Adherence to guideline-directed medical therapy among left ventricular systolic dysfunction patients in out patient department of Shahid Gangalal National Heart Centre, Kathmandu, Nepal.

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Background and Aims: Heart Failure (HF) with reduced Ejection Fraction (HFrEF) is defined as the clinical diagnosis of HF and left ventricular ejection fraction (LVEF) $\leq$ 40%, also referred to as systolic HF. Guideline-directed medical therapy (GDMT) has shown to reduce mortality for HFrEF. We aim to evaluate adherence to GDMT treatment in our outpatients.
Methods: It was a cross-sectional observational study. All patients who attended the Department of preventive medicine and cardiac rehabilitation for medical counseling from October 2016 to May 2018 and have already completed 3 months of follow up for HF were included in this study. Performa was designed to collect patient information which included; age, gender, NYHA functional class, LVEF, systolic and diastolic blood pressure, pulse rate, creatinine, potassium and drugs with doses were recorded.
Results: Among the 451 patients, ninety-nine (65.6%) were male and 52 (34.4%) were female. The mean age was 56.2±4.2 years. Most of the patients were in NYHA class II 114 (75.5%) and in Sinus rhythm 119 (79.4%). Mean LVEF was 26.6±6.1%. Dilated Cardiomyopathy was the most common clinical diagnosis in 76 (50.3%). Diuretic, Angiotensin-converting enzyme inhibitor (ACEI)/Angitensin receptor blocker (AB), Aldosterone Antagonist, β-blocker and digoxin were prescribed in 151 (100%), 140 (93.3%), 127 (84.1%), 114 (75.4%) and 46 (30.4%) patients respectively. The mean dose of furosemide, Enalapril, Losartan, carvedilol, bisoprolol and metoprolol succinate was 45.3mg, 4.0mg, 33.2mg, 33.6mg, 18.8mg, 3.0mg, and 27.5mg was respectively.
Conclusion: : Our center's adherence to GDMT in HFrEF patients is comparable to international studies. We still need more effort to re-emphasize the importance of GDMT by focusing on the optimization of drug doses during out-patient visits.

Keywords: ACEI; ARB; β-blocker; Guideline-directed medical therapy (GDMT); Heart Failure with reduced Ejection Fraction (HFrEF); Nepal.

Background

Heart Failure with reduced Ejection Fraction (HFrEF) is defined as the clinical diagnosis of Heart Failure (HF) and left ventricle ejection fraction (LVEF) $\leq$ 40%. Guideline-directed medical therapy (GDMT) such as the use of angiotensin-converting-enzyme-inhibitors (ACE-I) or angiotensin-receptor-blockers (ARB), beta-blockers (BB) and aldosterone antagonist (AA) have a class I indication for use in patients with HFrEF.[1] Digoxin is beneficial in decreasing hospitalizations whereas diuretics improve symptoms.[1] HF usually has a very poor outcome, but physician-adherence to Guideline-directed medical therapy (GDMT) usually helps improve the outcome.[2,3,4] Multiple studies have highlighted its growing importance towards the care of HF patients.[5,6]

Little is known about the use of guideline-directed medical therapy

(GDMT) in outpatients with heart failure (HF) and a left ventricular ejection fraction (EF) ≤40% (HFrEF) in Nepal. Our objective was to understand the use of GDMT in outpatients with HFrEF in our center.

Method

It was a single center, cross-sectional, observational study done at Shahid Gangalal National Heart Centre, Kathmandu, Nepal. All patients who attended the Department of preventive medicine and cardiac rehabilitation for medical counseling from 1st October 2016 to 31st May 2018 and have already completed at least 3 months of follow up for HF were included in this study. Approval from the Institutional Review Committee was obtained from the institution before the start of the study.

Performa was designed to collect patient information which included; age, gender, NYHA functional class, LVEF, systolic and diastolic blood pressure, pulse rate, creatinine (Cr), potassium and drugs with doses were recorded.

All the variables were entered into the Statistical Package for Social Sciences software, version 20 (IBM SPSS) for data analysis. Descriptive statistics were computed and presented as means and standard deviations for continuous variables like age and LVEF, categorical variables were reported in percentages.

Results

A total of 451 patients attended the medical counseling unit, among them 296 (65.6%) were male and 155 (34.4%) were female. The mean age was 56.2 ± 4.2 years. Most of the patients were in NYHA class II 340 (75.5%) and in Sinus rhythm 358 (79.4%). Mean LVEF was 26.6% ± 6.1. Details of clinical characteristics and features are shown in Tables 1 and 2.

Table 1: Clinical characteristics

Characteristic	n	%
Male	296	65.6
Female	155	34.4
Sinus Rhythm	358	79.4
Atrial fibrillation	92	20.4
Other	1	0.2
NYHA II	340	75.4
NYHA III	111	24.6
Heart rate≤60	33	7.3
Systolic BP≤90 (mmHg)	50	11.1
Cr>225 (μmol/L)	15	3.3

Table 2: Clinical parameters

Demographics	Mean + SD
Age (years)	56.2 ± 11.5
NYHA (class)	2.1 ± 0.8

Left Ventricular Internal Dimension (LVID) diastolic	6.4 ± 0.8
Left Atrial size (cm)	4.4 ± 0.6
LVEF (%)	26.6 ± 6.1
Systolic blood pressure (mmHg)	101.8 ± 11.3
Diastolic blood pressure (mmHg)	69.6 ± 9.1
Heart rate(bpm)	74.1 ± 10.6
Serum Creatinine (μmol/L)	91.4 ± 21.7

Dilated Cardiomyopathy (DCM) was the most common clinical diagnosis, in 76 (50.3%) followed by ischemic heart disease as shown in table 3.

Table 3: Causes of heart failure

Cause	No	%
Idiopathic (DCM)	227	50.3
Ischemic	164	36.4
Hypertensive	15	3.3
Peripartum	15	3.3
Others	30	6.7

Loop diuretics were used exclusively in all patients (100%) followed by ACEI/ARB (93.3%), AA (84.7%), Beta blockers (75.4%) and digoxin (30.4%), as show n in details in table 4. Vaccination was given to 132 patients (29.2%) during the hospital stay or at the time of out-patient department follow-up.

Table 4: Medications used

Drugs	No.	%
ACE/ARB	421	93.3
Beta blockers	340	75.4
Loop diuertics	451	100
Aldactone Antagonist	382	84.7
Vaccination	132	29.2

Mean doses and types of diuretics, ACE/ARB, β-blocker and AA used in patients in our study are shown in table 5. All 3 GDMT anti-HF drugs ACE/ARB + β-blocker and AA were used in 70.8% of patients in our study.

Table 5: Drugs used and mean doses

Drugs		No.	%	Mean Dose (per day)
ACEI	Enalapril	236	52.3	4.1 ± 1.7 mg

Adherence to guideline-directed medical therapy among left ventricular systolic dysfunction patients in outpatient department of Shahid Gangalal National Heart Centre, Kathmandu, Nepal.

31

	Ramipril	12	2.6	3.1 ± 2.5
ACEI total		248	54.9	
ARB	Losartan	161	35.7	33.2 ± 5.2 mg
	Telmisartan	12	2.6	30.0 ± 10.2
ARB total		173	38.4	
ACEI/ARB		421	93.3	
β-blocker	Carvedilol	167	37.0	16.2 ± 6.0 mg
	Metoprolol Succinate	86	19.1	21.5 ± 4.1 mg
	Bisoprolol	54	11.9	2.7 ± 1.5 mg
	Others	33	7.3	
β-blocker total		340	75.4	
Diuretics	Frusemide	409	90.6	55.3 ± 12.5 mg
	Torsemide	42	9.3	42.8 ± 10.3 mg
Diuretics total		451	100	
Aldosterone Antagonist	Spironolactone	370	82.0	33.4±6.3
	Epeleronone	9	2.0	32.3 ± 7.6
		379	84.0	
Digoxin		137	30.4	0.16 ± 0.02
ACEI/ARB+ β blocker+ AA		319	70.7	

Discussion

As emphasized in almost all international guidelines, GDMT in HF reduces morbidity and mortality. In our study, ACEI or ARB was prescribed in 93.3% of patients which were better than the study done in (69%) India[7] and similar to that in Nigeria (83%)[8] and South Africa (79%).[9] Interestingly, our study showed a higher rate of ACEI/ARB adherence than that noted in Japan[10] and rural Australia.[11] In our study, adherence to β-blocker was 75.4% which was higher than (34%) rural Australia[11] and (48%) Nigeria,[8] (57.8%) Japan[10] but lower than (78%) South Africa.[9] A retrospective study conducted in our center in 2016[12] showed the use of ACEI or ARB was 86.7%, β-blockers were used in 28.4% of patients which were lower than our current study. β-blocker prescribed in our study were mostly those recommended in Heart failure guideline[13] however in a small portion of patients (7.3%), β-blockers such as Atenolol and Metoprolol tartrate were used which are not the guideline-recommended drugs for the treatment of heart failure. So, proportion of patients who were prescribed guideline-recommended β-blocker use were 68.1%, which is still comparable to above mentioned international studies.

Aldactone antagonist (AA) was used in 84.1% patients in our study which was higher than similar studies done in (46.9%) Pakistan,[14] (41%) Nigerian[8] (79%) and South Africa.[9] This result was similar to another study done in our center,[12] which showed AA use of 83.9%.

Digoxin use in our study was 47.9%, its uses vary a lot, in a study done in Pakistan[14] it was 75%, (82%) in Nigerian study,[8] (67%) in

South African Study[9] and (27%) in Indian study.[7]

Diuretics reduce pulmonary edema and venous congestion, so it remains the first line of treatment in patients of HF. Diuretics (loop) were used in all the patients (100%) in our study among which Frusemide (90.6%) was the most common followed by Torsemide in 9.3% patients. In an Indian study[7] 91% of patients received Furosemide, 25% of patients received Torsemide.

A study was done by Shore. et al. in the US which included ischemic cardiomyopathy patients and non-ischemic Cardiomyopathy patients showed that ACEI was used in 90.7% vs 93%, β-blocker was used in 94.9% vs 93.9% and AA in 31.4% vs 34.5% patients.[15] In a study done in six European countries (France, Germany, Italy, The Netherlands, Spain, and the UK) ACEI (88%), diuretics (82%), cardiac glycosides (52%), β-blockers (58%), and AA (36%) were prescribed.[16] Our AA prescription rate was better than these two studies.

Despite concrete data to support the use of GDMT in all stages of HF there is considerable variation in the prescription of these therapies in patients with HF. Multiple factors influence the prescription of ß- blockers including concerns regarding advanced age, low LVEF, bradycardia, low BP; these may be the very people who stand to benefit from the GDMT.[16] Similarly ACEI and AA are known to be under-prescribed due to concerns regarding renal function and sometimes for no discernible reasons.[17,18] In a study done in our center in 2016,[12] β-blocker was prescribed to 28.4% of patients whereas use of all three were present in 19.9% of the total patients both of which were much lower as compared to our study β-blocker (75.4%), ACEI/ARB, β-blocker and AA (70%). This shows, progress though small, our center has made in the management of patients with heart failure with reduced ejection fraction. Our study showed that the mean dose of drugs used in heart failure in our center was more close to the initial dose or even low in some cases than to the maximum titrated level, as illustrated in recent heart failure guideline.[13] Since our study is a cross-sectional, observational study done in patients in their third month of follow-up, which was the first out-patient visit for more than half of the patients, most of the drugs might be still in the initial dose and yet to be uptitrated.

The limitations of this study are; it is an observational, non-randomized study that depends only on the data of a single center. Another limitation of our study is the lack of use of relatively newer drugs for the treatment of heart failure such as Angiotensin receptor-neprilysin inhibitor (ARNI) and I_f channel inhibitors, due to its unavailability or unaffordability. A prospective study with a good sample size after randomizations with most of the drugs for the treatment of heart failure in its fully optimized dose is needed for its proper implementation in heart failure, especially during the follow-up phase. Among the patients taking beta-blocker, 7.3% of the patients were prescribed atenolol and Metoprolol Tartrate, which are not recommended by current guidelines. So, this study provides a valuable reflection of our day-to-day practices and the need for improvement, focusing on the drug prescriptions during follow up outpatient visits.

Conclusion

Our center adherence to GDMT in HFrEF patients is comparable to international studies. We still need more effort to re-emphasize the importance of GDMT by focusing on the optimization of drug doses during out-patient visits.

Disclosure

The authors who were members of the editorial team were not involved in any steps in the editing / publication process.

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