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Research Article

Drug Utilization Study in Congestive Heart Failure at a Tertiary Care Hospital

Prasanna Kumar B. Jewargi[1], Ravi D. Mala[2]*
[1]Department of Pharmacology, Mahadevappa Rampure Medical College, Gulbarga-585103, India
[2]Department of Pharmacology, ESIC Medical College, Gulbarga-585106, India

***Corresponding author**
Ravi D. Mala
Email: ssneyar@rediffmail.com

Abstract: The incidence and prevalence of Congestive heart failure (CHF) is increasing. Several large clinical trials have found that pharmacological therapy results in decrease in mortality and morbidity. Despite the advances in drug therapy the morbidity and mortality of heart failure continues to remain high. Education of healthcare professionals on evidence based therapy plays an important role in successful heart failure programme. For a developing country like India, 70% of the population resides in rural areas, a national drug policy is needed for rational drug use. To achieve this, pattern of usage and monitoring drug use profile over a period of time is important. There are very few studies available pertaining to drug utilization in heart failure. Hence the present study. The study was conducted in a tertiary care hospital in South India May 2011 to August 2012. Detailed history, chief complaints, physical signs & symptoms and investigations were recorded. During this period 100 prescriptions were collected. The data was analyzed using SPPS software. Almost all the patients received Diuretics either by oral or parenteral route. Majority of the patients were treated with ACE inhibitors or ARBs. Initial therapy was with diuretics in most of the cases and ACE inhibitors in few, further modified in some cases based on the response and later on β blockers and other drugs were added. A wide range of drugs were used in our study, the frequently used once were Diuretics, ACE inhibitors, angiotensin receptor blockers, Bronchodilators and Hypolipidemic agents. It was observed that daily defined dose (DDD) value was highest for Furosemide (1.130) and then was with ramipril (0.791), the least DDD was with Metoprolol (0.015). The use of Pharmacoepidemiological data can aid the design, delivery & evaluation of interventions to improve the use of drugs in CHF patients & health outcomes of the patients.
Keywords: Congestive heart failure, Pharmacoepidemiology, Drug utilization, Furosemide.

INTRODUCTION

The incidence and prevalence of Congestive heart failure (CHF) is increasing. Several large clinical trials have found that pharmacological therapy results in decrease in mortality and morbidity. Despite the advances in drug therapy the morbidity and mortality of heart failure continues to remain high. Education of healthcare professionals on evidence based therapy plays an important role in successful heart failure programme [1].

In India CHF affects younger age group but in western countries it's a predominantly a disease of elderly. The important risk factors include hypertension, coronary artery disease, diabetes mellitus, valvular heart disease, cardiotoxic drugs, and obesity [1-3]. In India coronary artery disease, hypertension, valvular heart diseases, diabetes mellitus and muscle diseases are the common causes for heart failure. Another common cause of heart failure in India is Rheumatic heart disease [1].

In India, there is lack of data regarding the incidence prevalence of heart failure. With higher tendeny for cardiovascular diseases and ageing population, the mortality and morbidity of CHF is likely to be higher when comparing to the western population. Therefore, there is an urgent need to have a documentation of heart failure cases at the secondary, tertiary and national level. These will help in providing us the information related to heart failure, prevalence, incidence, causes and help in adopting various management strategies [1].

For a developing country like India, 70% of the population resides in rural areas; a national drug policy is needed for rational drug use. To achieve this, pattern of usage and monitoring drug use profile over a period of time is important [4]. There are very few studies available pertaining to drug utilization in heart failure.

According to WHO, drug utilization has been defined as the marketing, distribution, prescription and use of drugs in a society with a special emphasis on the

resulting medical, social and economical consequences [5]. The present study attempts to describe the drug utilization pattern in patients of congestive heart failure in a tertiary care hospital.

MATERIALS AND METHODS

The study was conducted in a tertiary care hospital in South India May 2011 to August 2012. The study was conducted after obtaining the permission from the ethical committee of our institution. Detailed history, chief complaints, physical signs & symptoms and investigations were recorded. The prescriptions were noted down. Then the patients were followed for adverse effects and prognosis until discharge or death. During this period 100 prescriptions were collected. The prescriptions were collected from the day of admission to the day of discharge or death. For calculating the length of stay day of admission was included and day of discharge was excluded. The data was analyzed using SPPS software (version 16).

RESULTS

The majority of the study subjects (56**%**) were male patients (Table-1).

Maximum numbers of cases were from 61-70 years (Table-2).

Table 1: Gender distribution of study subjects

Gender	Number of patients	%
Male	56	56
Female	44	44
Total	100	100

Table 2: Age wise distribution of patients

Age in years	No. of Patients	Percentage
01-10	2	2
11-20	3	3
21-30	7	7
31-40	6	6
41-50	16	16
51-60	23	23
61-70	24	24
71-80	14	14
81-90	5	5
>91	0	0

Table 3: Different Drugs used in patients

Name of Drug		No. of patients	Percentage
ACE inhibitors and angiotensin receptor blockers	Ramipril	51	51
	Enalapril	3	3
	Losartan	10	10
	Telmisartan	5	5
Diuretics	Furosemide	91	91
	Spironolactone	17	17
	Torasemide	25	25
	Hydrochlorothiazide	8	8
Beta Blockers	Metoprolol	7	7
	Carvedilol	33	33
Calcium channel blockers	Amlodipine	5	5
	Nifedipine	1	1
Hypolipidemics	Atorvastatin	47	47
	Rosuvastatin	7	7
Bronchodilators	Salbutamol	6	6
	Ipratropium bromide	31	31
	Ipratropium bromide & levosalbutamol	15	15
	Budesonide	15	15
	Deriphylline	6	6
Proton pump inhibitors	Pantoprazole	49	49
	Omeprazole	16	16
	Rabeprazole	8	8

H_2 Blocker	Ranitidine	1	1
Inotropic agents	Digoxin Dopamine Dobutamine	27 10 24	27 10 24
Antiplatelet Agents	Aspirin Clopidogrel	45 46	45 46
Antiarrhythmic drugs	Amiodarone	6	6
Antianginal drug	Ranolazine	1	1
Potassium Channel Opener	Nicorandil	1	1
Thrombolytic Agent	Streptokinase	1	1
Anticoagulants	Low molecular weight heparin	13	13
Hypoglycemics	Insulin	2	2
Antimicrobials	Antimicrobials	98	98
Oxygen	Oxygen	32	32
Benzodiazepines	Alprazolam	12	12
Tricyclic Antidepressants	Amitriptyline	1	1
Anti Emetics	Domperidone	3	3
	Ondansetron	10	10
NSAID	Paracetamol	8	8
Nutritional Supplements	Nutritional Supplements	10	10
Others	others	11	11

DRUG USE INDICATORS

Prescribing indicators

- Average number of drugs per encounter – 7.71
- Percentage of drugs prescribed by generic name – 8.71
- Percentage of encounters with an antibiotic prescribed – 12.71
- Percentage of encounters with an injection prescribed – 40.20
- Percentage of drugs prescribed from essential drugs list or formulary – 72.24

Patient care indicators

- Average consultation time – 11.94 min
- Average dispensing time – 18.15 sec
- Percentage of drugs actually dispensed – 96.23
- Patient's knowledge of correct dosage – 46 %

Facility indicators

- Availability of copy of essential drug list or formulary – Yes
- Availability of key drugs – 96 %

Complementary indicators

- Without drugs – 0
- Average drug cost (Rs) / Prescription – Rs.473.63
- Drug cost on injections / Prescription – Rs.407.62

DDD was calculated for the following drugs and was found to be as follows.

It was calculated as follows:

$$\text{DDD/100 bed days} = \frac{\text{Drug consumption in the study period X 100}}{\text{DDD X period of study X Bed Strength X Average Occupancy}}$$

Table 4: DDD of different drugs used in the study

Drug	ATC Code	Percentage of Drugs Prescribed	WHO DDD	DDD/100 bed days
Metoprolol	C07AB02	0.90	0.15g	0.015
Carvedilol	C07AG02	4.28	37.5mg	0.070
Furosemide	C03CA01	11.80	40mg	1.130
Torasemide	C03CA04	3.24	15mg	0.310
Spironolactone	C03DA01	2.20	75mg	0.057
Hydrochlorothiazide	C03AA03	1.03	25mg	0.030
Ramipril	C09AA05	6.61	2.5mg	0.791
Enalapril	C09AA02	0.38	10mg	0.022
Digoxin	C01AA05	3.50	0.25mg	0.251
Losartan	C09CA01	1.29	50mg	0.095
Telmisartan	C09CA07	0.64	40mg	0.037

DDD value was highest for Furosemide (1.130) and then was with ramipril (0.791), the least DDD was with Metoprolol (0.015).

DISCUSSION

A total 771 drugs were prescribed for 100 patients who are included in the study, of which 394 drugs were given by oral route, 310 drugs were given by parenteral route, and 67 drugs were given by inhalational route. 12% of patients received Alprazolam. Numerous clinical trials demonstrate that alprazolam is effective in the treatment of generalized anxiety. The usual stating dosage range is 0.75-1.5mg/day in divided doses [6]. 54% of patients received ACE inhibitors, of which 51% patients received ramipril and 3% of the patients received Enalapril.

The drugs that are most effective are the drugs which cause both venous and arterial dilatation most forms of heart failure have elevated preload and after load. The ACEI have effect on both preload and after load. In addition they cause a rise in bradykinin levels which result in the nitric oxide release and other important endogenous vasodilators [7]. Various prospective randomized placebo-controlled trials, particularly CONSENSUS I, V-HEFT II and SOLVD have shown improvement in symptoms and mortality in patients with mild to severe heart failure [8-10].

51% of the patients received ARBs, out of them 10% patients received Losartan and 5% patients received Telmisartan. The ARBs act at the angiotensisn II receptor level blocking the downstream effects of angiotensin II. ARBs can be used in treatment of heart failure instead of ACEI [11-13]. Added advantage of ARBs is they do not produce the brassy cough seen with the ACEI.

Diuretics were given to patients and Furosemide was the most commonly prescribed diuretic 91% of patients received Furosemide, 17% of patients received spironolactone, 25% of patients received Torsemide and 8% of patients received Hydrochlorothiazide. Diuretics remain the first line of treatment of edema or volume overload particularly in patients of CHF. Diuretics reduce pulmonary edema and venous congestion, and in some cases it may be the only drug needed in management of mild heart failure [14].

40% of the patients received Beta Blockers, of which 7% patients received Metoprolol & 33% received Carvedilol. The beneficial role of β- blockers in the treatment of heart failure is well established. Agents commonly used in clinical practice are sustained release metoprolol, bisoprolol, carvedilol, and nebivolol. Multiple large scale randomized placebo-controlled studies class II-IV heart failure patients like MERIT-HF, COPERNICUS, CIBIS and COMET trials have shown to reduce the mortality and morbidity [15-18].

The β-blockers were used in follow up patients, who are stabilized and not the newly diagnosed cases. β-blockers were started in low doses and then the gradually the dose was increased. 54% of patients were prescribed Hypolipidemic agents, 47% of them received Atorvastatin and 7% of them received Rosuvastatin.

Another major risk factor for CHF is atherosclerosis. Lipid lowering strategies alter plaque architecture, resulting in fewer macrophages and a larger collagen and smooth muscle cell – rich fibrous cap. Statins exert their major effects by lowering LDL-C and improving the lipid profile as [19], a variety of potentially cardioprotective effects are being ascribed to these drugs [20]. Statins are used mainly in patients who are affected by other co morbid conditions like myocardial infarction.

A total 73% of patients were prescribed bronchodilators, 6% of them received Salbutamol, 31% of them received Ipratropium bromide, 15% of them received a combination of Ipratropium bromide & Levosalbutamol, 15% of them received Budesonide, all these drugs were given to these patients by inhalational route and 6% of patients received Deriphylline.

A total of 73% of patients received Proton pump inhibitors (PPI), 49% of them received Pantoprazole, 16% of them received Omeprazole and 8% of patients received Rabeprzole. Most of these patients received these drugs by parenteral route. Out of 100 patients 1 patient received Ranitidine and was given by parenteral route. PPI and H2 blockers mainly help in reducing the gastric acid secretion and were mainly used in these patients to relieve the symptoms of gastritis and also to prevent gastritis.

Digoxin was prescribed to a total of 27% of patients. The Digitalis investigation Group, trial showed a decrease in the risk of death attributed to worsening of heart failure in the digoxin treated group compared to placebo in patients with mild to moderate heart failure. Greatest increase in contractility is apparent at serum levels of digoxin around 1.4 ng/ml [21]. The doses used in our study were sufficient to achieve the above mentioned serum levels. The randomized trials RADIANCE and the DIG trial showed significant reduction in hospitalizations for worsening heart failure but no reduction in mortality [22, 23].

Two inotropic agents were used Dopamine & Dobutamine, 10% of patients received Dopamine, 24% of patients received Dobutamine. Dopamine and Dobutamine are the positive inotropic agents most are used for the short term for support of circulation. So, these drugs are used in acute heart failure only.

Although Inotropic agents temporarily stabilize the haemodynamic status, their long term use is associated with increased mortality [2, 24].

Anti-platelet agent clopidogrel was prescribed for 46% of study subjects & aspirin in a dose of 75-325mg/day for its antiplatelet effect was prescribed for 45% of patients. Most of the patients in whom these two drugs were prescribed had an previous or present attack of MI and were on antiplatelet therapy. The CAPRIE trial has shown that clopidogrel 75 mg daily for 3 years post MI is superior to 325mg/day of Aspirin, in terms of reduction in the rate of subsequent atherothrombotic events [25].

13% of the patients received low molecular weight (LMW) heparin subcutaneously. LMW Heparin has been shown to be effective in the treatment of venous thrombosis, pulmonary embolism and unstable angina [26]. Although expensive, the cost- benefit ratio of LMW is acceptable. LMWs were mainly used in those patients who had a prior attack of acute myocardial infarction.

98% of patients received antimicrobial agents. Most commonly used AMA was Ceftriaxone in 30% of patients, A fixed dose combination of piperacillin & Tazobactum was used in 16% of patients, and cefotaxime in 12% of patients and a fixed dose combination of cefoperazone & sulbactum was also used in 12% of patients. Most of these AMA were prescribed as prophyaxis.

Patients who were treated with atorvastatin or rosuvastatin received either less or more than the adequate doses. For example they were given 10mg/day of atorvastatin. Patients remained on their initial dose and are not titrated to achieve their target LDL-C levels and start treatment with that dose. For example if the patients LDL-C is 175mg/dl and the goal is 100mg/dl, then it requires approximately 40% reduction and hence according to the table, the patient should be started on a dose of 10mg/day of Atorvastatin [27]. In our study the dose was not calculated according to LDL-C levels and hence it was irrational.

An average of 7.71 drugs were prescribed for each patient during their hospital stay. The large number of drugs used proves that modern medicine seems to believe in the "most is the best". Out of the 771 drugs prescribed only 8.71% (63) of the drugs were prescribed by generic name showing that most of the drugs were prescribed by brand names which were costlier making the treatment costly and also shows the higher influence of pharmaceutical companies on the doctors. 12.71% (98) of the drugs prescribed were antibiotics, most of them were given by parenteral route and were given prophylactically. 40.20% (310) of the drugs prescribed were given by the parenteral route. Making the whole treatment costlier & most of these drugs were AMA & PPIs. 72.24% (557) of the total drugs prescribed were from the essential drugs list.

Average consultation time was found to be 11.94 min and the average dispensing time was 18.15 sec, a total of 96.23% of the drugs prescribed were dispensed and 56% of the patients had adequate knowledge about the dose and route of the administration of the drugs prescribed. The area in which interventional measures are needed is patient education and knowledge. 46% of patients lacked adequate knowledge of dosage schedule, possibly due to communication error. Pharmacists can be urged to spend more time with dispensing since at the moment only 18.15 sec are spent for each encounter. This simple measure would probably help patients understand their dosage schedule better.

The non – drug prescription percentage was 0%, the injections cost 86.06 % of the total showing that their inclusion in prescription leads to a higher costing which is inevitable. Average drug cost in rupees per prescription was found to be Rs. 473.63, while the average drug cost on injections was Rs. 407.62

CONCLUSION

The drug utilization studies like this provides a good tool in Pharmacoepidemiology, a good research methodology for building evidence and very helpful in assessing & changing policy for improving the condition of the patients in building a healthy society with limited burden. The use of Pharmacoepidemiological data can aid the design, delivery & evaluation of interventions to improve the use of drugs in CHF patients & health outcomes of the patients.

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