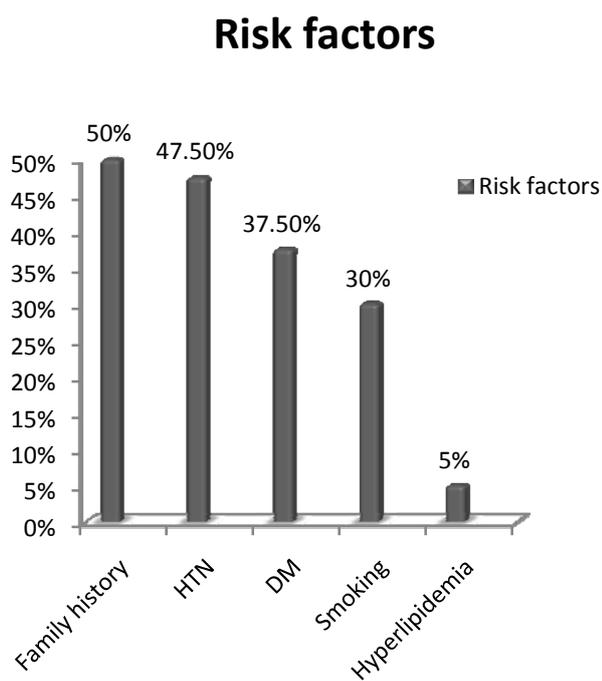


Figure 3 shows %age of different risk factors in CHF patient

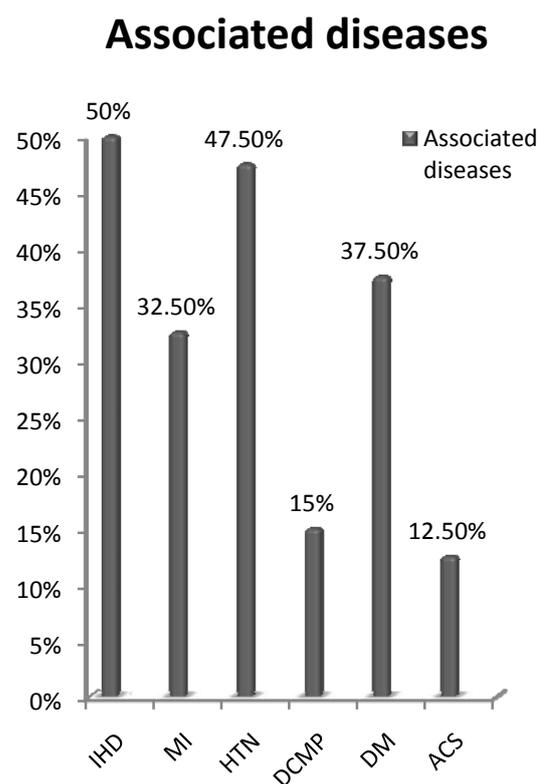


Figure 4 shows %age of associated diseases with CHF

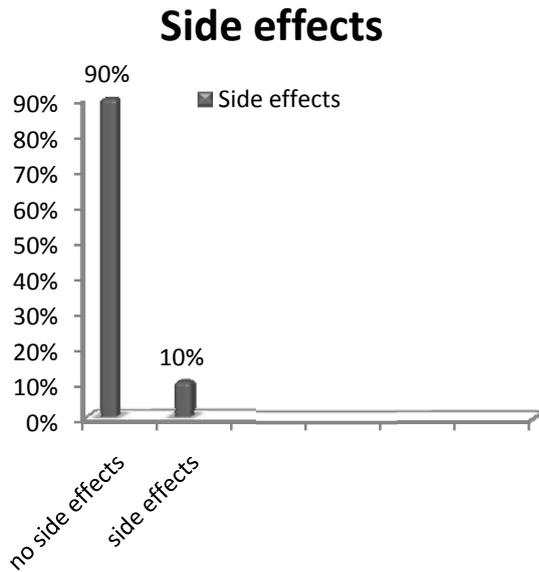


Figure 5 shows %age of patients showing side effects of ACE inhibitors

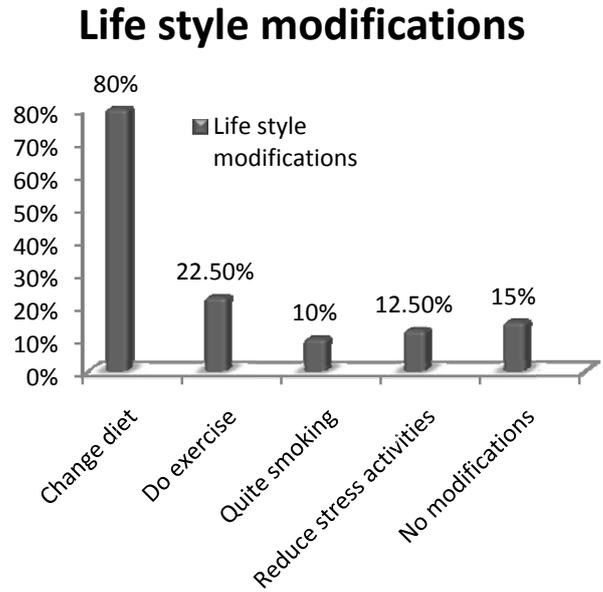


Figure 7 shows %age of pt who change their life style along with drug therapy

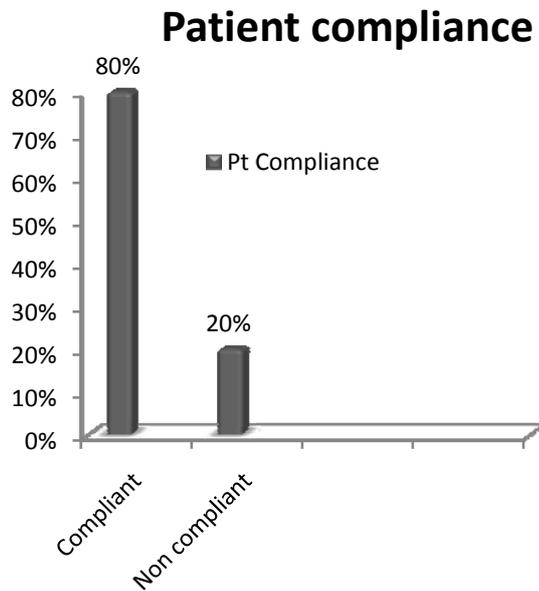


Figure 6 shows %age of pt compliance with Drug therapy

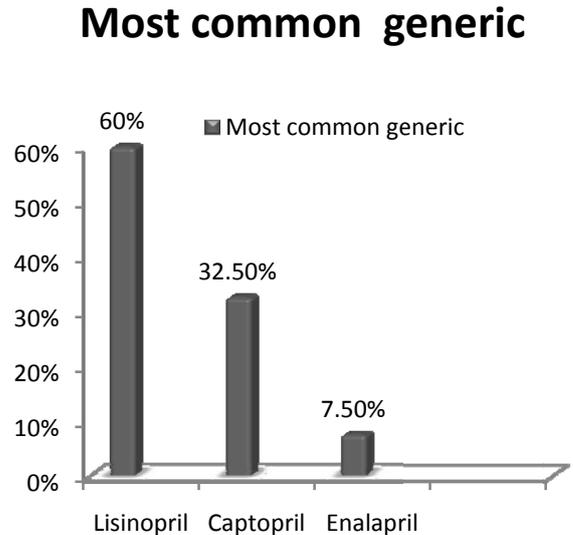


Figure 8 shows the % age of most common generics used

DISCUSSION:

Heart failure is a malignant condition with high rates of morbidity and mortality even in so called mild cases. The most effective medical treatments for heart failure are diuretics,

usually a loop diuretic, and angiotensin converting enzyme inhibitors [16]. Quality of life of heart failure patients is severely impaired. ACE I are used as first line therapy and there monitoring is very much important.

Because they provide relief of symptoms and reduce mortality, angiotensin-converting enzyme (ACE) inhibitors have become a highly recommended part of the pharmacologic treatment of patients with congestive heart failure (CHF) [17]. In our study data of 40 pts who were suffering from CHF and are on ACE I therapy were collected. Mainly male were affected i.e. about 60% patients were male as heart diseases are prevailing more in man than women. The risk factors associated with this is mainly family history that is about 50% of the pt have family history of cardiac diseases and about 47.5% of the patients were hypertensive. There are many underlying physiological & pathological causes but apparently the most significant is stress in Pakistan especially due to many problems like socio economical reasons & family problems etc. Diabetes is also one of the alarming risk factor about 37.5% of the pt's have DM this can be due to improper diet and HTN as well .30% of the patients were smokers also which serves as a risk for CHF.

More than 50% of the patients were complaining of shortness of breath, edema, PND & orthopenia. Some have cough & lack of appetite also. 90% of the patients suffer no side effects after taking ACE inhibitors. Only 10% of the patients have side effects like mild hypotension at the start of therapy which can be cope up with dose adjustment & some have occasional mild cough or hyperkalemia very rarely CHF rarely occurs alone mostly patients were having other associated diseases in which IHD is the most common one and HTN ranks second highest while about 32.5% patients were suffering from MI. These diseases can also act like precipitating factors.

80% of the patient show compliance and 20% were non compliant. Non-compliance was due to many reason some pt hesitate to take drug due to poly pharmacy some forget to take medicine & few patient do not take drug regularly due to socio economic factors .In addition to treatment therapy life style modifications is also very necessary so 80% of the patients change there diet i.e. restrict salt and fatty food. 22.5% of the pt do exercise and only 10% of the pt quit smoking & 12.5% of the

patients reduce there stress activities. The most commonly ACE I use were lisinopril & captopril with 60% & 32.5% respectively while enalapril was used only in 7.5% patients so the improvement in outcome in heart failure is a class effect of ACE inhibitors .

Dose of ACE II is affected by many factors it usually starts from low dose in close monitoring so as to prevent sudden hypotension which is a major side effect & after close monitoring if the patient condition is stable then its dose is increases gradually. Dose is also affected by change in urea creatinine level if these variables are high then dose should be low. Serum electrolytes also play a major role in managing ACE I dose. BMI should also considered while dose management. Captopril is short acting so its dose is high while lisinopril and enalapril are long acting so they are given in low dose as compare to captopril.

CONCLUSION:

Congestive heart failure (CHF) is an imbalance in pump function in which the heart fails to adequately maintain the circulation of blood. CHF is the end result of many heart diseases it is the common cause of hospitalizations. In my study we concluded that ACE INHIBITORS are widely used in preventing heart failure. They are integral part of CHF patient's prescription. They reduce hospitalization, improve symptoms & prognosis. ACE inhibitors are being used rationally in the hospitals we visited. The most commonly used ACE I in these hospitals are Lisinopril, captopril and enalapril. The therapy is started under close supervision. Initially low doses are given so as to prevent sudden hypotension then the dose is titrated slowly according to patient condition to achieve maintenance dose. Most of the patients have no major side effects but some suffer from cough & few were suffering from sudden hypotension at initial dose. Serum electrolyte, creatinine levels and blood pressure are monitored while initiating the therapy. These levels were not monitored regularly after the patient discharged, which should be monitored. Patients are recommended to take low salt & low fat diet.

Pharmacist role is very much important in monitoring ACE I therapy in CHF patients. There was no clinical pharmacist in these hospitals. Pharmacist should be there as a part of heart health care team so that ACE inhibitors use become rational and best therapeutic outcomes can be achieved.

ACKNOWLEDGMENTS:

The authors are very grateful to Dr. Bushra Mateen, Vice Chancellor, Lahore College for Women University Lahore, for her support and concern for our pharmacy department. Deepest gratitude to Dr. Hafeez, Head of Pharmacy Department, Lahore College for Women University for his support to this work. Special thanks to Dr Asma of services hospital for her guidance.

REFERENCES:

- [1]. Jay. N. Cohn “The Management of Chronic Heart Failure” *N Engl J Med* 1996; 335:490-498.
- [2]. Wheeldon NM, MacDonald TM, Flucker CJ et al. “Echocardiography in chronic heart failure in the community” *Quarterly Journal of Medicine* 1993 86: 287-9.
- [3]. Francis GS, Tang WH. “Pathophysiology of congestive heart failure” *Rev Cardiovasc Med.* 2003; 4(suppl 2):S14-S20
- [4]. Gautam V. Ramani, Patricia A. Uber, Mandeep R. Mehra, “Chronic Heart Failure: Contemporary Diagnosis and Management” *Mayo Clinic Proceedings* 2010 vol. 85 no. 2 180-195
- [5]. Nadia Giannetti “Management of congestive heart failure: How well are we doing?” *CMAJ* • 2001; 165 (3)
- [6]. Kantner TR “ACE inhibitors in Congestive Heart failure” *J Fam Pract* 1992; 35(3):305-14.
- [7]. Halawa B “Pharmacologic treatment of chronic congestive heart failure” *Przegl Lek* 1996; 53(3):119-23
- [8]. Opie LH “Fundamental role of angiotensin-converting enzyme inhibitors in the management of congestive heart failure” *Am J Cardiol.* 1995; 75(18):3F-6F
- [9]. Riegger A.J.G “ACE Inhibitors in Congestive Heart Failure” *Cardiology* 1989; 76 (Suppl. 2):42-49 (DOI: 10.1159/000174558)
- [10]. José López-Sendón, John McMurray et al “angiotensin converting enzyme inhibitors in cardiovascular disease” *Eur Heart J* (2004) 25 (16): 1454-1470.
- [11]. Opie LH “Fundamental role of angiotensin-converting enzyme inhibitors in the management of congestive heart failure” *Am J Cardiol.* 1995; 75(18):3F-6F
- [12]. Quinn, Beverly MSN, RN “Pharmacological Treatment of Heart Failure” 2007 - Volume 30 - Issue 4 - p 299–306 doi: 10.1097/01.CNQ.0000290363.57677.98
- [13]. MacFadyena R J, Fraser C G, Struthersb A D “Intermittent non-adherence with ACE inhibitor treatment and its implications for clinical trials results” *Heart* 2001; 85:213-214 doi:10.1136/heart.85.2.213
- [14]. Wendy A. Gattis,; David J. Whellan, ; Christopher M. O'Connor “Reduction in Heart Failure Events by the Addition of a Clinical Pharmacist to the Heart Failure Management Team” *Arch Intern Med.* 1999;159:1939-1945
- [15]. Michael D. Murray, James Young, Shawn Hoke,; Wanzhu Tu, et al “Pharmacist Intervention to Improve Medication Adherence in Heart Failure” *Ann Intern Med.* 2007 vol. 146 no. 10 714-725
- [16]. Dargie H J, McMurray J .J .V “Diagnosis and management of heart failure” *BMJ* 1994; 308: 321
- [17]. Edward F. Philbin, Costa Andreou, Thomas A. Rocco, Laura J. Lynch, et al. *American Journal of Cardiology* Volume 77, Issue 10 , Pages 832-838, 15; 1996