Introduction

Heart Failure (HF) has been declared as a new epidemic [1]. The worldwide prevalence and incidence rates of HF are approaching epidemic proportions, as evidenced by the relentless increase in the number of HF hospitalizations, the growing number of HF-attributable deaths, and the spiraling costs associated with the care of HF patients. Worldwide, HF affects nearly 23 million people. In the United States, HF affects approximately 4.7 million persons (1.5 to 2 percent of the total population), with approximately 550,000 incident cases of HF diagnosed annually [2]. Estimates of the prevalence of symptomatic HF in the general European population are similar to those in the United States and range from 0.4 to 2 percent [3]. The prevalence of HF follows an exponential pattern, rising with age, and affects 6 to 10 percent of people older than 65 years. Data from the Framingham Heart Study have suggested that the overall incidence of HF has declined among women but not among men [4]. In North America and Europe, the lifetime risk of developing HF is approximately 1 in 5 for a 40-year-old. The overall prevalence of HF is thought to be increasing, in part because our current therapies of cardiac disorders, such as myocardial infarction, valvular heart disease, and arrhythmias, are allowing patients to survive longer. Little is known with respect to the prevalence or risk of developing HF in Pakistan because of the lack of population-based studies. The situation in other under-developed countries and developing countries are the same [5]. It is the leading cause of morbidity and mortality in patients over the age of 65 years [6]. The overall mortality rate remains higher than for many cancers, including those involving the bladder, breast, uterus and prostate. The five year survival is about 50% [7]. In the Framingham Study, the median survival was 1.7 years for men and 3.2 years for women, with only 25 percent of men and 38 percent of women surviving 5 years [2]. European studies have confirmed a similarly poor long-term prognosis [3]. In the United States alone approximately 260,000 patients die of heart failure each year [4]. Age is one of the strongest and most consistent predictors of adverse outcome in HF [8]. The role of gender and HF prognosis remains a controversial issue with respect to HF outcomes. Nonetheless, the aggregate data suggest that women with HF have a better overall prognosis than men [8]. It is extraordinarily difficult to determine which prognostic variable is most important in predicting an individual patient's outcome in clinical trials or, more importantly, during the daily management of an individual patient. The goals of the treatment are to stabilize the patient, improve cardiac output and tissue perfusion, to minimize symptoms and delay progression of the disease.

Cardiac glycosides (digoxin) are used to improve cardiac contractility [9]. Diuretics are used to improve the congestive symptoms [10]. To counter the neurohormonal activation angiotensin-converting enzyme inhibitors are of paramount importance in the management of congestive heart failure [11]. To counter sympathetic stimulation, beta blockers therapy has been shown to benefit patients in heart failure [12]. Addition of beta blockers to treatment regimen improves the time to all-cause mortality and cardiovascular hospital admission in heart failure patients [13]. Over all angiotensin-converting enzyme inhibitors and beta blockers has resulted in significant improvement in the management of heart failure patients [14]. Still there is increased risk of sudden cardiac death (due to arrhythmias) in patients with congestive heart failure [15]. Atrial fibrillation occurs in 15 to 30 percent of patients with HF, and is a frequent cause of cardiac decompensation. A variety of arrhythmias, especially frequently ventricular extra systoles [16], ventricular tachycardia [17], left
bundle branch block [18], and atrial fibrillation [19], have been shown to be predictors of mortality and sudden death. Most anti arrhythmic agents, with the exception of amiodarone and dofetilide, have negative inotropic effects and are proarrhythmic. Amiodarone is a class III anti arrhythmic that has little or no negative inotropic and/or proarrhythmic effects and is effective against most supra ventricular arrhythmias. Patients have shown improved survival in diluted cardiomyopathies when they were put on amiodarone and those who were on intra cardiac defibrillators received few shocks when remain on amiodarone [20]. One year mortality after admission is still 25% [21]. In Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) implantable cardioverter defibrillators significantly reduced mortality as compared to amiodarone [22]. We conducted this study to see whether we will be able to affect mortality with amiodarone in our setup compared to placebo.

Material and Methods

Heart failure patients came to the Cardiology Department Hayat Abad Medical Complex Peshawar through OPD or casualty, having functional class II and III on history and physical examination and ejection fraction of 35% or less on echocardiography were selected. After explaining the purpose of study, patients meet the inclusion criteria were randomly divided into two groups (group A and group B). Demographic characteristics were recorded. Group A was put on conventional therapy and placebo (folic acid 5 mg) while Group B on conventional therapy and Amiodarone. The dose of Amiodarone was based on weight. Oral loading dose of 800 mg daily was given for one week and 400 mg daily for three weeks. Patients weighed more than 90.9 kg were receive 400 mg daily, patients weighed 68.2 to 90.9 kg were receive 300 mg daily, and patients less than 68.2 kg were receive 200 mg daily.

Statistical analysis

Statistical analysis was performed on SPSS 22. Chi square and T test applied for statistical analysis. Kaplan Mayer survival curve applied to see the mortality difference between the two groups.

Results

Total of 200 patients were studied, they were divided into two groups. Group A “Placebo” , Group B “Amiodarone”. The base line characteristics are presented in table 1. There was no significant difference between the two groups. Kaplan Mayer survival curve was not significance for mortality between the two groups. The events and survival plots are presented in figure 1A and figure 1B. There 98 patients in group A and 102 patients in group B. Age distribution in group A was 48-80 years, mean 62.81 years. While in group B 45-78 years mean 60.40. There were 54 (54%) and 47 (47%) patients of coronary artery disease in group A and group B respectively. 54 (54%) patients were in NYHA class II and 46 (46%) were in NYHA class III in group A. Where as in group B 55 (55%) patients were in class II and n=45 (45%) patients in class III. Diabetes was found in 36% and 27% in group A and group B respectively.

Association of Pulmonary Disease between Placebo and Amiodarone was n=15 (15%) and n=18 (18%) respectively. 49 patients in group A and 52 patients in group B were hypertensive. Atrial Fibrillation was found in 49 patients in group A and 52 in group B. none sustain Ventricular Tachycardia (VT) was noted in both groups. There were total 12 episodes of VT in group A and 9 episodes in group B.

The mean creatinine in the patients was 1.6 in group A and 1.5 in group B. All patients were on standard medical therapy including angiotensin converting enzyme inhibitors, beta blockers and diuretics. 5% patient in placebo group and 7% in Amiodarone group were on digoxin. At the end of 2 years period, there are 19 deaths in group A patients and 17 deaths in group B patients.

Discussion

Survival is markedly shortened in patients with heart failure, which accounts for a substantial portion of all deaths from cardiovascular diseases. The overall 5 years mortality for all patients with heart failure is approximately 50 percent [17], and one year mortality in patients with end-stage heart failure may be as high as 75% [18]. The major cause of death in these patients is arrhythmia [23]. Amiodarone is known to be

<table>
<thead>
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<th>Baseline characteristics</th>
<th>GROUP A</th>
<th>GROUP B</th>
<th>P value</th>
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<tbody>
<tr>
<td>Male</td>
<td>63</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>35</td>
<td>29</td>
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<td>0.233</td>
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</tr>
<tr>
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<td>1</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>12</td>
<td>09</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Table 1: Presentation of Baseline Characteristics of Group A (Placebo) and Group B (Amiodarone)

Figure 1A and 1B: The events and survival plots
effective in controlling life-threatening arrhythmias [19,24]. There is also evidence that the drug may be effective in reducing cardiac-related and overall mortality in survivors of myocardial infarction [25,26]. Cleland et al. [27] and Chatterjee [28] reported improved survival in patients with heart failure treated with amiodarone, whereas a small, prospective, randomized trial reported by Nicklas et al. [29] found no benefit.

Patients who have an ICD receive fewer shocks if they are treated with Amiodarone compared with conventional therapy [30]. In patients with congestive heart failure, amiodarone therapy improved survival in one study in which heart failure was mainly due to non-ischemic cardiomyopathies, whereas no benefit was observed in another study where heart failure was mainly due to Ischemic cardiomyopathies [31].

In another study, Amiodarone increased the left ventricular ejection fraction by 42 percent at two years [32], confirming the results of previous studies [33]. These data are consistent with the observation that amiodarone may improve the capacity for exercise in patients with heart failure [34]. The observed improvement in systolic function may be related to the drug's property of lengthening the period of repolarization [35].

Despite the fact that amiodarone is effective in suppressing ventricular arrhythmias and improving ventricular function, it did not reduce the incidence of sudden death or prolong survival among patients with heart failure, except for a trend toward reduced mortality among those with non-ischemic cardiomyopathy [32]. However, the finding of other study shows that there is no beneficial effect of amiodarone on survival, despite the use of appropriate dosage and reasonable compliance rate over longer periods [31].

In Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) [22], there was improved survival in patients who are on AICD (mortality was reduced by 23 percent) as compared to those who were on conventional therapy and on amiodarone.

In our study we see that there is no difference in overall mortality among two groups. The two years mortality remains the same. There is no difference in survival among the patients in ischemic and non-ischemic patients in both groups. The mortality remains the same in diabetics and non-diabetics. We do not see any improvement in NYHA functional class on repeated echocardiography in both the groups. When we place our study in relation to those other studies we see that in one study there is a trend toward reduced mortality among those with non-ischemic cardiomyopathy [32]. However no benefit was seen in another, primarily ischemic cardiomyopathy patients.

Conclusion
Heart failure patients die due to pump failure or due to arrhythmias that is VT or VF. Preventing VF in these patients we can save a significant number of patients. Conventionally arrhythmias are treated with drugs, electric cardioversion or radiofrequency ablation. We attempted to show any significant difference in mortality by adding Amiodarone to the convention treatment of heart failure (ACEI, beta blockers, diuretics, and digoxin) in standard doses but there was no statistically significant difference in all causes mortality in both groups.

References


