STUDY ON THE PRESCRIBING PATTERNS OF DRUGS USED IN HEART FAILURE

Mitu Baskota, B. S. Rao, Rajani Shakya

Department of Pharmacy, Kathmandu University, Dhulikhel, Kavre,
P.O. Box: 6250, Kathmandu, Nepal

Corresponding author E-Mail: profsrao@ku.edu.np, pharmacy@ku.edu.np

ABSTRACT

Heart failure is the common cardiovascular diseases among people of south Asian Origin including Nepal. The prevalence of Heart failure increases with age and accounts for most of the adult hospital admissions. The objective of the study was to study the prescribing patterns of drugs used in the heart failure. The study included both the in-patients and outpatients conducted at 2 different hospitals inside the Kathmandu valley and one outside the valley, Dhulikhel. The period of study was nearly four months and the number of patients included was 156, which included total of 71 Males (52.59 %) and 64 Females (47.4%). Subjects of age groups 45-65 (45%) were found to be more susceptible to heart failure. Significant age, smoking & alcohol use, associated disease family history of disease related factors in the prevalence of heart failure were seen. The various drugs used frequently were, Diuretics, Cardiac glycosides, ACE-I, A II Receptor Blockers and Anti-Coagulants with respect to overall utilization. In the combination of drugs, was ACE-I +Diuretics + Digoxin was used most frequently. ACE-I was not appropriately prescribed as per the literature facts that they have various benefits in the treatment of congestive Heart failure and hence was underused. Ramipril, Lisinopril were also considered in the prescriptions in spite of their new entries. ARB, though similar in properties to the ACE accounts for a very small proportion of drug use profile, where high cost and lower availability may be accounted. Beta-blockers were also prescribed extensively.

KEY WORDS: Heart failure or Congestive Heart Failure, Hypertension, Ischemic Heart Disease, Dilated Cardiomyopathy, Valvular Heart Disease, Rheumatic Heart Disease,

INTRODUCTION

Heart failure represents a major public health problem in industrialized nations. It appears to be the only common cardiovascular condition that is increasing in prevalence and incidence. In the United States, heart failure is responsible for almost 1 million hospital admissions and 40,000 deaths annually. In Nepal, it is found to be about 3% in people aged 45 years or more (Kontam, 1994).

Heart failure is a term used to describe the state that develops when the heart cannot maintain an adequate cardiac output or can do so only at the expense of elevated filling pressure (Edwards). It occurs when the heart loses its ability to pump enough blood throughout the body.

Heart Failure is being described as a next epidemic (Roger Walker, 2004). It remains the major public health problem in the industrialized world and is becoming an increasingly

important problem in developing countries (Susan Aldridge, 2003). Heart failure is often a progressive condition and can worsen over time (Timmis Adam).

It is an increasingly important cause of cardiovascular morbidity and mortality and the risk increases dramatically with age. The heart loses some of its pumping ability as a natural consequence of aging. It affects approximately 10 of every 1,000 people over the age of 65 (Rich, 1997). However, a number of other factors contribute to the potentially life threatening loss of pumping activity. Patients with CAD, Hypertension, DM, and exposure to cardio-toxic drugs, alcohol abuse, or a family history of cardio-myopathy are at high risk for HF.

Heart failure can often be successfully treated from medical therapies to heart transplantation. The medical management in clinical practice varies considerably within the medical specialty. Treatment usually requires a program of rest, proper diet, lifestyle modification and one or more of the prescription drugs including ACE-Inhibitors, Beta-blockers, Digitalis, Diuretics and Vasodilators.

Diuretics and angiotensin converting enzyme (ACE) inhibitors, when combined with non-pharmacological measures, remain the basis of treatment in patients with congestive heart failure (Matthew 1997). Digoxin has a possible role in some of these patients, however, and the potential benefits of B-blockers and spironolactone (an aldosterone antagonist) in chronic heart failure are now increasingly recognized.

MATERIALS AND METHOD

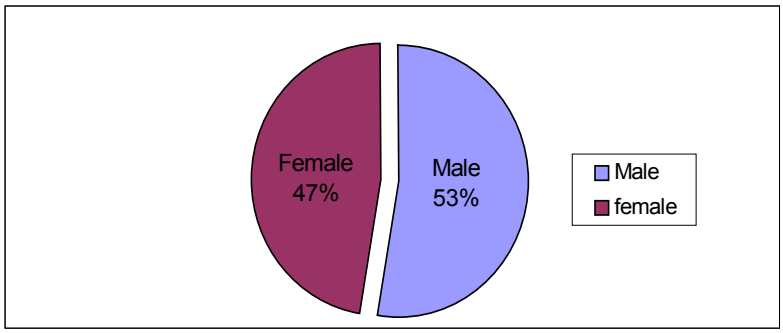
Study design & setting:
A prospective, qualitative and observational study including a total of 135 patients, above 18 years of age, diagnosed of HF were collected from 3 hospitals in Kathmandu and Dhulikhel from the period of Feb 2005 to May 2005. The main objective of the study was to assess the prescribing patterns of drugs used in heart failure, based on the types of disease, number of drugs given and the cost of the drugs used in the therapy and its comparison with respect to three different hospitals.

Selected patients included persons above 18 years of age diagnosed of heart failure and on drug therapy, while persons below the age of 18 and with other medical complications were excluded. The data collection was done by developing a structured questionnaire for interview with the patient and by studying the patient's history records available in the hospital.

Patient's age, sex, smoking and alcohol use status, associated diseases and the hereditary links with the diseases were studied along with the total number and class of drugs prescribed and their cost.

General characteristics of the patients

Fig.1: Sex wise distribution of the subjects



Among the total population of 135 patients, 71 males and 64 females were observed. This showed that the prevalence of men (53%) was found to be higher than females (47%) indicating that men are more prone to heart failure than females. This fact is supported by other studies which says that the risk of developing HF in males is slightly greater than in females Timmis Adam).

Age wise categorization of the patients

Heart Failure progresses with the advancing age. There is a greater prevalence, which increases with the higher age. When categorized age-wise, maximum number of patients (45%) were from the age group 46-65 years, followed by 28% in more than 65 years of age. There were significantly lower number of patients in the younger ages, 8% in the age group 18 – 25 and 19% in the age group 25-45.

The above result is possibly due to the fact that as the age progress, the person become old and weak and there are chances possible reasons for him to get associated diseases. It tends to affect the elderly subjects and often leads to prolonged disability. The condition affects 1% of people of age 50 and about 5% of people of age 75[7]

Risk factors

Heart failure is closely associated with the majority of risk factors. There is an increased risk for the development of the disease in case of alcohol abuse, smoking, overweight / obesity, increased blood sugar and blood cholesterol level, exposure to cardio-toxic drugs and use (abuse) of cocaine. These are also termed as secondary risk factors.

Alcohol-use status of the patients

Alcohol users constitute 9.63% of the population. Although alcohol is one of the risk factors 57.78 % have never taken alcohol. This group mainly consists of females. Although 32.59% used to take earlier but have left now.

Alcohol consumption along with smoking causes decrease in the pumping efficiency of the heart. Though the exact mechanism is not known it is however claimed that excess of alcohol can cause weakening of the heart muscle, which develops to a heart failure. It is suggested that alcohol use reduction is one of the major life style modifications. This has a positive effect in reducing the symptoms in HF. This also suggests that a number of people are following the advice of their cardiologists in reducing their alcohol intake.

Smoking status of the Patients
Smoking is one of risk factors for HF but about 41.5% of the patients are non-smokers. About 46.7% used to smoke but have left after being diagnosed, on advice of the physician. The patients who smoke constitute 11.8%.

Smoking causes decrease in the pumping action of the heart. It contributes to elevated blood pressure due to higher level of thromboxane, a vasoconstrictor, which in turn leads to the development of HF, although no specific data are available. Cessation of smoking is one of the major step in improving the lifestyle is suggested by the international guidelines. Most of the people are towards quitting smoking.

Disease Associated risk for Heart failure
Patients, at a high risk for development of HF symptoms includes; Hypertension (HTN), Diabetes Mellitus (DM), Ischemic heart Diseases (IHD). Others like Valvular Heart Disease (VHD), Rheumatic Heart Disease (RHD), and Family history of cardiac disorders also contribute to the high risk for the occurrence of HF.

Table1: Distribution of Associated Diseases according Sex of Patients

ASSOCIATED DISEASES	MALE	FEMALE
Diabetes mellitus (DM)	4	6
Hypertension (HTN)	12	11
Ischemic Heart Disease (IHD)	18	10
DM + HTN	3	2
DM + IHD	4	5
HTN + IHD	8	3
DM + HTN + IHD	1	2
Others	4	1
NO/ not significant	19	25

In the Tables of major risk factors, the patients with Ischemic heart disease (20.7%) contributed the majority among patients who developed into the heart failure, followed by Hypertension in about 15.5% and Diabetes in 7.4% of the patients. Whereas there were about 32.6% of the patients without any associated diseases as risk factors. Even for patients with combination of the diseases was comparatively less.

Categorisation according to the type of HF (etiology wise)
Heart failure may be final & most severe manifestation of nearly every form of cardiac disease including; coronary artherosclerosis, Myocardial infarction, Valvular heart disease, Hypertension, Congenital heart disease, cardiomyopathies. It refers to a clinical syndrome rather than a specific diagnosis.

Table 2: Distribution according to HF category

Disease	No. of subjects (n)	Percentage (%)
DCM	33	24.44
RHD	39	28.89
IHD	36	26.67
HTN	15	11.11
VHD	12	8.89
TOTAL	135	100.00

The patients diagnosed of HF had progressed from Rheumatic Heart Disease (28.89 %) & Ischemic Heart Disease (26.7%), while some of them from DCM (24.4%) and HTN (11.1%). A very few accounted for valvular heart diseases (8.9%).

Drug use characterisation

Drugs Prescribed
The most commonly prescribed drugs, either alone or in combination of the following classes as per the disease they have been diagnosed of:

Ischemic heart disease

Anticoagulants	:	Aspirin / Clopidogrel / Warfarin
Diuretics	:	Frusemide (lasix) / Spironolactone / Amifru / lasilactone
ACE-I	:	Enalapril / Lisinopril / Ramipril / Captopril
or		
ARB	:	Losartan Potassium/sodium
B-Blockers	:	Atenolol /Carvedilol / Metoprolol
Nitrates	:	Isosorbide di/mono nitrates

Dilated Cardiomyopathy:

Diuretics	:	Frusemide / Spironolactone / amiloride + furosemide
Anti-coagulants	:	Aspirin / Clopidogrel / Warfarin
Cardiac glycosides	:	Digoxin
ACE-I or	:	Enalapril / Ramipril
ARB	:	Losartan Potassium/sodium
B-Blockers	:	Carvedilol / Metoprolol

Hypertension

Diuretics	:	Frusemide / Spironolactone / Amiloride + furosemide
ACE-I	:	Enalapril / Ramipril or ARB: Losartan

Valvular Heart disease

Cardiac glycosides	:	Digoxin
ACE-I	:	Enalapril / Ramipril or Losartan
Diuretics	:	Frusemide / Spironolactone / Amiloride + furosemide
Anti-coagulants	:	Aspirin / Clopidogrel / Warfarin

Rheumatic Heart disease

Diuretics	:	Frusemide / Spironolactone / Amiloride + furosemide
ACE-I	:	Enalapril / Ramipril or Losartan Potassium/sodium
Cardiac glycosides	:	Digoxin
Penicillin:	:	Injection Benzathine Penicillin IM

Among the drugs prescribed as per the disease, I found that Diuretics, ACE- inhibitors are used in all form of disease.

Digoxin is added in case of Dilated cardiomyopathy, Valvular disease and Rheumatic heart disease. Oral anticoagulants, like aspirin is given along with the drugs mentioned above in case of Dilated cardiomyopathy and Ischemic Heart Disease, and also in some cases of valvular heart disease. B-Blockers were added in some cases of Dilated Cardiomyopathy and Ischemic Heart Diseases. Nitrates were also given incase of IHD. Penicillin is given in case of Rheumatic heart disease.

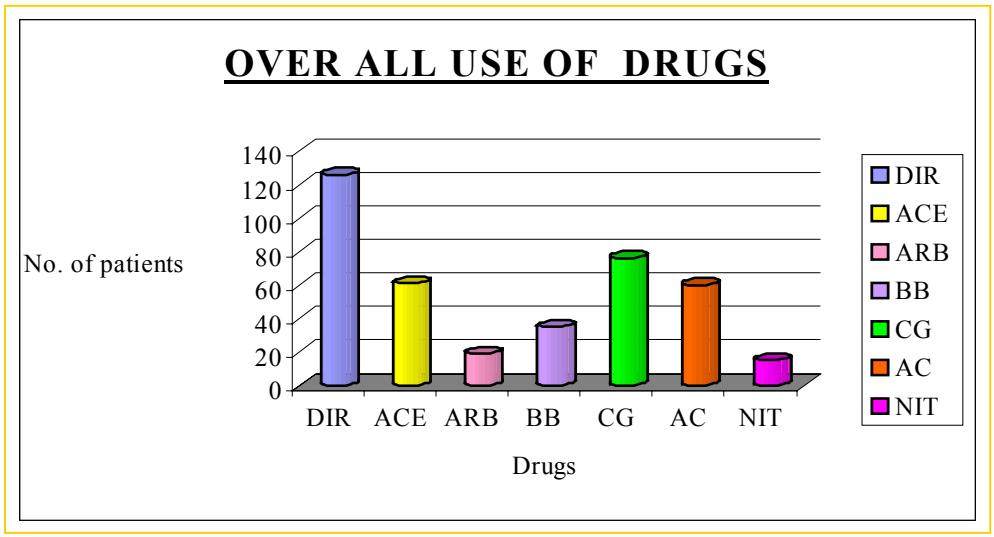
As per the AHCPR (Agency for Health Care Policy and Research) guidelines, for treatment of patients with heart failure, depending upon the severity it is reasonable to start treatment with ACE-I alone in patients who have mild exertional breathlessness without edema. Diuretics may be added if overload is present or symptoms persist.

For more severe symptoms, triple therapy with ACE-I, Diuretics and Digoxin ie cardiac glycosides is recommended. Treatment with an ACE-I significantly reduces the incidence of symptomatic heart failure and incidence of symptomatic heart failure and the rate of associated hospitalization. If congestion still persists, then vasodilators such as hydralazine and Nitrates can also be added

Distribution patterns of overall use of drugs in HF

Among the drugs prescribed according to the class, most commonly used was found to be Diuretics, 32.14%, followed by cardiac glycosides, 19.38%, ACE-I, 15.56%, anticoagulants 15.30% and so on.

Fig2: **Distribution patterns of overall use of drugs in HF**



Use of Individual drugs in HF

Within each class of drugs used, the most commonly prescribed drugs were: Diuretics: Frusemide (16.4%); ACE-I: Enalapril (11.8%); B-blocker: Atenolol (4.04%); Anti-coagulants: Aspirin (12.58%). Among ARB only Losartan (4.48%) was used.

This may also be due to the trends of prescribing patterns in the hospital and may also be due to easy availability and low cost.

Table 3: Use if Individual Drugs in HF

Drugs Class	Individual drugs	No. of subjects (n)
ACE-Inhibitors	Enalapril	53
	Captopril	2
	Ramipril	4
	lisinopril	3
ARB	Losartan	20
B-Blockers	Atenolol	18
	Carvedilol	4
	Metoprolol	13
Cardiac glycoides	Digoxin	77
Diuretics	Frusemide	73
	Spironolcat one	17
	Frusemide+ Spironolact one	17
	Frusemide + Amiloride	46
Oral anticoagulants	Aspirin	57
	Clopidogrel	9
	Warfarin	16
	Heparin	2
Nitrates	Isosorbide mononitrate	10
	isosorbide dinitrate	5

Number of Drugs prescribed in a regimen

In overall observation, drugs were used mostly in mono-therapy as well as combination therapy but it is seen that combination therapy of 3-drug therapy (40.74%) is used the most followed by 4-drug therapy (28.89%) and 2-drug therapy (21.48%).

In overall observation, drugs were used mostly in mono-therapy as well as combination therapy but it is seen that combination therapy of 3-drug therapy (40.74%) is used the most followed by 4-drug therapy (28.89%) and 2-drug therapy (21.48%). Generally the number of drug increases as the severity of the disease increases.

Fig:3 Distribution of number of drugs prescribed in a regimen

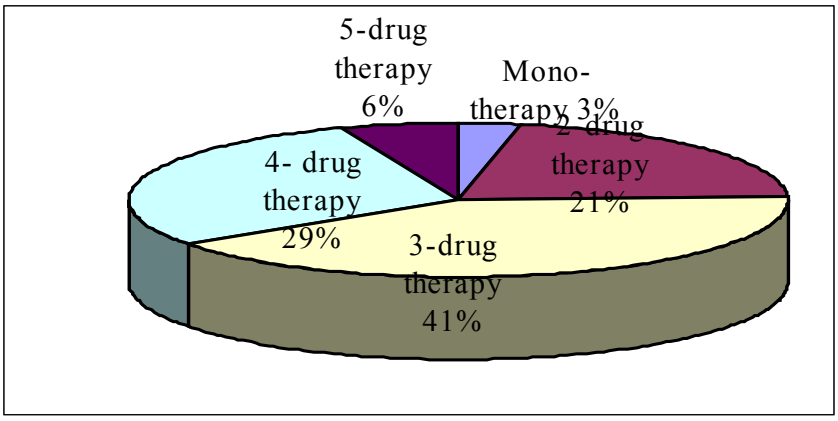


Table 4: Use of Two drug combinations prescribed in a regimen

DRUG COMBINATION	number	%
ACE-I + Diuretics	11	35.48
Diuretics + Digoxin	17	54.84
Diuretics + B-blockers	2	6.45
ACE-I + Digoxin	1	3.23

In this type, the most commonly prescribed drug combination is Diuretics and Digoxin (54.8%), followed by ACE-I and Diuretics with 35.5%. These combinations are usually prescribed in mild cases.

Table 5: Use of Three drug combinations prescribed in a regimen

DRUG COMBINATION	number	%
ACE-I+ DIR + DIG	18	31.58
ACE-I+ DIR + AC	10	17.54
BB + ACE-I + DIR	2	3.51
BB + AC + DIR	2	3.51
DIR + DIG + AC	17	29.82
DIR + BB + AC	4	7.02
ACE-I+ BB + NIT	2	3.51
ACE-I + BB + CG	2	3.51

As the most prescribed drugs combination, we have ACE-I + Diuretics + Digoxin prescribed in higher proportion (31.57%), followed by Diuretics + Digoxin +anticoagulants with 29.8%. This also concludes that the prescribing physicians have followed the AHCPR guidelines.

Table 6: Use of Four drug combinations prescribed in a regimen

DRUG COMBINATION	number	%
ACE-I + DIR + DIG + AC	14	35.0
BB + ACE-I + DIR + AC	6	15.0
ACE-I + DIR + DIG + NIT	3	7.5
ACE-I + DIR + AC + NIT	7	17.5
BB + ACE-I + DIR + CG	6	15.0
NIT + BB + AC + DIR	4	10.0

This is one of the most commonly prescribed combination and ACE-I, Diuretics, Digoxin and Anticoagulants (35%) combination was most widely used, followed by ACE-I+ Diuretics + Anticoagulants + Nitrates (17.5%). In all the combinations, Ace-I and Diuretics were used.

Table 7: Use of Five drug combinations prescribed in a regimen

DRUG COMBINATION	number	%
ACE-I + DIR + DIG + AC + BB	4	66.67
ACE-I + DIR + DIG + AC + NIT	1	16.67
ACE-I + DIR + BB + AC + NIT	2	33.33

Generally this combination is used to include almost all types of drug with different actions. From the tables & graphs, it was found that, among the five drug regimen, the combination of ACE-I, Diuretics, Digoxin, Anticoagulants & B-blockers were prescribed more than the other two.

Cost analysis

Cost of different drugs used in the prescription was collected in different hospitals, obtained from their own pharmacy. This study was carried out just to compare the differences in the cost of drug (in rupees per tablet) that the patients have to pay in different hospitals for their therapy.

1. There is not much variation in the price of the same drugs in different hospitals. But to certain extent SGNHC is near to the average while MNH and DH represents for the higher side and lower side
2. In SGNHC and MNH, there is a trend of prescribing the drugs in their brand name which results in the variations in their costs. DH follows prescribing the drugs in the generic name which results in not much variation in the cost of the drugs and hence, is available at a cost somewhat cheaper than the other two hospitals.

Conclusion

Heart Failure is caused due to various underlying diseases among which, Rheumatic Heart Disease and Ischemic Heart Diseases are most common followed by Dilated Cardiomyopathy, Hypertension and a few caused by Valvular Heart Disease.

A combination therapy proves to be more effective than a single drug. A combination of up to 5 drugs is in practice, the most common being Three-drug and Four-drug therapy.

Among the class of drugs prescribed, Diuretics occupy a large proportion, followed by Cardiac glycosides, ACE-Inhibitors and anti-coagulants. Digoxin is the most common individual drugs prescribed, followed by Frusemide, Aspirin and Enalapril. All these are cheaper causing fairly less economic burden to the patient Penicillin has been used in combination with other drugs in most of the RHD cases. CCB, are used for patients with HTN and Lipid Lowering Drugs like Atorvastatin is given in IHD as well as DCM cases.

Newer drugs like, Ramipril, Lisinopril (ACE) and Losartan (ARB) are coming at rapid pace and are used as equally and as effectively as Enalapril. Amiodarone is also coming up for HF due to arrhythmic cases.

Recommendation

In order to achieve the appropriate goal of treatment, it is necessary for discouraging complex treatment with the minimum cost so that more people can benefit to overcome. In the treatment of HF, life style modification and prevention of precipitating factors should be encouraged along with the medications prescribed Awareness of the disease and treatment is equally important.

Acknowledgement

The help and support of Dr. Bhagwan Koirala, Executive Director, Shahid Gangalal national Heart center, Dr. Man Bahadur KC, Head of Department, Department of Cardiology, Dr. Abanibhusan Upadyaya, Consultant Cardiologist, Dr. Denis Shrestha MD and Dr. Rajendra Koju, M.D. Department of cardiology & clinical co-ordinator of Dhulikhel is gratefully acknowledged.

REFERENCES

1. Kontam MA., Dracup K., Baker DW et al., 1994. Heart failure: Evaluation and Care of Patients with Left ventricular Failure, Agency for Health Care Policy & Research, US. Clinical practice guidelines, 11 (AHCPR), 94-0612.

2. Edwards CRW., Bonchier IAD., Haslet C., Chilvers ER., 2000. Davidson's Principles and Practices of Medicines.

3. Walker R., Edwards C., 2004. Clinical Pharmacy and Therapeutics.

4. Aldridge S., 2003. Heart Failure in South Asian People. British Medical Journal.

5. Timmis Adam D., Anthony W., Nathan., 1995. Essential Cardiology.

6. Rich MW., 1997. Epidemiology, Pathophysiology and Etiology of Congestive Heart Failure in older adults. J Am Geriatre, Soc, 45, 968-974.

7. Matthew J., Sorrentino., 1997. Drug therapy for Congestive Heart Failure- Appropriate choices can prolong life. Postgraduate Medicine, 101, 1.